UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-Q

(Mark One)

☒ QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Quarterly Period Ended September 30, 2023

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____

Commission file number 000-19125

Ionis Pharmaceuticals, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**33-0336973**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
2855 Gazelle Court, Carlsbad, California	**92010**
(Address of Principal Executive Offices)	(Zip Code)

760-931-9200

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol	Name of each exchange on which registered
Common Stock, $.001 Par Value	"IONS"	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer ☒	Accelerated Filer ☐
Non-accelerated Filer ☐	Smaller Reporting Company ☐ Emerging Growth Company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12(b)-2 of the Securities Exchange Act of 1934). Yes ☐ No ☒

The number of shares of voting common stock outstanding as of October 27, 2023 was 143,472,119.

IONIS PHARMACEUTICALS, INC.
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TRADEMARKS

"Ionis," the Ionis logo, and other trademarks or service marks of Ionis Pharmaceuticals, Inc. appearing in this report are the property of Ionis Pharmaceuticals, Inc. "Akcea," the Akcea logo, and other trademarks or service marks of Akcea Therapeutics, Inc. appearing in this report are the property of Akcea Therapeutics, Inc., Ionis' wholly owned subsidiary. This report contains additional trade names, trademarks and service marks of others, which are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this report may appear without the ® or TM symbols.

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share data)

	September 30, 2023 (unaudited)	December 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	$ 352,060	$ 276,472
Short-term investments	1,883,522	1,710,397
Contracts receivable	142,359	25,538
Inventories	25,634	22,033
Other current assets	181,075	168,254
Total current assets	2,584,650	2,202,694
Property, plant and equipment, net	70,928	74,294
Right-of-use assets	174,310	181,544
Deposits and other assets	104,083	75,344
Total assets	$ 2,933,971	$ 2,533,876
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 5,615	$ 17,921
Accrued compensation	33,781	49,178
Accrued liabilities	118,968	140,101
Income taxes payable	31,070	6,249
Current portion of deferred contract revenue	204,824	90,577
Other current liabilities	9,952	7,535
Total current liabilities	404,210	311,561
Long-term deferred contract revenue	249,272	287,768
1.75 percent convertible senior notes, net	561,609	—
0 percent convertible senior notes, net	624,594	622,242
0.125 percent convertible senior notes, net	44,287	544,504
Liability related to sale of future royalties, net	512,700	—
Long-term lease liabilities	173,038	178,941
Long-term obligations	48,801	15,973
Total liabilities	2,618,511	1,960,989
Stockholders' equity:		
Common stock, $0.001 par value; 300,000,000 shares authorized, 143,393,493 and 142,057,736 shares issued and outstanding at September 30, 2023 (unaudited) and December 31, 2022, respectively	143	142
Additional paid-in capital	2,148,002	2,059,850
Accumulated other comprehensive loss	(46,037)	(57,480)
Accumulated deficit	(1,786,648)	(1,429,625)
Total stockholders' equity	315,460	572,887
Total liabilities and stockholders' equity	$ 2,933,971	$ 2,533,876

See accompanying notes.

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except for per share amounts)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$ 67,253	$ 61,647	$ 178,511	$ 175,092
Other commercial revenue	16,828	10,763	51,235	47,787
Total commercial revenue	84,081	72,410	229,746	222,879
Research and development revenue:				
Collaborative agreement revenue	44,167	69,250	173,513	157,282
Eplontersen joint development revenue	15,959	18,107	59,883	55,317
Total research and development revenue	60,126	87,357	233,396	212,599
Total revenue	144,207	159,767	463,142	435,478
Expenses:				
Cost of sales	2,191	1,515	6,071	10,430
Research, development and patent	215,330	182,990	643,070	524,875
Selling, general and administrative	69,951	34,416	161,608	102,345
Total operating expenses	287,472	218,921	810,749	637,650
Loss from operations	(143,265)	(59,154)	(347,607)	(202,172)
Other income (expense):				
Investment income	23,935	7,524	63,355	13,447
Interest expense	(4,203)	(2,139)	(8,102)	(6,391)
Interest expense related to sale of future royalties	(17,779)	—	(50,948)	—
Gain (loss) on investments	(1,943)	2,347	(1,753)	(10,616)
Other income (expense)	2,447	4,713	13,857	(7,923)
Loss before income tax expense	(140,808)	(46,709)	(331,198)	(213,655)
Income tax expense	(6,602)	(283)	(25,825)	(3,637)
Net loss	$ (147,410)	$ (46,992)	$ (357,023)	$ (217,292)
Basic and diluted net loss per share	$ (1.03)	$ (0.33)	$ (2.50)	$ (1.53)
Shares used in computing basic and diluted net loss per share	143,317	141,950	143,052	141,782

See accompanying notes.

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Net loss	$ (147,410)	$ (46,992)	$ (357,023)	$ (217,292)
Unrealized gains (losses) on debt securities, net of tax	5,029	(8,734)	11,421	(29,508)
Currency translation adjustment	(153)	(399)	22	(964)
Comprehensive loss	$ (142,534)	$ (56,125)	$ (345,580)	$ (247,764)

See accompanying notes.

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)
(Unaudited)

Description	Common Stock Shares	Common Stock Amount	Additional Paid in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at June 30, 2022	141,831	$ 142	$ 2,008,794	$ (54,007)	$ (1,330,203)	$ 624,726
Net loss	—	—	—	—	(46,992)	(46,992)
Change in unrealized losses, net of tax	—	—	—	(8,734)	—	(8,734)
Foreign currency translation	—	—	—	(399)	—	(399)
Issuance of common stock in connection with employee stock plans	203	—	2,567	—	—	2,567
Stock-based compensation expense	—	—	23,837	—	—	23,837
Payments of tax withholdings related to vesting of employee stock awards and exercise of employee stock options	(17)	—	(644)	—	—	(644)
Balance at September 30, 2022	142,017	$ 142	$ 2,034,554	$ (63,140)	$ (1,377,195)	$ 594,361
Balance at June 30, 2023	143,167	$ 143	$ 2,118,309	$ (50,913)	$ (1,639,238)	$ 428,301
Net loss	—	—	—	—	(147,410)	(147,410)
Change in unrealized losses, net of tax	—	—	—	5,029	—	5,029
Foreign currency translation	—	—	—	(153)	—	(153)
Issuance of common stock in connection with employee stock plans	226	—	3,729	—	—	3,729
Stock-based compensation expense	—	—	25,964	—	—	25,964
Balance at September 30, 2023	143,393	$ 143	$ 2,148,002	$ (46,037)	$ (1,786,648)	$ 315,460

See accompanying notes.

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)
(Unaudited)

Description	Common Stock Shares	Common Stock Amount	Additional Paid in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2021	141,210	$ 141	$ 1,964,167	$ (32,668)	$ (1,159,903)	$ 771,737
Net loss	—	—	—	—	(217,292)	(217,292)
Change in unrealized losses, net of tax	—	—	—	(29,508)	—	(29,508)
Foreign currency translation	—	—	—	(964)	—	(964)
Issuance of common stock in connection with employee stock plans	1,138	1	6,029	—	—	6,030
Stock-based compensation expense	—	—	74,575	—	—	74,575
Payments of tax withholdings related to vesting of employee stock awards and exercise of employee stock options	(331)	—	(10,217)	—	—	(10,217)
Balance at September 30, 2022	142,017	$ 142	$ 2,034,554	$ (63,140)	$ (1,377,195)	$ 594,361
Balance at December 31, 2022	142,058	$ 142	$ 2,059,850	$ (57,480)	$ (1,429,625)	$ 572,887
Net loss	—	—	—	—	(357,023)	(357,023)
Change in unrealized gains, net of tax	—	—	—	11,421	—	11,421
Foreign currency translation	—	—	—	22	—	22
Issuance of common stock in connection with employee stock plans	1,335	1	8,679	—	—	8,680
Stock-based compensation expense	—	—	79,473	—	—	79,473
Balance at September 30, 2023	143,393	$ 143	$ 2,148,002	$ (46,037)	$ (1,786,648)	$ 315,460

See accompanying notes.

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)
(Unaudited)

	Nine Months Ended September 30,	
	2023	**2022**
Operating activities:		
Net loss	$ (357,023)	$ (217,292)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	7,748	11,301
Amortization of right-of-use operating lease assets	7,234	1,970
Amortization of other assets	1,904	1,805
Amortization of premium (discount) on investments, net	(20,396)	9,072
Amortization of debt issuance costs	4,666	4,035
Non-cash royalty revenue related to sale of royalties	(27,814)	—
Non-cash interest related to sale of future royalties	50,541	—
Stock-based compensation expense	79,473	74,575
Loss on investments	1,429	228
Gain on early retirement of debt	(13,389)	—
Non-cash losses related to disposal of property, plant and equipment	14,646	528
Non-cash losses related to other assets	849	1,155
Changes in operating assets and liabilities:		
Contracts receivable	(116,814)	55,251
Inventories	(3,601)	4,161
Other current and long-term assets	(18,325)	(988)
Income taxes payable	24,821	(20)
Accounts payable	(12,462)	5,607
Accrued compensation	(15,397)	(8,400)
Accrued liabilities and other current liabilities	(24,219)	38,263
Deferred contract revenue	75,751	(55,426)
Net cash used in operating activities	(340,378)	(74,175)
Investing activities:		
Purchases of short-term investments	(1,353,100)	(1,223,791)
Proceeds from sale of short-term investments	1,193,724	764,101
Purchases of property, plant and equipment	(24,624)	(11,582)
Acquisition of licenses and other assets, net	(3,414)	(3,511)
Net cash used in investing activities	(187,414)	(474,783)
Financing activities:		
Proceeds from equity, net	8,680	6,030
Payments of tax withholdings related to vesting of employee stock awards and exercise of employee stock options	—	(10,217)
Proceeds from issuance of 1.75 percent convertible senior notes	575,000	—
1.75 percent convertible senior notes issuance costs	(14,175)	—
Repurchase of $504.4 million principal amount of 0.125 percent convertible senior notes	(487,943)	—
Proceeds from sale of future royalties	500,000	—
Payments of transaction costs related to sale of future royalties	(10,434)	—
Proceeds from real estate transaction	32,352	—
Principal payments on mortgage debt	(122)	(89)
Net cash provided by (used in) financing activities	603,358	(4,276)
Effects of exchange rates on cash	22	(964)
Net increase (decrease) in cash and cash equivalents	75,588	(554,198)
Cash and cash equivalents at beginning of period	276,472	869,191
Cash and cash equivalents at end of period	$ 352,060	$ 314,993
Supplemental disclosures of cash flow information:		
Interest paid	$ 952	$ 2,204
Income taxes paid	$ 714	$ 2
Supplemental disclosures of non-cash investing and financing activities:		
Amounts accrued for capital and patent expenditures	$ 341	$ 3,032
Right-of-use assets obtained in exchange for lease liabilities	$ —	$ 657

See accompanying notes.

IONIS PHARMACEUTICALS, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
September 30, 2023
(Unaudited)

1. Organization and Basis of Presentation

Organization and Business Activity

We incorporated in California on January 10, 1989. In conjunction with our initial public offering, we reorganized as a Delaware corporation in April 1991. We are a leader in the discovery and development of RNA-targeted therapeutics.

Basis of Presentation

We prepared the unaudited interim condensed consolidated financial statements for the three and nine months ended September 30, 2023 and 2022 on the same basis as the audited financial statements for the year ended December 31, 2022. We included all normal recurring adjustments in the financial statements, which we considered necessary for a fair presentation of our financial position at such dates and our operating results and cash flows for those periods. Our operating results for the interim periods may not be indicative of what our operating results will be for the entire year. For more complete financial information, these financial statements, and notes thereto, should be read in conjunction with the audited financial statements for the year ended December 31, 2022 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or SEC.

In our condensed consolidated financial statements, we included the accounts of Ionis Pharmaceuticals, Inc. and the consolidated results of our wholly owned subsidiary, Akcea Therapeutics, Inc. and its wholly owned subsidiaries (“we”, “us” or “our”).

We operate as a single segment, Ionis operations, because our chief decision maker reviews operating results on an aggregate basis and manages our operations as a single operating segment.

Use of Estimates

We prepare our condensed consolidated financial statements in conformity with accounting principles generally accepted in the United States, or U.S., that require us to make estimates and assumptions that affect the amounts reported in our condensed consolidated financial statements and accompanying notes. Actual results could differ from our estimates.

2. Significant Accounting Policies

Our significant accounting policies have not changed substantially from those included in our Annual Report on Form 10-K for the year ended December 31, 2022, other than as discussed below.

Liability Related to Sale of Future Royalties

In January 2023, we entered into a royalty purchase agreement with Royalty Pharma Investments, or Royalty Pharma, to monetize a portion of our future SPINRAZA and pelacarsen royalties we are entitled to under our arrangements with Biogen and Novartis, respectively. Refer to Note 11, *Liability Related to Sale of Future Royalties*, for further details on the agreement.

Under our agreement with Royalty Pharma, we record upfront payments and milestone payments we receive from the sale of future royalties as a liability, net of transaction costs. We record royalty payments made to Royalty Pharma as a reduction of the liability and amortize the transaction costs over the estimated life of the royalty stream. We account for the associated interest expense under the effective interest rate method, while continuing to recognize the full amount of royalty revenue in the period in which the counterparty sells the related product and recognizes the related revenue.

We calculate the liability related to the sale of future royalties, effective interest rate and the related interest expense using our current estimate of anticipated future royalty payments under the arrangement, which we periodically reassess based on internal projections and information from our partners who are responsible for commercializing the medicines. If there is a material change in our estimate, we will prospectively adjust the liability related to the sale of future royalties, effective interest rate and the related interest expense.

Recently Adopted Accounting Standards

We do not expect any recently issued accounting standards to have a material impact to our financial results.

3. Supplemental Financial Data

Inventories

Our inventory consisted of the following (in thousands):

	September 30, 2023	December 31, 2022
Raw materials:		
Raw materials - clinical	$ 18,427	$ 17,061
Raw materials - commercial	4,380	2,699
Total raw materials	22,807	19,760
Work in process	2,651	2,109
Finished goods	176	164
Total inventory	$ 25,634	$ 22,033

Accrued Liabilities

Our accrued liabilities consisted of the following (in thousands):

	September 30, 2023	December 31, 2022
Clinical development expenses	$ 89,217	$ 116,460
In-licensing expenses	7,560	7,945
Commercial expenses	8,575	3,498
Other miscellaneous expenses	13,616	12,198
Total accrued liabilities	$ 118,968	$ 140,101

4. Revenues

During the three and nine months ended September 30, 2023 and 2022, our revenues were comprised of the following (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$ 67,253	$ 61,647	$ 178,511	$ 175,092
Other commercial revenue:				
TEGSEDI and WAYLIVRA revenue, net	8,286	5,920	25,420	22,467
Licensing and other royalty revenue	8,542	4,843	25,815	25,320
Total other commercial revenue	16,828	10,763	51,235	47,787
Total commercial revenue	84,081	72,410	229,746	222,879
Research and development revenue:				
Collaborative agreement revenue	44,167	69,250	173,513	157,282
Eplontersen joint development revenue	15,959	18,107	59,883	55,317
Total research and development revenue	60,126	87,357	233,396	212,599
Total revenue	$ 144,207	$ 159,767	$ 463,142	$ 435,478

Refer to Note 5, *Collaborative Arrangements and Licensing Agreements*, for further details on our collaborative agreement revenue.

5. Collaborative Arrangements and Licensing Agreements

Below, we have included our AstraZeneca, Biogen, GSK, Novartis, Roche and Sobi collaborations, which are the collaborations with substantive changes during 2023 from those included in Part IV, Item 15, Note 7, *Collaborative Arrangements and Licensing Agreements*, of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2022.

AstraZeneca

We have two collaborations with AstraZeneca, one focused on the joint development and commercialization of eplontersen for the treatment of transthyretin amyloidosis, or ATTR, and one focused on the treatment of cardiovascular, renal and metabolic diseases. From inception through September 30, 2023, we have received nearly $650 million from these collaborations.

We are jointly developing and preparing to commercialize eplontersen with AstraZeneca in the U.S. In addition, we granted AstraZeneca exclusive rights to commercialize eplontersen outside the U.S. In the second quarter of 2023, we earned a $20 million license fee payment when we licensed rights to Latin America for eplontersen to AstraZeneca. We recognized the upfront payment in full in the second quarter of 2023 because AstraZeneca had full use of the license without any continuing involvement from us. We will achieve the next payment of $50 million upon regulatory approval in the U.S. under this collaboration.

Under our collaboration for cardiovascular, renal and metabolic diseases, AstraZeneca has licensed multiple medicines from us. AstraZeneca is responsible for global development, regulatory and commercialization activities and costs for each of the medicines it has licensed from us. In the second quarter of 2023, we earned a $20 million milestone payment when AstraZeneca initiated a Phase 2b study for ION839, an investigational ligand-conjugated antisense, or LICA, medicine designed to inhibit the production of patatin-like phospholipase domain-containing 3, or PNPLA3, protein. We recognized this milestone payment as R&D revenue in full in the second quarter of 2023 because we did not have any remaining performance obligations related to the milestone payment. We will achieve the next payment of up to $30 million if AstraZeneca licenses a medicine under this collaboration.

During the three and nine months ended September 30, 2023 and 2022, we earned the following revenue from our relationship with AstraZeneca (in thousands, except percentages):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue from our relationship with AstraZeneca	$ 15,959	$ 18,107	$ 99,885	$ 55,718
Percentage of total revenue	11%	11%	22%	13%

We did not have any deferred contract revenue from our relationship with AstraZeneca at September 30, 2023 or December 31, 2022.

Biogen

We have several strategic collaborations with Biogen focused on using antisense technology to advance the treatment of neurological disorders. We developed and licensed to Biogen SPINRAZA, our approved medicine to treat people with spinal muscular atrophy, or SMA. Under our 2013 strategic neurology collaboration, Biogen developed QALSODY (tofersen), our recently approved medicine in the U.S. to treat patients with superoxide dismutase 1 amyotrophic lateral sclerosis, or SOD1-ALS. Under our collaborations, we and Biogen are currently developing numerous investigational medicines to treat neurodegenerative diseases in addition to SMA and SOD1-ALS, including medicines in development to treat people with amyotrophic lateral sclerosis, or ALS, Angelman Syndrome, or AS, Alzheimer's disease, or AD, and Parkinson's disease, or PD. In addition to these medicines, our collaborations with Biogen include a substantial research pipeline that addresses a broad range of neurological diseases. From inception through September 30, 2023, we have received more than $3.6 billion in payments from our Biogen collaborations.

Under our 2013 strategic neurology collaboration, we earned a $16 million milestone payment from Biogen when the U.S. Food and Drug Administration, or FDA, approved Biogen's New Drug Application, or NDA, for QALSODY in the second quarter of 2023. We recognized this milestone payment as R&D revenue in full in the second quarter of 2023 because we did not have any remaining performance obligations related to the milestone payment. Under our collaboration agreement with Biogen, we are eligible to receive tiered royalties ranging from 11 percent to 15 percent on sales of QALSODY. Following the NDA approval in April 2023, we began earning royalties from QALSODY sales, which we recognize as other commercial revenue in our condensed consolidated statements of operations. We will achieve the next milestone payment for QALSODY of $20 million if the European Medicines Agency approves Biogen's Marketing Authorization Application, filing of QALSODY.

Under our 2012 neurology collaboration, we achieved $21 million in milestone payments from Biogen when Biogen advanced ION582, our investigational antisense medicine for the potential treatment of AS, in the third quarter of 2023. We are recognizing these milestone payments as revenue as we perform services based on our effort to satisfy our R&D services performance obligation relative to the total effort expected to satisfy our performance obligation for ION582.

During the three and nine months ended September 30, 2023 and 2022, we earned the following revenue from our relationship with Biogen (in thousands, except percentages):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue from our relationship with Biogen	$ 94,695	$ 88,959	$ 262,599	$ 259,713
Percentage of total revenue	66%	56%	57%	60%

In October 2023, we earned a milestone payment of $9 million from Biogen when we advanced ION582 under our 2012 neurology collaboration. We will achieve the next payment of $70 million if Biogen licenses ION582 under this collaboration.

Our condensed consolidated balance sheets at September 30, 2023 and December 31, 2022 included deferred contract revenue of $316.8 million and $351.2 million, respectively, from our relationship with Biogen.

GSK

In March 2010, we entered into a collaboration with GSK using our antisense drug discovery platform to discover and develop new medicines against targets for serious and rare diseases, including infectious diseases and some conditions causing blindness. Our collaboration with GSK currently includes bepirovirsen, our medicine in development for the treatment of hepatitis B virus, or HBV, infection. In the third quarter of 2019, following positive Phase 2 results, GSK licensed our HBV program. GSK is responsible for all global development, regulatory and commercialization activities and costs for the HBV program. From inception through September 30, 2023, we have received more than $105 million in an upfront payment and payments related to the HBV program.

In the first quarter of 2023, we earned a $15 million milestone payment when GSK initiated a Phase 3 program of bepirovirsen. We recognized this milestone payment as R&D revenue in full in the first quarter of 2023 because we did not have any remaining performance obligations related to the milestone payment. We will achieve the next payment of $15 million if the FDA accepts an NDA filing of bepirovirsen for review.

During the three and nine months ended September 30, 2023 and 2022, we earned the following revenue from our relationship with GSK (in thousands, except percentages):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue from our relationship with GSK	$ —	$ —	$ 15,000	$ —
Percentage of total revenue	0%	0%	3%	0%

We did not have any deferred contract revenue from our relationship with GSK at September 30, 2023 or December 31, 2022.

Novartis

In January 2017, we initiated a collaboration with Novartis to develop and commercialize pelacarsen, an investigational medicine for patients with elevated lipoprotein(a), or Lp(a)-driven cardiovascular disease, or CVD. Novartis is responsible for conducting and funding development and regulatory activities for pelacarsen, including a global Phase 3 cardiovascular outcomes study, which Novartis initiated in December 2019.

In August 2023, we entered into a collaboration and license agreement with Novartis for the discovery, development and commercialization of a novel medicine for patients with Lp(a)-driven CVD. Novartis is solely responsible for the development, manufacturing and potential commercialization of the next generation Lp(a) therapy. In September 2023, this agreement received clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976. Novartis paid us a $60 million upfront payment in October 2023 and we are eligible to receive development, regulatory and commercial milestone payments and tiered royalties ranging from 10 percent to 20 percent on net sales of any product resulting from this collaboration.

At the commencement of this collaboration, we identified one performance obligation, which was to perform R&D services for Novartis. We included the upfront payment in our transaction price for our R&D services performance obligation. We are recognizing revenue for our R&D services performance obligation as we perform services based on our effort to satisfy our performance obligation relative to our total effort expected to satisfy our performance obligation. We will achieve the next payment of $5 million if we designate a development candidate under this collaboration.

From inception through September 30, 2023, we have received more than $275 million in payments from our Novartis collaborations.

During the three and nine months ended September 30, 2023 and 2022, we earned the following revenue from our relationship with Novartis (in thousands, except percentages):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue from our relationship with Novartis	$ 1,908	$ —	$ 2,023	$ —
Percentage of total revenue	1%	0%	0%	0%

Our condensed consolidated balance sheet at September 30, 2023 included deferred contract revenue of $58.1 million from our relationship with Novartis. We did not have any deferred contract revenue from our relationship with Novartis at December 31, 2022.

Roche

We have three collaborations with Hoffmann-La Roche Inc and F. Hoffmann-La Roche Ltd, collectively Roche: one to develop treatments for Huntington's disease, or HD, one to develop IONIS-FB-L_{Rx} for the treatment of complement-mediated diseases, and one to develop RNA-targeted programs for AD and HD.

In September 2023, we entered into an agreement with Roche to develop two undisclosed early-stage programs for RNA-targeting investigational medicines for the treatment of AD and HD. Under the agreement, we are responsible for advancing the two programs through preclinical studies and Roche is responsible for clinical development, manufacturing and commercialization of the medicines if they receive regulatory approval. Roche paid us a $60 million upfront payment in October 2023 and we are eligible to receive development, regulatory and commercial milestone payments and tiered royalties up to the mid-teens on net sales of any product resulting from this collaboration.

We identified two performance obligations under this new agreement, comprised of R&D services for each of the two separate programs. We included the upfront payment in our transaction price for our R&D services performance obligations. We are recognizing revenue for our R&D services performance obligations as we perform services based on our effort to satisfy our performance obligations relative to our total effort expected to satisfy our performance obligations. We will achieve the next payment of $7.5 million if we advance a medicine under this collaboration.

From inception through September 30, 2023, we have received more than $285 million in payments from our Roche collaborations.

During the three and nine months ended September 30, 2023 and 2022, we earned the following revenue from our relationship with Roche (in thousands, except percentage amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
R&D revenue	$ 8,858	$ 41,504	$ 16,979	$ 65,360
Percentage of total revenue	6%	26%	4%	15%

Our condensed consolidated balance sheets at September 30, 2023 and December 31, 2022 included deferred contract revenue of $68.0 million and $22.4 million, respectively, from our relationship with Roche.

Swedish Orphan Biovitrum AB (Sobi)

We began commercializing TEGSEDI and WAYLIVRA in Europe in January 2021 and TEGSEDI in North America in April 2021 through distribution agreements with Swedish Orphan Biovitrum AB, or Sobi. Under our agreements, we are responsible for supplying finished goods inventory to Sobi and Sobi is responsible for selling each medicine to the end customer. In exchange, we earn a distribution fee on net sales from Sobi for each medicine.

In October 2023, our distribution agreement for TEGSEDI in North America was terminated. During the three and nine months ended September 30, 2023 and 2022, we earned the following revenue from our distribution agreement with Sobi for TEGSEDI in North America (in thousands, except percentage amounts).

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
TEGSEDI revenue from our distribution agreement with Sobi in North America	$ 794	$ 1,008	$ 2,189	$ 3,443
Percentage of total revenue	1%	1%	2%	1%

6. Basic and Diluted Net Loss Per Share

Basic net loss per share

We calculated our basic net loss per share for the three and nine months ended September 30, 2023 and 2022 by dividing our net loss by our weighted-average number of common shares outstanding during the period.

Diluted net loss per share

For the three and nine months ended September 30, 2023 and 2022, we incurred a net loss; therefore, we did not include dilutive common equivalent shares in the computation of diluted net loss per share because the effect would have been anti-dilutive. Common stock from the following would have had an anti-dilutive effect on net loss per share:

- 1.75 percent convertible senior notes, or 1.75% Notes;
- 0 percent convertible senior notes, or 0% Notes;
- Note hedges related to the 0% Notes;
- 0.125 percent convertible senior notes, or 0.125% Notes;
- Note hedges related to the 0.125% Notes;
- Dilutive stock options;
- Unvested restricted stock units, or RSUs;
- Unvested performance restricted stock units, or PRSUs; and
- Employee Stock Purchase Plan, or ESPP.

Additionally as of September 30, 2023, we had warrants related to our 0% and 0.125% Notes outstanding. We will include the shares issuable under these warrants in our calculation of diluted earnings per share when the average market price per share of our common stock for the reporting period exceeds the strike price of the warrants.

7. Investments

The following table summarizes the contract maturity of the available-for-sale securities we held as of September 30, 2023:

One year or less	72%
After one year but within two years	20%
After two years but within three and a half years	8%
Total	100%

As illustrated above, at September 30, 2023, 92 percent of our available-for-sale securities had a maturity of less than two years.

All of our available-for-sale debt securities are available to us for use in our current operations. As a result, we categorize all of these securities as current assets even though the stated maturity of some individual securities may be one year or more beyond the balance sheet date.

We invest in debt securities with strong credit ratings and an investment grade rating at or above A-1, P-1 or F-1 by Standard & Poor’s, Moody’s or Fitch, respectively.

At September 30, 2023, we had an equity ownership interest of less than 20 percent in seven private companies and three public companies with which we conduct business.

The following is a summary of our investments (in thousands):

September 30, 2023	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Available-for-sale debt securities:				
Corporate debt securities (1)	$ 535,408	$ 13	$ (4,492)	$ 530,929
Debt securities issued by U.S. government agencies	267,503	—	(1,429)	266,074
Debt securities issued by the U.S. Treasury (1)	520,013	1	(3,027)	516,987
Debt securities issued by states of the U.S. and political subdivisions of the states	23,906	—	(242)	23,664
Total debt securities with a maturity of one year or less	1,346,830	14	(9,190)	1,337,654
Corporate debt securities	195,674	183	(3,160)	192,697
Debt securities issued by U.S. government agencies	56,365	—	(507)	55,858
Debt securities issued by the U.S. Treasury	297,501	—	(3,364)	294,137
Debt securities issued by states of the U.S. and political subdivisions of the states	4,164	53	(51)	4,166
Total debt securities with a maturity of more than one year	553,704	236	(7,082)	546,858
Total available-for-sale debt securities	$ 1,900,534	$ 250	$ (16,272)	$ 1,884,512
Equity securities:				
Publicly traded equity securities included in other current assets (2)	$ 11,897	$ (1,252)	$ (4,083)	$ 6,562
Privately held equity securities included in deposits and other assets (3)	23,115	25,001	(5,125)	42,991
Total equity securities	35,012	23,749	(9,208)	49,553
Total available-for-sale debt and equity securities	$ 1,935,546	$ 23,999	$ (25,480)	$ 1,934,065

December 31, 2022	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Available-for-sale debt securities:				
Corporate debt securities (1)	$ 513,790	$ 23	$ (4,365)	$ 509,448
Debt securities issued by U.S. government agencies	133,585	—	(1,829)	131,756
Debt securities issued by the U.S. Treasury (1)	512,655	23	(5,124)	507,554
Debt securities issued by states of the U.S. and political subdivisions of the states	57,484	18	(686)	56,816
Other municipal debt securities	6,008	—	(14)	5,994
Total debt securities with a maturity of one year or less	1,223,522	64	(12,018)	1,211,568
Corporate debt securities	227,631	14	(10,143)	217,502
Debt securities issued by U.S. government agencies	34,339	—	(1,040)	33,299
Debt securities issued by the U.S. Treasury	245,030	—	(4,109)	240,921
Debt securities issued by states of the U.S. and political subdivisions of the states	18,314	116	(329)	18,101
Total debt securities with a maturity of more than one year	525,314	130	(15,621)	509,823
Total available-for-sale debt securities	$ 1,748,836	$ 194	$ (27,639)	$ 1,721,391
Equity securities:				
Publicly traded equity securities included in other current assets (2)	$ 11,897	$ —	$ (1,358)	$ 10,539
Privately held equity securities included in deposits and other assets (3)	23,115	17,257	—	40,372
Total equity securities	35,012	17,257	(1,358)	50,911
Total available-for-sale debt and equity securities	$ 1,783,848	$ 17,451	$ (28,997)	$ 1,772,302

(1) Includes investments classified as cash equivalents in our condensed consolidated balance sheets.

(2) Our publicly traded equity securities are included in other current assets. We recognize publicly traded equity securities at fair value. In the nine months ended September 30, 2023, we recognized a $4.0 million unrealized loss in our condensed consolidated statements of operations related to a decrease in the fair value of our investments in publicly traded companies.

(3) Our privately held equity securities are included in deposits and other assets. We recognize our privately held equity securities at cost minus impairments, plus or minus changes resulting from observable price changes in orderly transactions for the identical or similar investment of the same issuer, which are Level 3 inputs. In the nine months ended September 30, 2023, we recorded a net gain of $2.6 million in our condensed consolidated statements of operations related to changes in the fair value of our investments in privately held companies.

The following is a summary of our investments we consider to be temporarily impaired at September 30, 2023 (in thousands, except for number of investments):

		Less than 12 Months of Temporary Impairment		More than 12 Months of Temporary Impairment		Total Temporary Impairment	
	Number of Investments	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses
Corporate debt securities	370	$ 469,095	$ (2,390)	$ 207,073	$ (5,262)	$ 676,168	$ (7,652)
Debt securities issued by U.S. government agencies	98	293,408	(1,242)	24,531	(694)	317,939	(1,936)
Debt securities issued by the U.S. Treasury	68	557,489	(3,420)	225,634	(2,971)	783,123	(6,391)
Debt securities issued by states of the U.S. and political subdivisions of the states	85	11,644	(73)	12,973	(220)	24,617	(293)
Total temporarily impaired securities	621	$ 1,331,636	$ (7,125)	$ 470,211	$ (9,147)	$ 1,801,847	$ (16,272)

We believe that the decline in value of these securities is temporary and is primarily related to the change in market interest rates since purchase rather than underlying credit deterioration for any of the issuers. We believe it is more likely than not that we will be able to hold our debt securities with declines in value to maturity. Therefore, we intend to hold these securities to maturity and anticipate full recovery of our debt securities' amortized cost basis at maturity.

8. Fair Value Measurements

The following tables present the major security types we held at September 30, 2023 and December 31, 2022 that we regularly measure and carry at fair value. The following tables segregate each security type by the level within the fair value hierarchy of the valuation techniques we utilized to determine the respective security's fair value (in thousands):

	At September 30, 2023	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)
Cash equivalents (1)	$ 269,255	$ 269,255	$ —
Corporate debt securities (2)	723,626	—	723,626
Debt securities issued by U.S. government agencies (3)	321,932	—	321,932
Debt securities issued by the U.S. Treasury (2)	811,124	811,124	—
Debt securities issued by states of the U.S. and political subdivisions of the states (2)	27,830	—	27,830
Publicly traded equity securities included in other current assets (4)	6,562	6,562	—
Total	$ 2,160,329	$ 1,086,941	$ 1,073,388

	At December 31, 2022	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)
Cash equivalents (1)	$ 211,655	$ 211,655	$ —
Corporate debt securities (5)	726,950	—	726,950
Debt securities issued by U.S. government agencies (2)	165,055	—	165,055
Debt securities issued by the U.S. Treasury (2)	748,475	748,475	—
Debt securities issued by states of the U.S. and political subdivisions of the states (2)	74,917	—	74,917
Other municipal debt securities (2)	5,994	—	5,994
Publicly traded equity securities included in other current assets (4)	10,539	10,539	—
Total	$ 1,943,585	$ 970,669	$ 972,916

The following footnotes reference lines in our condensed consolidated balance sheets:

(1) Included in cash and cash equivalents in our condensed consolidated balance sheets.

(2) Included in short-term investments in our condensed consolidated balance sheets.

(3) $1.0 million was included in cash and cash equivalents, with the difference included in short-term investments, in our condensed consolidated balance sheets.

(4) Included in other current assets in our condensed consolidated balance sheets.

(5) $11.0 million was included in cash and cash equivalents, with the difference included in short-term investments, in our condensed consolidated balance sheets.

Convertible Notes

Our 1.75% Notes, 0% Notes and 0.125% Notes had a fair value of $605.3 million, $620.1 million and $42.4 million at September 30, 2023, respectively. Our 0% Notes and 0.125% Notes had a fair value of $587.3 million and $498.9 million at December 31, 2022, respectively. We determine the fair value of our notes based on quoted market prices for these notes, which are Level 2 measurements because the notes do not trade regularly.

9. Stock-based Compensation Expense

We measure stock-based compensation expense for equity-classified awards, principally related to stock options, RSUs, PRSUs and stock purchase rights under our ESPP based on the estimated fair value of the award on the date of grant. We recognize the value of the portion of the award that we ultimately expect to vest as stock-based compensation expense over the requisite service period in our condensed consolidated statements of operations. We reduce stock-based compensation expense for estimated forfeitures at the time of grant and revise in subsequent periods if actual forfeitures differ from those estimates. We use the Black-Scholes model to estimate the fair value of stock options granted and stock purchase rights under our ESPP.

On the grant date, we use our stock price and assumptions regarding a number of variables to determine the estimated fair value of stock-based payment awards. These variables include, but are not limited to, our expected stock price volatility over the term of the awards, and actual and projected employee stock option exercise behaviors.

We recognize compensation expense for stock options, RSUs, PRSUs and stock purchase rights under the ESPP using the accelerated multiple-option approach. Under the accelerated multiple-option approach (also known as the graded-vesting method), we recognize compensation expense over the requisite service period for each separately vesting tranche of the award as though the award were in substance multiple awards, which results in the expense being front-loaded over the vesting period.

For the nine months ended September 30, 2023 and 2022, we used the following weighted-average assumptions in our Black-Scholes calculations:

Employee Stock Options:

	Nine Months Ended September 30,	
	2023	**2022**
Risk-free interest rate	3.7%	1.9%
Dividend yield	0.0%	0.0%
Volatility	47.1%	54.9%
Expected life	6.3 years	6.3 years

Ionis Board of Director Stock Options:

	Nine Months Ended September 30,	
	2023	**2022**
Risk-free interest rate	3.8%	2.9%
Dividend yield	0.0%	0.0%
Volatility	53.0%	56.2%
Expected life	7.7 years	7.4 years

ESPP:

	Nine Months Ended September 30,	
	2023	**2022**
Risk-free interest rate	5.3%	1.2%
Dividend yield	0.0%	0.0%
Volatility	36.0%	50.1%
Expected life	6 months	6 months

RSUs:

The fair value of RSUs is based on the market price of our common stock on the date of grant. The RSUs we have granted to employees vest annually over a four-year period. The RSUs we granted to our board of directors prior to June 2020 vest annually over a four-year period. The RSUs we granted after June 2020 to our board of directors fully vest after one year. The weighted-average grant date fair value of RSUs granted to employees for the nine months ended September 30, 2023 and 2022 was $39.78 and $34.88 per share, respectively.

PRSUs:

Beginning in 2020, we added PRSU awards to the compensation for our Chief Executive Officer, Dr. Brett Monia. In 2022, we added PRSU awards to the compensation for our other Section 16 officers. Beginning in 2023, we added PRSU awards to the compensation for all executive officers.

Under the terms of the PRSUs we granted in 2020 through 2022, one third of the PRSUs may vest at the end of three separate performance periods spread over the three years following the date of grant (i.e., the one-year period commencing on the date of grant and ending on the first anniversary of the date of grant, the two-year period commencing on the date of grant and ending on the second anniversary of the date of grant and the three-year period commencing on the date of grant and ending on the third anniversary of the date of grant) based on our relative total shareholder return, or TSR, as compared to a peer group of companies, and as measured, in each case, at the end of the applicable performance period. Under the terms of the grants, no number of PRSUs is guaranteed to vest and the actual number of PRSUs that will vest at the end of each performance period may be anywhere from zero percentto 150 percent of the target number depending on our relative TSR.

Under the terms of the PRSUs we granted in 2023, 100 percent of the PRSUs may vest at the end of the three-year performance period based on our relative TSR as compared to a peer group of companies and as measured at the end of the performance period. Under the terms of the grants, no number of PRSUs is guaranteed to vest and the actual number of PRSUs that will vest at the end of each performance period may be anywhere from zero to 200 percent of the target number depending on our relative TSR.

We determined the fair value of the PRSUs using a Monte Carlo model because the performance target is based on our relative TSR, which represents a market condition. The weighted-average grant date fair value of PRSUs granted to our executive officers for the nine months ended September 30, 2023 and 2022 were $58.99 and $42.28 per share, respectively.

The following table summarizes stock-based compensation expense for the three and nine months ended September 30, 2023 and 2022 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Cost of sales	$ 118	$ 163	$ 355	$ 376
Research, development and patent expense	18,727	17,733	57,543	55,315
Selling, general and administrative expense	7,119	5,941	21,575	18,884
Total stock-based compensation expense	$ 25,964	$ 23,837	$ 79,473	$ 74,575

As of September 30, 2023, total unrecognized estimated stock-based compensation expense related to non-vested stock options, RSUs and PRSUs was $44.1 million, $62.2 million and $7.3 million, respectively. Our actual expenses may differ from these estimates because we will adjust our unrecognized stock-based compensation expense for future forfeitures, including any PRSUs that do not vest. We expect to recognize the cost of stock-based compensation expense related to our non-vested stock options, RSUs and PRSUs over a weighted average amortization period of 1.2 years, 1.4 years and 1.7 years, respectively.

10. Income Taxes

Beginning in 2022, the Tax Cuts and Jobs Act of 2017, or TCJA, requires taxpayers to amortize research and development expenditures over five years pursuant to Internal Revenue Code, or IRC, Section 174. Additionally, we expect to reflect the royalty purchase agreement with Royalty Pharma as a taxable sale, requiring us to include the proceeds from the sale, net of currently deductible issuance costs, as taxable income in 2023. The resulting tax liability is partially offset by the utilization of our R&D tax credits.

We recorded income tax expense of $6.6 million and $25.8 million for the three and nine months ended September 30, 2023, respectively, compared to $0.3 million and $3.6 million for the same periods in 2022, respectively. The increase in income tax expense for the three and nine months ended September 30, 2023, compared to the same periods in 2022, relates primarily to the impact of the Royalty Pharma transaction.

We continue to maintain a full valuation allowance on all our net deferred tax assets.

11. Liability Related to Sale of Future Royalties

In January 2023, we entered into a royalty purchase agreement with Royalty Pharma to monetize a portion of our future SPINRAZA and pelacarsen royalties we are entitled to under our arrangements with Biogen and Novartis, respectively. As a result, we received an upfront payment of $500 million and we are eligible to receive up to $625 million in additional milestone payments. Under the terms of the agreement, Royalty Pharma will receive 25 percent of our SPINRAZA royalty payments from 2023 through 2027, increasing to 45 percent of royalty payments in 2028, on up to $1.5 billion in annual sales. In addition, Royalty Pharma will receive 25 percent of any future royalty payments on pelacarsen. Royalty Pharma's royalty interest in SPINRAZA will revert to us after total SPINRAZA royalty payments to Royalty Pharma reach either $475 million or $550 million, depending on the timing and occurrence of FDA approval of pelacarsen.

We recorded the upfront payment of $500 million as a liability related to the sale of future royalties, net of transaction costs of $10.4 million, which we are amortizing over the estimated life of the arrangement using the effective interest rate method. We recognize royalty revenue in the period in which the counterparty sells the related product and recognizes the related revenue. We record royalty payments made to Royalty Pharma as a reduction of the liability.

We determine the effective interest rate used to record interest expense under this agreement based on an estimate of future royalty payments to Royalty Pharma. As of September 30, 2023, the estimated effective interest rate under the agreement was 13.5 percent.

The following is a summary of our liability related to sale of future royalties for the nine months ended September 30, 2023 (in thousands):

Proceeds from sale of future royalties	$ 500,000
Royalty payments to Royalty Pharma	(27,814)
Interest expense related to sale of future royalties	50,541
Liability related to sale of future royalties as of September 30, 2023	522,727
Issuance costs related to sale of future royalties	(10,434)
Amortization of issuance costs related to sale of future royalties as of September 30, 2023	407
Net liability related to sale of future royalties as of September 30, 2023	$ 512,700

There are numerous factors, most of which are not within our control, that could materially impact the amount and timing of royalty payments from Biogen and Novartis, and result in changes to our estimate of future royalty payments to Royalty Pharma. Such factors include, but are not limited to the commercial sales of SPINRAZA, the regulatory approval and commercial sales of pelacarsen, competing products or other significant events.

12. Convertible Debt

1.75 Percent Convertible Senior Notes

In June 2023, we completed a $575.0 million offering of convertible senior notes and used $420.4 million of the net proceeds from the issuance of the 1.75% Notes to repurchase $434.1 million in principal of our 0.125% Notes. In the third quarter of 2023, we used $67.8 million of the residual proceeds to repurchase an additional $70.3 million in principal of our 0.125% Notes. We expect to use the remaining net proceeds to settle the 0.125% Notes that remain outstanding.

At September 30, 2023, we had the following 1.75% Notes outstanding (in millions except interest rate and price per share data):

	1.75% Notes
Outstanding principal balance	$ 575.0
Unamortized debt issuance costs	$ 13.4
Maturity date	June 2028
Interest rate	1.75 percent
Effective interest rate	2.3 percent
Conversion price per share	$ 53.73
Total shares of common stock subject to conversion	10.7

0 Percent Convertible Senior Notes and Call Spread

In April 2021, we completed a $632.5 million offering of convertible senior notes. We used $257.0 million of the net proceeds from the issuance of the 0% Notes to repurchase $247.9 million in principal of our 1% convertible senior notes, or 1% Notes.

At September 30, 2023, we had the following 0% Notes outstanding (in millions except interest rate and price per share data):

	0% Notes
Outstanding principal balance	$ 632.5
Unamortized debt issuance costs	$ 7.9
Maturity date	April 2026
Interest rate	0 percent
Effective interest rate	0.5 percent
Conversion price per share	$ 57.84
Effective conversion price per share with call spread	$ 76.39
Total shares of common stock subject to conversion	10.9

In conjunction with the April 2021 offering, we entered into a call spread transaction, which was comprised of purchasing note hedges and selling warrants, to minimize the impact of potential economic dilution upon conversion of our 0% Notes by increasing the effective conversion price on our 0% Notes. We increased our effective conversion price to $76.39 with the same number of underlying shares as our 0% Notes. The call spread cost us $46.9 million, of which $136.7 million was for the note hedge purchase, offset by $89.8 million we received for selling the warrants. Similar to our 0% Notes, our note hedges are subject to adjustment. Additionally, our note hedges are exercisable upon conversion of the 0% Notes. The note hedges will expire upon maturity of the 0% Notes, or April 2026. The note hedges and warrants are separate transactions and are not part of the terms of our 0% Notes. The holders of the 0% Notes do not have any rights with respect to the note hedges and warrants.

We recorded the amount we paid for the note hedges and the amount we received for the warrants in additional paid-in capital in our condensed consolidated balance sheets. Refer to Part IV, Item 15, Note 1, *Organization and Significant Accounting Policies*, of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2022 for our Call Spread accounting policy. We reassess our ability to continue to classify the note hedges and warrants in shareholders' equity at each reporting period.

0.125 Percent Convertible Senior Notes and Call Spread

As discussed above, in June 2023, we repurchased $434.1 million of our 0.125% Notes. In the third quarter of 2023, we used $67.8 million of residual net proceeds from the issuance of the 1.75% Notes to repurchase an additional $70.3 million of our 0.125% Notes. As a result, the remaining principal balance of our 0.125% Notes was $44.5 million as of September 30, 2023. Additionally, in the three and nine months ended September 30, 2023, we recorded a $2.1 million and $13.4 million gain on the early retirement of debt, respectively, which we recorded as other income in our condensed consolidated statements of operations. The gain on the early retirement of our debt is the difference between the amounts paid to repurchase our 0.125% Notes and the net carrying balance of the liability at the time that we completed the repurchases.

At September 30, 2023, we had the following 0.125% Notes outstanding with interest payable semi-annually (in millions except interest rate and price per share data):

	0.125% Notes
Outstanding principal balance	$ 44.5
Unamortized debt issuance costs	$ 0.2
Maturity date	December 2024
Interest rate	0.125 percent
Effective interest rate	0.5 percent
Conversion price per share	$ 83.28
Effective conversion price per share with call spread	$ 123.38
Total shares of common stock subject to conversion	0.5

In conjunction with the issuance of our 0.125% Notes in December 2019, we entered into a call spread transaction, which was comprised of purchasing note hedges and selling warrants, to minimize the impact of potential economic dilution upon conversion of our 0.125% Notes by increasing the effective conversion price on our 0.125% Notes. We increased our effective conversion price to $123.38 with the same number of underlying shares as our 0.125% Notes. The call spread cost us $52.6 million, of which $108.7 million was for the note hedge purchase, offset by $56.1 million we received for selling the warrants. Similar to our 0.125% Notes, our note hedges are subject to adjustment. Additionally, our note hedges are exercisable upon conversion of the 0.125% Notes. The note hedges will expire upon maturity of the 0.125% Notes, or December 2024. The note hedges and warrants are separate transactions and are not part of the terms of our 0.125% Notes. The holders of the 0.125% Notes do not have any rights with respect to the note hedges and warrants. As of September 30, 2023, the note hedges and warrants remain outstanding.

We recorded the amount we paid for the note hedges and the amount we received for the warrants in additional paid-in capital in our condensed consolidated balance sheets. We reassess our ability to continue to classify the note hedges and warrants in shareholders' equity at each reporting period.

Other Terms of Convertible Senior Notes

The 1.75%, 0% and 0.125% Notes are convertible under certain conditions, at the option of the note holders. We can settle conversions of the notes, at our election, in cash, shares of our common stock or a combination of both. We may not redeem the notes prior to maturity, and we do not have to provide a sinking fund for them. Holders of the notes may require us to purchase some or all of their notes upon the occurrence of certain fundamental changes, as set forth in the indentures governing the notes, at a purchase price equal to 100 percent of the principal amount of the notes to be purchased, plus any accrued and unpaid interest.

13. Real Estate Transactions

In October 2022, we concurrently entered into two purchase and sale agreements with a real estate investor. In the same month, we closed the first transaction in which we sold the facilities at our headquarters in Carlsbad, California, which includes our primary R&D facility, for a purchase price of $263.4 million. In connection with this transaction, we leased back our headquarters facilities for an initial lease term of 15 years with options to extend the lease for two additional terms of five years each.

In August 2023, we closed the second transaction and transferred legal ownership of two lots of undeveloped land adjacent to our headquarters to the real estate investor for a purchase price of $33 million. In connection with this transaction, we entered into a build-to-suit lease agreement with the same real estate investor to lease a new R&D facility. The lessor will develop and construct a new building composed of R&D and office space. We will design and construct tenant improvements to customize the facility's interior space. We will lease the facility for an initial term of 15 years with options to extend the lease for two additional terms of five years each. The lease will commence once the structure of this new facility is completed.

Since the building is under construction and unavailable to lease, we are unable to complete the sale-leaseback evaluation under ASC 842, *Leases*. As a result, the land remains in our condensed consolidated balance sheets and we accounted for the proceeds as a financial liability. We will reassess the transaction under the sale-leaseback accounting guidance when the facilities are available for lease commencement.

In October 2022, we entered into a build-to-suit lease agreement to lease a development chemistry and manufacturing facility to be constructed by the lessor in Oceanside, California. We capitalized costs that we incurred related to the design and development of tenant improvements as construction-in-progress in our condensed consolidated balance sheets. In August 2023, we reached a mutual agreement with the lessor to terminate the lease agreement. As a result, we recorded a charge of $18 million, primarily associated with the impairment of construction-in-progress assets, within selling, general and administrative, or SG&A, expense in our condensed consolidated statements of operations.

14. Legal Proceedings

From time to time, we are involved in legal proceedings arising in the ordinary course of our business. Periodically, we evaluate the status of each legal matter and assess our potential financial exposure. If we consider the potential loss from any legal proceeding to be probable and we can reasonably estimate the amount, we accrue a liability for the estimated loss. The outcome of any proceeding is not determinable in advance. Therefore, we are required to use significant judgment to determine the probability of a loss and whether the amount of the loss is reasonably estimable. Our assessment of a potential liability and the amount of accruals we recorded are based only on the information available to us at the time. As additional information becomes available, we reassess the potential liability related to the legal proceeding and may revise our estimates.

There are no pending material legal proceedings to which we are a party or of which our property is the subject.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

In this Report on Form 10-Q, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us," means Ionis Pharmaceuticals, Inc. and its wholly owned subsidiary, Akcea Therapeutics, Inc.

Forward-Looking Statements

In addition to historical information contained in this Report on Form 10-Q, the Report includes forward-looking statements regarding our business and the therapeutic and commercial potential of QALSODY (tofersen), SPINRAZA (nusinersen), TEGSEDI (inotersen), WAYLIVRA (volanesorsen), eplontersen, olezarsen, donidalorsen, zilganersen, ulefnersen (ION363), pelacarsen, bepirovirsen, IONIS-FB-L_{Rx}, our technologies and our other products in development. Any statement describing our goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, including those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this report and described in additional detail in our annual report on Form 10-K for the year ended December 31, 2022, which is on file with the U.S. Securities and Exchange Commission and is available from us, and those identified within Part II Item 1A. Risk Factors of this Report. Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors currently known by us. As a result, you are cautioned not to rely on these forward-looking statements.

Overview

We were founded over 30 years ago to deliver innovative medicines for diseases with great medical need. Today, we are building on our advancements in RNA-targeted therapeutics to deliver our medicines to the market that have the potential to transform the lives of people with devastating diseases. We currently have four marketed medicines: QALSODY, SPINRAZA, TEGSEDI and WAYLIVRA. On April 25, 2023, the U.S. Food and Drug Administration, or FDA, granted Biogen accelerated approval of QALSODY for the treatment of superoxide dismutase 1 amyotrophic lateral sclerosis, or SOD1-ALS. Additionally, the FDA accepted our New Drug Application, or NDA, of eplontersen for polyneuropathy caused by hereditary TTR amyloidosis, or ATTRv-PN. eplontersen's Prescription Drug User Fee Act, or PDUFA, date is December 22, 2023. We also have a rich innovative late- and mid-stage pipeline primarily focused on our leading cardiovascular and neurology franchises. In the first nine months of 2023, we expanded our late-stage pipeline with the initiations of Roche's Phase 3 study of IONIS-FB-L_{Rx} in patients with immunoglobulin A nephropathy, or IgAN, and GSK's Phase 3 program of bepirovirsen. In addition, we recently advanced zilganersen, our wholly owned medicine for the treatment of Alexander disease, or AxD, into the Phase 3 portion of our ongoing study. In September 2023, we reported positive data from the Phase 3 Balance study of olezarsen in patients with familial chylomicronemia syndrome, or FCS, showing dose-dependent reductions in APOCIII, statistically significant reductions in triglycerides, and substantial reductions in acute pancreatitis attacks and a favorable safety and tolerability profile. Based on these results, we plan to file for regulatory approval with the U.S. FDA and with the European Medicines Agency, or EMA, in 2024.

We believe our substantial and sustainable revenue and strong balance sheet enable us to continue investing in our commercial readiness efforts for multiple late-stage medicines and our innovative pipeline. By continuing to focus on these priorities, we believe we are well positioned to drive future growth and to deliver increasing value for patients and shareholders.

Marketed Medicines

SPINRAZA is the global market leader for the treatment of patients with spinal muscular atrophy, or SMA, a progressive, debilitating and often fatal genetic disease. Our partner, Biogen, is responsible for commercializing SPINRAZA worldwide. From inception through September 30, 2023, we have earned more than $2.0 billion in revenues from our SPINRAZA collaboration, including more than $1.6 billion in royalties on sales of SPINRAZA.

TEGSEDI is a once weekly, self-administered subcutaneous medicine approved in the U.S., Europe, Canada and Brazil for the treatment of patients with ATTRv-PN, a debilitating, progressive, and fatal disease. We launched TEGSEDI in the United States, or U.S., and the European Union, or EU, in late 2018. In 2021, we began selling TEGSEDI in Europe through our distribution agreement with Swedish Orphan Biovitrum AB, or Sobi, and in the second quarter of 2021, Sobi began distributing TEGSEDI in the U.S. and Canada. In October 2023, our distribution agreement for TEGSEDI in North America was terminated. In Latin America, PTC Therapeutics International Limited, or PTC, is commercializing TEGSEDI in Brazil and is pursuing access in additional Latin American countries through its exclusive license agreement with us.

WAYLIVRA is a once weekly, self-administered, subcutaneous medicine that received conditional marketing authorization in May 2019 from the European Commission, or EC, as an adjunct to diet in adult patients with genetically confirmed FCS and at high risk for pancreatitis. We launched WAYLIVRA in the EU in the third quarter of 2019. In 2021, we began selling WAYLIVRA in Europe through our distribution agreement with Sobi. In Latin America, PTC is commercializing WAYLIVRA in Brazil for two indications, FCS and familial partial lipodystrophy, or FPL, and is pursuing access in additional Latin American countries through its exclusive license agreement with us.

QALSODY is an antisense medicine that received accelerated approval in April 2023 from the FDA for the treatment of adult patients with SOD1-ALS, a rare, neurodegenerative disorder that causes progressive loss of motor neurons leading to death. Our partner, Biogen, is responsible for commercializing QALSODY worldwide. The EMA is currently reviewing QALSODY for approval in the EU.

Medicines in Registration and Phase 3 Studies

We currently have nine medicines in Phase 3 studies for eleven indications, which include:

- Eplontersen: our medicine in development for transthyretin amyloidosis, or ATTR
  - We are currently conducting a broad Phase 3 development program for ATTRv-PN and ATTR cardiomyopathy, or ATTR-CM, and additional studies supporting our ATTR development program
    - The FDA accepted the NDA of eplontersen in the U.S. for ATTRv-PN with a PDUFA date of December 22, 2023, and eplontersen is currently under regulatory review by the EMA and Health Canada for ATTRv-PN
    - In November 2023, we presented new positive data showing continued benefit in secondary endpoints from the Phase 3 NEURO-TTRansform study in patients with ATTRv-PN at EU-ATTR congress
    - In October 2023, the EMA granted orphan drug designation to eplontersen for the treatment of ATTR in the EU
    - In September 2023, *The Journal of the American Medical Association (JAMA)* published positive results from the Phase 3 NEURO-TTRansform study in patients with ATTRv-PN showing eplontersen halted disease progression and continuously improved quality of life at 35-, 66- and 85-week analyses
    - In July 2023, we completed enrollment of the Phase 3 CARDIO-TTRansform study of eplontersen in patients with ATTR-CM

- Olezarsen: our medicine in development for FCS and severe hypertriglyceridemia, or SHTG
  - We are currently conducting a broad Phase 3 development program for olezarsen that includes the Phase 3 Balance study in patients with FCS, three Phase 3 studies supporting development for the treatment of SHTG (CORE, CORE2 and ESSENCE) and a Phase 2b supporting study
    - In September 2023, we reported positive results from the Phase 3 Balance study in patients with FCS showing statistically significant triglyceride lowering and a substantial reduction in acute pancreatitis events in addition to a favorable safety and tolerability profile
    - In January 2023, the FDA granted fast track designation to olezarsen for the treatment of patients with FCS

- Donidalorsen: our medicine in development for hereditary angioedema, or HAE
  - We are currently conducting the Phase 3 OASIS-HAE study in patients with HAE and the Phase 3 OASIS-Plus supportive study for HAE patients previously treated with other prophylactic therapies
    - In September 2023, the FDA granted orphan drug designation to donidalorsen for the treatment of HAE
    - In June 2023, we completed enrollment of the Phase 3 OASIS-HAE study of donidalorsen in patients with hereditary angioedema; we remain on track for data in the first half of 2024
    - We reported positive data from the Phase 2 study and Phase 2 open-label extension, or OLE, study throughout 2022 and early 2023, including new topline two-year OLE data in June 2023

- Ulefnersen (ION363): our medicine in development for amyotrophic lateral sclerosis, or ALS, with mutations in the fused in sarcoma gene, or FUS
  - We are currently conducting a Phase 3 study of ulefnersen in juvenile and adult patients with FUS-ALS
    - In August 2023, the FDA granted orphan drug designation to ulefnersen for the treatment of FUS-ALS

- QALSODY: our medicine to treat patients with SOD1-ALS that is approved in the U.S., under regulatory review in the EU and in development for presymptomatic patients
  - In April 2023, the FDA granted Biogen accelerated approval of QALSODY for patients with SOD1-ALS
  - The EMA is currently reviewing QALSODY's Marketing Authorization Application, or MAA, in the EU

- Pelacarsen: our medicine in development to treat patients with elevated lipoprotein(a), or Lp(a)-driven cardiovascular disease, or CVD
  - Novartis is developing pelacarsen, including conducting the ongoing Lp(a) HORIZON Phase 3 cardiovascular outcome study in patients with elevated Lp(a)-driven CVD
    - In July 2022, Novartis achieved full enrollment in the Lp(a) HORIZON study

- Bepirovirsen: our medicine in development for hepatitis B virus, or HBV
  - GSK is developing bepirovirsen, including conducting the ongoing B-Well Phase 3 program in patients with HBV
    - In October 2023, GSK reported positive results from the Phase 2b B-Together study followed by pegylated interferon in patients with chronic HBV
    - In June 2023, GSK presented durable response data from the Phase 2 B-Sure long-term follow-up study of bepirovirsen in complete responder patients from the Phase 2b B-Clear study of patients with HBV

- IONIS-FB-L_{Rx}: our medicine in development for IgAN and geographic atrophy, or GA
  - In the second quarter of 2023, Roche advanced IONIS-FB-L_{Rx} into Phase 3 development in patients with IgAN
  - In October 2023, we reported positive interim data from the ongoing Phase 2 study of IONIS-FB-L_{Rx} in patients with IgAN
  - In June 2023, we completed enrollment in the Phase 2 GOLDEN study of IONIS-FB-L_{Rx} in patients with GA

- Zilganersen: our medicine in development for AxD
  - In September 2023, we advanced zilganersen into the Phase 3 portion of its ongoing study for patients with AxD

Critical Accounting Estimates

We prepare our condensed consolidated financial statements in conformity with accounting principles generally accepted in the U.S. As such, we make certain estimates, judgments and assumptions that we believe are reasonable, based upon the information available to us. These judgments involve making estimates about the effect of matters that are inherently uncertain and may significantly impact our quarterly or annual results of operations and financial condition. Each quarter, our senior management reviews the development, selection and disclosure of such estimates with the audit committee of our board of directors. The following are our significant accounting estimates, which we believe are the most critical to aid in fully understanding and evaluating our reported financial results:

- Assessing the propriety of revenue recognition and associated deferred revenue; and
- Determining the appropriate cost estimates for unbilled preclinical studies and clinical development activities

There have been no other material changes to our critical accounting policies and estimates from the information provided in Part II, Item 7, *Management's Discussion and Analysis of Financial Condition and Results of Operations*, included in our Annual Report on Form 10-K for the year ended December 31, 2022.

Results of Operations

The following is a summary of our financial results (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Total revenue	$ 144.2	$ 159.8	$ 463.1	$ 435.5
Total operating expenses	$ 287.5	$ 218.9	$ 810.7	$ 637.7
Loss from operations	$ (143.3)	$ (59.2)	$ (347.6)	$ (202.2)
Net loss	$ (147.4)	$ (47.0)	$ (357.0)	$ (217.3)

Revenue

Total revenues for the three and nine months ended September 30, 2023 were $144.2 million and $463.1 million, respectively, compared to $159.8 million and $435.5 million for the same periods in 2022 and were comprised of the following (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$ 67.3	$ 61.6	$ 178.5	$ 175.1
Other commercial revenue:				
TEGSEDI and WAYLIVRA revenue, net	8.3	5.9	25.4	22.5
Licensing and other royalty revenue	8.5	4.9	25.8	25.3
Total other commercial revenue	16.8	10.8	51.2	47.8
Total commercial revenue	84.1	72.4	229.7	222.9
R&D revenue:				
Amortization from upfront payments	18.0	18.1	46.8	54.0
Milestone payments	16.2	14.9	89.8	59.7
License fees	4.6	35.0	24.6	37.0
Other services	5.3	1.3	12.3	6.6
Collaborative agreement revenue	44.1	69.3	173.5	157.3
Eplontersen joint development revenue	16.0	18.1	59.9	55.3
Total R&D revenue	60.1	87.4	233.4	212.6
Total revenue	$ 144.2	$ 159.8	$ 463.1	$ 435.5

Commercial revenue for the three and nine months ended September 30, 2023 included $67 million and $179 million from SPINRAZA royalties, respectively, which were relatively consistent compared to the same periods in 2022. Our commercial revenue in the three and nine months ended September 30, 2023 also included royalties from the U.S. launch of QALSODY.

R&D revenue decreased for three months ended September 30, 2023 and increased for the nine months ended September 30, 2023 compared to the same periods in 2022 due to the timing of certain partner payments. The decrease for the three months comparison was due to the $35 million license fee for IONIS-FB-L_{Rx} that we earned from Roche in the three months ended September 30, 2022. The increase for the nine months comparison was driven by increased partner payments in 2023 compared to 2022.

Eplontersen Collaboration with AstraZeneca

Our financial results for the three and nine months ended September 30, 2023 and 2022 reflected the cost-sharing provisions related to our collaboration with AstraZeneca to develop and commercialize eplontersen for the treatment of ATTR. Under the terms of the collaboration agreement, AstraZeneca is currently paying 55 percent of the costs associated with the ongoing global Phase 3 development program. Because we are leading and conducting the Phase 3 development program, we are recognizing as R&D revenue the 55 percent of cost-share funding AstraZeneca is responsible for, net of our share of AstraZeneca's development expenses, in the same period we incur the related development expenses.

As AstraZeneca is responsible for the majority of the medical affairs and commercial costs in the U.S. and all costs associated with bringing eplontersen to market outside the U.S., we are recognizing cost-share funding we receive from AstraZeneca related to these activities as a reduction of our medical affairs and commercialization expenses, which we classify as R&D and selling, general and administrative, or SG&A, expenses, respectively. We expect our medical affairs and commercialization expenses to increase as eplontersen advances toward the market under our collaboration with AstraZeneca.

Our revenue and expenses under this collaboration were as follows (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Eplontersen joint development revenue	$ 16.0	$ 18.1	$ 59.9	$ 55.3
Research and development expenses related to Phase 3 development expenses for eplontersen	32.4	36.2	117.8	107.3
Medical affairs expenses for eplontersen	1.1	0.5	2.9	1.4
Commercialization expenses for eplontersen	4.5	0.8	8.3	1.5

Operating Expenses

Our operating expenses were as follows (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Operating expenses, excluding non-cash compensation expense related to equity awards	$ 261.6	$ 195.1	$ 731.3	$ 563.1
Non-cash compensation expense related to equity awards	25.9	23.8	79.4	74.6
Total operating expenses	$ 287.5	$ 218.9	$ 810.7	$ 637.7

Operating expenses, excluding non-cash compensation expense related to equity awards, for the three and nine months ended September 30, 2023 increased compared to the same periods in 2022. Our R&D expenses increased as we advanced our pipeline, which included an increase in the costs associated with our clinical studies as most of our Phase 3 studies were either fully enrolled or approaching full enrollment at the end of September 2023. Our SG&A expenses increased due to expenses related to our launch preparation activities for eplontersen, olezarsen and donidalorsen. We expect our operating expenses, excluding non-cash compensation expense related to equity awards, to slightly increase in the fourth quarter of 2023 as we continue to advance our late-stage medicines in development and prepare for commercialization.

To analyze and compare our results of operations to other similar companies, we believe it is important to exclude non-cash compensation expense related to equity awards from our operating expenses. We believe non-cash compensation expense related to equity awards is not indicative of our operating results or cash flows from our operations. Further, we internally evaluate the performance of our operations excluding it.

Cost of Sales

Our cost of sales is comprised of costs related to our commercial revenue, which consisted of manufacturing costs, including certain fixed costs, transportation and freight, indirect overhead costs associated with the manufacturing and distribution of TEGSEDI and WAYLIVRA and certain associated period costs.

Our cost of sales were as follows (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Cost of sales, excluding non-cash compensation expense related to equity awards	$ 2.1	$ 1.3	$ 5.8	$ 9.9
Non-cash compensation expense related to equity awards	0.1	0.2	0.3	0.5
Total cost of sales	$ 2.2	$ 1.5	$ 6.1	$ 10.4

Research, Development and Patent Expenses

Our research, development and patent expenses consist of expenses for drug discovery, drug development, manufacturing and development chemistry and R&D support expenses.

The following table sets forth information on research, development and patent expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Research, development and patent expenses, excluding non-cash compensation expense related to equity awards	$ 196.5	$ 165.3	$ 585.5	$ 469.6
Non-cash compensation expense related to equity awards	18.8	17.7	57.6	55.3
Total research, development and patent expenses	$ 215.3	$ 183.0	$ 643.1	$ 524.9

Drug Discovery

We use our proprietary technologies to generate information about the function of genes and to determine the value of genes as drug discovery targets. We use this information to direct our own drug discovery research, and that of our partners. Drug discovery is also the function that is responsible for advancing our core technology. This function is also responsible for making investments in complementary technologies to expand the reach of our technologies.

Our drug discovery expenses were as follows (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Drug discovery expenses, excluding non-cash compensation expense related to equity awards	$ 26.6	$ 25.0	$ 78.8	$ 68.6
Non-cash compensation expense related to equity awards	4.0	4.2	11.9	12.8
Total drug discovery expenses	$ 30.6	$ 29.2	$ 90.7	$ 81.4

Drug discovery expenses, excluding non-cash compensation expense related to equity awards, increased in the three and nine months ended September 30, 2023 compared to the same periods in 2022 as we continued to advance our research programs.

Drug Development

The following table sets forth drug development expenses, including expenses for our marketed medicines and those in Phase 3 development for which we have incurred significant costs (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
TEGSEDI and WAYLIVRA	$ 3.0	$ 3.9	$ 5.6	$ 9.4
Eplontersen	25.1	24.5	90.8	75.8
Olezarsen	38.5	18.3	96.6	39.7
Donidalorsen	6.9	5.5	19.4	9.1
Ulefnersen	2.5	2.3	7.7	5.8
Other development projects	28.2	31.6	81.4	91.7
Development overhead expenses	28.3	22.5	83.8	63.3
Total drug development, excluding non-cash compensation expense related to equity awards	132.5	108.6	385.3	294.8
Non-cash compensation expense related to equity awards	8.6	7.6	25.7	15.6
Total drug development expenses	$ 141.1	$ 116.2	$ 411.0	$ 310.4

Our development expenses, excluding non-cash compensation expense related to equity awards, increased for the three and nine months ended September 30, 2023 compared to the same periods in 2022 primarily due to our advancing late-stage pipeline and full or nearly full enrollment of multiple Phase 3 studies.

We may conduct multiple clinical trials on a drug candidate, including multiple clinical trials for the various indications we may be studying. Furthermore, as we obtain results from trials, we may elect to discontinue clinical trials for certain drug candidates in certain indications in order to focus our resources on more promising drug candidates or indications. Our Phase 1 and Phase 2 programs are clinical research programs that fuel our Phase 3 pipeline. When our medicines are in Phase 1 or Phase 2 clinical trials, they are in a dynamic state in which we may adjust the development strategy for each medicine. Although we may characterize a medicine as "in Phase 1" or "in Phase 2," it does not mean that we are conducting a single, well-defined study with dedicated resources. Instead, we allocate our internal resources on a shared basis across numerous medicines based on each medicine's particular needs at that time. This means we are constantly shifting resources among medicines. Therefore, what we spend on each medicine during a particular period is usually a function of what is required to keep the medicines progressing in clinical development, not what medicines we think are most important. For example, the number of people required to start a new study is large, the number of people required to keep a study going is modest and the number of people required to finish a study is large. However, such fluctuations are not indicative of a shift in our emphasis from one medicine to another and cannot be used to accurately predict future costs for each medicine. Because we always have numerous medicines in preclinical and varying stages of clinical research, the fluctuations in expenses from medicine to medicine, in large part, offset one another. If we partner a medicine, it may affect the size of a trial, its timing, its total cost and the timing of the related costs.

Medical Affairs

Our medical affairs function is responsible for funding and coordinating investigator-sponsored trials, communicating scientific and clinical information to healthcare providers, medical professionals and patients, and managing publications.

Our medical affairs expenses were as follows (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Medical affairs expenses, excluding non-cash compensation expense related to equity awards	$ 4.9	$ 3.8	$ 13.8	$ 11.4
Non-cash compensation expense related to equity awards	0.8	0.6	2.7	1.3
Total medical affairs expenses	$ 5.7	$ 4.4	$ 16.5	$ 12.7

Medical affairs expenses, excluding non-cash compensation expense related to equity awards, increased in the three and nine months ended September 30, 2023 compared to the same periods in 2022. We expect medical affairs expenses, excluding non-cash compensation expense related to equity awards, to increase in the fourth quarter of 2023 as we advance our late-stage pipeline.

Manufacturing and Development Chemistry

Expenditures in our manufacturing and development chemistry function consist primarily of personnel costs, specialized chemicals for oligonucleotide manufacturing, validation batches to support regulatory approvals, laboratory supplies and outside services. Our manufacturing and development chemistry function is responsible for providing drug supplies to drug development and our collaboration partners. Our manufacturing procedures include testing to satisfy good laboratory and good manufacturing practice requirements.

Our manufacturing and development chemistry expenses were as follows (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Manufacturing and development chemistry expenses, excluding non-cash compensation expense related to equity awards	$ 12.3	$ 14.0	$ 49.2	$ 53.4
Non-cash compensation expense related to equity awards	2.2	2.3	6.5	7.6
Total manufacturing and development chemistry expenses	$ 14.5	$ 16.3	$ 55.7	$ 61.0

R&D Support

In our research, development and patent expenses, we include support costs such as rent, repair and maintenance for buildings and equipment, utilities, depreciation of laboratory equipment and facilities, amortization of our intellectual property, information technology costs, procurement costs and waste disposal costs. We call these costs R&D support expenses.

The following table sets forth information on R&D support expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Personnel costs	$ 6.2	$ 5.3	$ 19.4	$ 15.4
Occupancy	7.2	4.1	21.4	12.3
Patent expenses	0.9	0.9	2.8	3.1
Insurance	0.9	1.0	2.7	2.8
Computer software and licenses	0.8	0.1	2.0	1.1
Other	4.2	2.5	10.1	6.7
Total R&D support expenses, excluding non-cash compensation expense related to equity awards	20.2	13.9	58.4	41.4
Non-cash compensation expense related to equity awards	3.2	3.0	10.8	10.4
Total R&D support expenses	$ 23.4	$ 16.9	$ 69.2	$ 51.8

R&D support expenses, excluding non-cash compensation expense related to equity awards, increased in the three and nine months ended September 30, 2023 compared to the same periods in 2022. The increase was primarily related to increased occupancy and personnel costs to support advancing our pipeline and our technology. In October 2022, we executed a sale and leaseback transaction for our headquarters in Carlsbad, California. As a result, beginning in the fourth quarter of 2022, our occupancy costs increased because we began incurring rent expense for these facilities.

Selling, General and Administrative Expenses

SG&A expenses include personnel and outside costs associated with the pre-commercialization and commercialization activities for our medicines and costs to support our company, our employees and our stockholders including, legal, human resources, investor relations and finance. Additionally, we include in selling, general and administrative expenses such costs as rent, repair and maintenance of buildings and equipment, depreciation and utilities costs that we need to support the corporate functions listed above. We also include fees we owe under our in-licensing agreements related to SPINRAZA and QALSODY.

The following table sets forth information on SG&A expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Selling, general and administrative expenses, excluding non-cash compensation expense related to equity awards	$ 62.9	$ 28.5	$ 140.0	$ 83.6
Non-cash compensation expense related to equity awards	7.1	5.9	21.6	18.8
Total selling, general and administrative expenses	$ 70.0	$ 34.4	$ 161.6	$ 102.4

SG&A expenses, excluding non-cash compensation expense related to equity awards, increased in the three and nine months ended September 30, 2023 compared to the same periods in 2022 due to increased expenses related to our go-to-market activities for eplontersen, olezarsen and donidalorsen. In addition, we recorded a one-time expense of $18 million when we terminated a build-to-suit lease agreement in August 2023. Refer to Part I, Item 1, Note 13, *Real Estate Transactions*, in the Notes to our condensed consolidated financial statements for further details on the lease termination.

Investment Income

The following table sets forth information on investment income (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Investment income	$ 23.9	$ 7.5	$ 63.4	$ 13.4

Our investment income increased primarily due to an increase in interest rates associated with our investments in debt securities and an increase in our cash available for investment during the three and nine months ended September 30, 2023 compared to the same periods in 2022. Our cash balance increased due to the $500 million upfront payment we received in January 2023 from our royalty purchase agreement with Royalty Pharma Investments, or Royalty Pharma, and net proceeds we received from the debt offering in June 2023. These increases were partially offset by the repurchase of $504 million in principal of our 0.125% Notes during the nine months ended September 30, 2023.

Interest Expense

The following table sets forth information on interest expense (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Convertible notes:				
Non-cash amortization of debt issuance costs	$ 1.6	$ 1.3	$ 4.3	$ 4.0
Interest expense payable in cash	2.5	0.2	3.5	0.5
Interest on mortgage for primary R&D and manufacturing facilities	0.1	0.6	0.3	1.9
Total interest expense	$ 4.2	$ 2.1	$ 8.1	$ 6.4

In June 2023, we completed a $575.0 million offering of our 1.75% Notes and repurchased $434.1 million in principal of our 0.125% Notes. As a result, beginning in the second quarter of 2023, our interest expense related to our convertible notes increased because we began incurring interest expense for our 1.75% Notes.

Interest Expense Related to Sale of Future Royalties

We recorded $17.8 million and $50.9 million of interest expense related to the sale of future royalties in the three and nine months ended September 30, 2023, respectively, as a result of the Royalty Pharma transaction, in which we sold a minority interest in our future royalties to Royalty Pharma for a $500 million upfront payment and $625 million of potential future payments. Refer to Part I, Item 1, Note 11, *Liability Related to Sale of Future Royalties*, in the Notes to our condensed consolidated financial statements for further details.

Gain (Loss) on Investments

The following table sets forth information on gain (loss) on investments (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Gain (loss) on investments	$ (1.9)	$ 2.3	$ (1.8)	$ (10.6)

The period-over-period fluctuations in our gain (loss) on investments were driven by changes in the fair value of our investments in privately held and publicly traded biotechnology companies. The loss on investments in the nine months ended September 30, 2022 was primarily driven by losses on our investments in publicly traded biotechnology companies.

Other Expense

In June 2023, we completed a $575.0 million offering of our 1.75% Notes and used $420.4 million of the net proceeds to repurchase $434.1 million in principal of our 0.125% Notes. In the third quarter of 2023, we used $67.8 of the residual proceeds to repurchase an additional $70.3 million in principal of our 0.125% Notes. As a result of these repurchases, we recorded a $13.4 million gain on early retirement of debt for the nine months ended September 30, 2023, which reflects the difference between the amounts we paid to repurchase portions of our 0.125% Notes and the net carrying balance of the liability at the time that we repurchased the debt. Refer to Part I, Item 1, Note 12, *Convertible Debt*, in the Notes to our condensed consolidated financial statements for further details regarding our convertible debt.

In the second quarter of 2022, we recorded a non-operating expense of $12.5 million related to a settlement agreement for a litigation claim. Refer to Part IV, Item 15, Note 9, *Legal Proceedings*, of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2022 for further details regarding the litigation.

Income Tax Expense

Beginning in 2022, the Tax Cuts and Jobs Act of 2017, or TCJA, requires taxpayers to amortize research and development expenditures over five years pursuant to Internal Revenue Code, or IRC, Section 174. Additionally, we expect to reflect the royalty purchase agreement with Royalty Pharma as a taxable sale, requiring us to include the proceeds from the sale, net of currently deductible issuance costs, as taxable income in 2023. The resulting tax liability is partially offset by the utilization of our R&D tax credits.

We recorded income tax expense of $6.6 million and $25.8 million for the three and nine months ended September 30, 2023, respectively, compared to $0.3 million and $3.6 million for the same periods in 2022, respectively. The increase in income tax expense for the three and nine months ended September 30, 2023, compared to the same periods in 2022, relates primarily to the impact of the Royalty Pharma transaction.

We continue to maintain a full valuation allowance on all our net deferred tax assets.

Net Loss and Net Loss per Share

We had a net loss of $147.4 million and $357.0 million for the three and nine months ended September 30, 2023, respectively. We had a net loss of $47.0 million and $217.3 million for the same periods in 2022. The period-over-period fluctuations in our net loss were driven by factors discussed in the sections above. Basic and diluted net loss per share for the three and nine months ended September 30, 2023 were $1.03 and $2.50, respectively, compared to $0.33 and $1.53 for the same periods in 2022.

Liquidity and Capital Resources

We have financed our operations primarily from research and development collaborative agreements. We also finance our operations from commercial revenue from royalties, most notably from SPINRAZA, and TEGSEDI and WAYLIVRA commercial revenue. From our inception through September 30, 2023, we have earned approximately $6.9 billion in revenue. We have also financed our operations through the sale of our equity securities, the issuance of long-term debt and the sale of future royalties. From the time we were founded through September 30, 2023, we have raised net proceeds of approximately $2.1 billion from the sale of our equity securities. Additionally, from our inception through September 30, 2023, we have borrowed approximately $2.7 billion under long-term debt arrangements and received proceeds of $0.5 billion from the sale of future royalties to finance a portion of our operations.

Our cash, cash equivalents and short-term investments, working capital and long-term obligations increased from December 31, 2022 to September 30, 2023. As discussed above, in the nine months ended September 30, 2023, we repurchased $504.4 million in principal of our 0.125% Notes. In the third quarter of 2023, we closed a real estate transaction for a total purchase price of $33.0 million. In the second quarter of 2023, we issued $575.0 million of 1.75% Notes (due in June 2028). In the first quarter of 2023, we received an upfront payment of $500.0 million when we entered into a royalty purchase agreement with Royalty Pharma and recorded a corresponding long-term liability related to the sale of future royalties.

The following table summarizes our contractual obligations, excluding our liability related to the sale of future royalties, as of September 30, 2023. The table provides a breakdown of when obligations become due. We provide a more detailed description of the major components of our debt in the paragraphs following the table:

Contractual Obligations

	Payments Due by Period (in millions)		
(selected balances described below)	**Total**	**Less than 1 year**	**More than 1 year**
1.75% Notes (principal and interest payable)	$ 625.4	$ 10.1	$ 615.3
0% Notes (principal payable)	632.5	—	632.5
0.125% Notes (principal and interest payable)	44.7	0.1	44.6
Operating leases	284.6	20.3	264.3
Building mortgage payments (principal and interest payable)	10.3	0.5	9.8
Other obligations (principal and interest payable)	0.8	0.1	0.7
Total	$ 1,598.3	$ 31.1	$ 1,567.2

Our contractual obligations consist primarily of our convertible debt. In addition, we also have facility leases, a facility mortgage, equipment financing arrangements and other obligations. We have not entered into, nor do we currently have, any off-balance sheet arrangements (as defined under SEC rules).

Convertible Debt and Call Spread

Refer to Part I, Item 1, Note 12, *Convertible Debt*, in the Notes to our condensed consolidated financial statements for the significant terms of each convertible debt instrument.

Operating Facilities

In July 2017, we purchased the building that houses our primary R&D facility for $79.4 million and our manufacturing facility for $14.0 million. We financed the purchase of these two facilities with mortgage debt of $60.4 million in total. Our manufacturing facility mortgage, which has an interest rate of 4.20 percent, matures in August 2027.

In October 2022, we concurrently entered into two purchase and sale agreements with a real estate investor. In the same month, we closed the first transaction in which we sold and leased back the facilities at our headquarters, which includes our primary R&D facility, for a purchase price of $263.4 million. We used a portion of the sale proceeds from our primary R&D facility to extinguish our mortgage debt on the facility of $51.3 million. In August 2023, we closed the second transaction and transferred legal ownership of two lots of undeveloped land adjacent to our headquarters to the real estate investor for a purchase price of $33 million. In connection with this transaction, we entered into a build-to-suit lease agreement with the same real estate investor to lease a new R&D facility.

In October 2022, we entered into a build-to-suit lease agreement to lease a development chemistry and manufacturing facility in Oceanside, California. In August 2023, we reached a mutual agreement with the lessor to terminate the lease agreement. We do not believe the termination of the lease impacts our ability to successfully commercialize our medicines. Refer to Part I, Item 1, Note 13, *Real Estate Transactions*, in the Notes to our condensed consolidated financial statements for further details on these agreements.

Operating Leases

Refer to our Leases accounting policy in Part IV, Item 15, Note 4, *Long-Term Obligations and Commitments*, of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2022 for further details on our operating leases.

Liability Related to Sale of Future Royalties

Refer to Part I, Item 1, Note 11, *Liability Related to Sale of Future Royalties*, in the Notes to our condensed consolidated financial statements for further details on our royalty purchase agreement with Royalty Pharma.

Other Obligations

In addition to contractual obligations, we had outstanding purchase orders as of September 30, 2023 for the purchase of services, capital equipment and materials as part of our normal course of business.

We may enter into additional collaborations with partners which could provide for additional revenue to us and we may incur additional cash expenditures related to our obligations under any of the new agreements we may enter into. We currently intend to use our cash, cash equivalents and short-term investments to finance our activities. However, we may also pursue other financing alternatives, like issuing additional shares of our common stock, issuing debt instruments, refinancing our existing debt, or securing lines of credit. Whether we use our existing capital resources or choose to obtain financing will depend on various factors, including the future success of our business, the prevailing interest rate environment and the condition of financial markets generally.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to changes in interest rates primarily from our investments in certain short-term investments. We primarily invest our excess cash in highly liquid short-term investments of the U.S. Treasury and reputable financial institutions, corporations, and U.S. government agencies with strong credit ratings. We typically hold our investments for the duration of the term of the respective instrument. We do not utilize derivative financial instruments, derivative commodity instruments or other market risk sensitive instruments, positions or transactions to manage exposure to interest rate changes. Accordingly, we believe that, while the securities we hold are subject to changes in the financial standing of the issuer of such securities, we are not subject to any material risks arising from changes in interest rates, foreign currency exchange rates, commodity prices, equity prices or other market changes that affect market risk sensitive instruments.

We are also exposed to changes in foreign currency exchange rates as we have foreign subsidiaries with functional currencies other than the U.S. dollar. We translate our subsidiaries' functional currencies into our reporting currency, the U.S. dollar. As a result, our financial position, results of operations and cash flows can be affected by market fluctuations in the foreign currencies to U.S. dollar exchange rate, which are difficult to predict. A hypothetical 10 percent change in foreign exchange rates during any of the periods presented would not have had a material impact on our condensed consolidated financial statements.

ITEM 4. CONTROLS AND PROCEDURES

We maintain disclosure controls and procedures that are designed to ensure that information we are required to disclose in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. We design and evaluate our disclosure controls and procedures recognizing that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance and not absolute assurance of achieving the desired control objectives.

As of our most recently completed fiscal year and as of the end of the period covered by this Quarterly Report on Form 10-Q, we carried out an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer. Based on our evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of September 30, 2023. There have been no significant changes in our internal controls or in other factors that could significantly affect internal controls subsequent to September 30, 2023.

We also performed an evaluation of any changes in our internal controls over financial reporting that occurred during our last fiscal quarter and that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting. We conducted this evaluation under the supervision of and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer. That evaluation did not identify any changes in our internal controls over financial reporting that occurred during our latest fiscal quarter and that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

PART II — OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

For details of legal proceedings, refer to Part I, Item 1, Note 14, *Legal Proceedings*, in the Notes to our condensed consolidated financial statements.

ITEM 1A. RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the following information about the risks described below, together with the other information contained in this report and in our other public filings in evaluating our business. If any of the following risks actually occur, our business could be materially harmed, and our financial condition and results of operations could be materially and adversely affected. As a result, the trading price of our securities could decline, and you might lose all or part of your investment. We have marked with an asterisk those risk factors that reflect substantive changes from the risk factors included in our Annual Report on Form 10-K for the year ended December 31, 2022.

Summary of Risk Factors

There are a number of risks related to our business and our securities. Some of the principal risks related to our business include the following:

- Our ability to generate substantial revenue from the sale of our medicines;
- The availability of adequate coverage and payment rates for our medicines;
- Our and our partners' ability to compete effectively;
- Our ability to successfully manufacture our medicines;
- Our ability to successfully develop and obtain marketing approvals for our medicines;
- Our ability to secure and maintain effective corporate partnerships;
- Our ability to sustain cash flows and achieve consistent profitability;
- Our ability to protect our intellectual property;
- Our ability to maintain the effectiveness of our personnel;
- The impacts of the COVID-19 pandemic and ongoing wars between Russia/Ukraine and Israel/Hamas; and
- The other factors set forth below.

Risks Related to the Commercialization of our Medicines

We have limited experience as a company in commercializing medicines and we will have to invest significant resources to develop our capabilities. If we are unable to establish effective marketing, sales, market access, distribution, and related functions, or enter into agreements with third parties to commercialize our medicines, we may not be able to generate revenue from our medicines.

We currently rely on third parties for the commercialization of our marketed medicines, have limited experience as a company in commercializing medicines and will have to invest significant financial and management resources to develop the infrastructure required to successfully commercialize our medicines. There are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. We will also need to scale-up existing internal support functions to aid our commercialization efforts, in particular, regulatory affairs and medical affairs. Any failure to effectively build or maintain the infrastructure required to successfully commercialize our medicines, including our sales, marketing, market access, distribution, and related capabilities, or scale-up our existing support functions, could adversely impact the revenue we generate from our medicines. In addition, if we choose to rely on third parties to assist us in commercializing our medicines, we may not be able to enter into collaborations or hire consultants or external service providers on acceptable financial terms, or at all. If we continue to engage third parties to assist us in the commercialization of our medicines, our product revenues and profitability may be lower than if we commercialized such medicines ourselves.

If the market does not accept our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our other medicines in development, we are not likely to generate substantial revenues or become consistently profitable.

Even if our medicines are authorized for marketing, our success will depend upon the medical community, patients and third-party payers accepting our medicines as medically useful, cost-effective, safe and convenient. Even when the FDA or foreign regulatory authorities authorize our or our partners' medicines for commercialization, doctors may not prescribe our medicines to treat patients. Furthermore, we and our partners may not successfully commercialize additional medicines.

Additionally, in many of the markets where we or our partners may sell our medicines in the future, if we or our partners cannot agree with the government or other third-party payers regarding the price we can charge for our medicines, we may not be able to sell our medicines in that market. Similarly, cost control initiatives by governments or third-party payers could decrease the price received for our medicines or increase patient coinsurance to a level that makes our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development, economically unviable. If the pricing of any of our medicines decreases for any reason, it will reduce our revenue for such medicine. For example, Biogen has in the past disclosed that SPINRAZA revenue decreased in part due to lower pricing in the U.S. and certain rest-of-world markets.

The degree of market acceptance for our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development, depends upon a number of factors, including the:

- receipt and scope of marketing authorizations;
- establishment and demonstration in the medical and patient community of the efficacy and safety of our medicines and their potential advantages over competing products;
- cost and effectiveness of our medicines compared to other available therapies;
- patient convenience of the dosing regimen for our medicines; and
- reimbursement policies of government and third-party payers.

Based on the profile of our medicines, physicians, patients, patient advocates, payers or the medical community in general may not accept or use any of the medicines that we may develop.

For example, TEGSEDI requires periodic blood and urine monitoring and is available in the U.S. only through a risk evaluation and mitigation strategy ("REMS") program. In addition, the product label for TEGSEDI in the U.S. has a boxed warning for thrombocytopenia and glomerulonephritis. Our main competitors in the U.S. market for TEGSEDI are patisiran and vutrisiran, both marketed by Alnylam Pharmaceuticals, Inc. Neither patisiran nor vutrisiran has a boxed warning nor does either require use of a REMS program. Additionally, the product label for WAYLIVRA in the European Union, or EU, requires regular blood monitoring. In each case, these label requirements have negatively affected our ability to attract and retain patients for these medicines. If we or our partner cannot effectively maintain patients on TEGSEDI or WAYLIVRA, including due to limitations or restrictions on the ability to conduct periodic blood and urine monitoring of our patients as a result of the COVID-19 pandemic, we may not be able to generate substantial revenue from TEGSEDI or WAYLIVRA sales.

If government or other third-party payers fail to provide adequate coverage and payment rates for our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development, our revenue will be limited.*

In both domestic and foreign markets, sales of our current and future products will depend in part upon the availability of coverage and reimbursement from third-party payers. The majority of patients in the U.S. who would fit within our target patient populations for our medicines have their healthcare supported by a combination of Medicare coverage, other government health programs such as Medicaid, managed care providers, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new medicines when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be enough to make our medicines affordable. Even if favorable coverage status and adequate reimbursement rates are attained, less favorable coverage policies and reimbursement rates may be implemented in the future. Accordingly, QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development, will face competition from other therapies and medicines for limited financial resources. We or our partners may need to conduct post-marketing studies to demonstrate the cost-effectiveness of any future products to satisfy third-party payers. These studies might require us to commit a significant amount of management time and financial and other resources. In addition, third-party payers may never consider our future products as cost-effective and adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Third-party payers, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the U.S., no uniform policy of coverage and reimbursement for medicines exists among third-party payers. Therefore, coverage and reimbursement for medicines can differ significantly from payer to payer. For example, the Affordable Care Act, or ACA, was passed in March 2010, and substantially changed the way healthcare is financed by both governmental and private insurers and continues to significantly impact the U.S. pharmaceutical industry. There have been judicial and Congressional challenges to certain aspects of the ACA, as well as efforts to repeal or replace certain aspects of the ACA. It is unclear how future litigation and healthcare reform measures will impact the ACA and our business.

Further, we believe that future coverage, reimbursement and pricing will likely be subject to increased restrictions both in the U.S. and in international markets. In the U.S., recent health reform measures have resulted in reductions in Medicare and other healthcare funding, and there have been several recent U.S. Congressional inquiries, legislation and executive orders designed to, among other things, reduce drug prices, increase competition (including by enhancing support for generic and biosimilar drugs), lower out-of-pocket drug costs for patients, curtail spread pricing practices by pharmacy benefit managers, and foster scientific innovation to promote better health care and improved health. In addition, the Inflation Reduction Act of 2022, or the IRA, among other things, allows the U.S. Department of Health and Human Services, or HHS, to negotiate the price of certain single-source drugs covered under Medicare and imposes rebates under Medicare Part B and Medicare Part D. In an effort to curb Medicare patients' out-of-pocket costs for prescription drugs, the Part D redesign legislation requires manufacturers to contribute to the catastrophic coverage phase for Part D drugs as discounts through a manufacturer discount program. Furthermore, any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. Our future product sales may be subject to additional discounts from list price in the form of rebates and discounts provided to covered entities under the Public Health Service Act 340B drug pricing program. Changes to the 340B program or to Medicare or Medicaid programs at the federal or state level, including outcomes of ongoing litigation in our industry, may impact our product prices and rebate liability. Further, in February 2023, in response to President Biden's executive order released in October 2022, the Secretary of the U.S. Department of HHS selected three new models for testing by the Centers for Medicare & Medicaid Services Innovation Center to help lower the high cost of drugs, promote accessibility to life-changing drug therapies and improve quality of care. It is unclear whether or how these selected models or similar policy initiatives will impact prescription drug pricing in the future.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Third-party coverage and reimbursement for medicines may not be available or adequate in either the U.S. or international markets, which would negatively affect the potential commercial success of our products, our revenue and our profits.

If we or our partners fail to compete effectively, our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development, will not generate significant revenues.

Our competitors engage in drug discovery throughout the world, are numerous, and include, among others, major pharmaceutical companies and specialized biopharmaceutical firms. In addition, other companies are engaged in developing RNA-targeted technology. Our competitors may succeed in developing medicines that are:

- priced lower than our medicines;
- reimbursed more favorably by government and other third-party payers than our medicines;
- safer than our medicines;
- more effective than our medicines; or
- more convenient to use than our medicines.

These competitive developments could make our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development, obsolete or non-competitive.

Certain of our partners are pursuing other technologies or developing other medicines either on their own or in collaboration with others, including our competitors, to treat some of the same diseases our own collaborative programs target. Competition may negatively impact a partner's focus on and commitment to our medicines and, as a result, could delay or otherwise negatively affect the commercialization of our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our other medicines in development.

Many of our competitors have substantially greater financial, technical and human resources than we do. In addition, many of these competitors have significantly greater experience than we do in conducting preclinical testing and human clinical studies of new pharmaceutical products, in obtaining FDA and other regulatory authorizations of such products and in commercializing such products. Accordingly, our competitors may succeed in obtaining regulatory authorization for products earlier than we do or more successfully commercialize their products.

There are several pharmaceutical and biotechnology companies engaged in the development or commercialization in certain geographic markets of products against targets that are also targets of products in our development pipeline. For example:

- Onasemnogene abeparvovec and risdiplam compete with SPINRAZA;
- Patisiran, tafamidis, tafamidis meglumine and vutrisiran compete with TEGSEDI and could compete with eplontersen;
- Acoramidis could compete with TEGSEDI and eplontersen;
- ARO-APOC3, lomitapide and pegozafermin could compete with WAYLIVRA and olezarsen;
- Lanadelumab-flyo, C1 esterase inhibitor, berotralstat, C1 esterase inhibitor subcutaneous, garadacimab, and NTLA-2002 could compete with donidalorsen;
- Olpasiran and SLN360 could compete with pelacarsen; and
- NI-204 could compete with QALSODY.

SPINRAZA injection for intrathecal use is an antisense medicine indicated for the treatment of SMA patients of all ages approved in over 50 countries. Specifically, SPINRAZA faces competition from onasemnogene abeparvovec, a gene therapy product that was approved in the U.S. in May 2019 and in the EU in May 2020 for the treatment of SMA, as well as risdiplam, an oral product for the treatment of SMA that was approved in the U.S. in August 2020 and in the EU in March 2021. Biogen has in the past disclosed that SPINRAZA revenue decreased due to a reduction in demand as a result of increased competition and that future sales of SPINRAZA may be adversely affected by competing products.

Additionally, companies that are developing medicines that target the same patient populations as our medicines in development may compete with us to enroll participants in the clinical trials for such medicines, which could make it more difficult for us to complete enrollment for these clinical trials.

Our medicines could be subject to regulatory limitations following approval.

Following approval of a medicine, we and our partners must comply with comprehensive government regulations regarding the manufacture, marketing and distribution of medicines. Promotional communications regarding prescription medicines must be consistent with the information in the product's approved labeling. We or our partners may not obtain the labeling claims necessary or desirable to successfully commercialize our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development.

The FDA and foreign regulatory bodies have the authority to impose significant restrictions on an approved medicine through the product label and on advertising, promotional and distribution activities. For example:

- in the U.S., TEGSEDI's label contains a boxed warning for thrombocytopenia and glomerulonephritis;
- TEGSEDI requires periodic blood and urine monitoring; and
- in the U.S., TEGSEDI is available only through a REMS program.

Prescription medicines may be promoted only for the approved indication(s) in accordance with the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, when approved, the FDA or a foreign regulatory authority may condition approval on the performance of post-approval clinical studies or patient monitoring, which could be time consuming and expensive. For example, in connection with the conditional marketing approval for WAYLIVRA in the EU, we are required to conduct a post-authorization safety study to evaluate the safety of WAYLIVRA on thrombocytopenia and bleeding in FCS patients taking WAYLIVRA. If the results of such post-marketing studies are not satisfactory, the FDA, EC or other foreign regulatory authorities may withdraw marketing authorization or may condition continued marketing on commitments from us or our partners that may be expensive and time consuming to fulfill.

If we or others identify side effects after any of our medicines are on the market, or if manufacturing problems occur subsequent to regulatory approval, or if we, our manufacturers or our partners fail to comply with regulatory requirements, we or our partners may, among other things, lose regulatory approval and be forced to withdraw products from the market, need to conduct additional clinical studies, incur restrictions on the marketing, distribution or manufacturing of the product, and/or change the labeling of our medicines.

We depend on our collaborations with Biogen for the development and commercialization of SPINRAZA and QALSODY.*

We have entered into separate collaborative arrangements with Biogen to develop and commercialize SPINRAZA and QALSODY. We entered into these collaborations primarily to:

- fund our development activities for SPINRAZA and QALSODY;
- seek and obtain regulatory approvals for SPINRAZA and QALSODY; and
- successfully commercialize SPINRAZA and QALSODY.

We are relying on Biogen to obtain additional regulatory approvals for SPINRAZA and QALSODY, generate additional clinical data for SPINRAZA and QALSODY, manufacture SPINRAZA and QALSODY, successfully launch QALSODY and continue to successfully commercialize SPINRAZA. In general, we cannot control the amount and timing of resources that Biogen devotes to our collaborations. If Biogen fails to further develop SPINRAZA or QALSODY, obtain additional regulatory approvals for SPINRAZA or QALSODY, manufacture SPINRAZA or QALSODY, successfully launch QALSODY or continue to successfully commercialize SPINRAZA, or if Biogen's efforts in any of these respects are ineffective, revenues for SPINRAZA or QALSODY would be negatively affected.

In addition, our collaborations with Biogen may not continue for various reasons. Biogen can terminate our collaborations at any time. If Biogen stops developing or commercializing SPINRAZA or QALSODY, we would have to seek or spend additional funding, and SPINRAZA's or QALSODY's commercialization may be harmed.

We depend on our collaboration with AstraZeneca for the joint development and commercialization of eplontersen.

We have entered into a collaborative arrangement with AstraZeneca to develop and commercialize eplontersen. Under the terms of the collaboration agreement, we and AstraZeneca will co-develop and co-commercialize eplontersen in the U.S. and AstraZeneca will have the sole right to commercialize eplontersen in all other countries, except for certain Latin American countries. Prior to co-commercializing eplontersen in the U.S., we will need to negotiate a co-commercialization agreement with AstraZeneca to govern the parties' performance of co-commercialization, which agreement will include a commercial plan and budget. As a company we do not have experience with co-commercialization arrangements. We also do not have control over the amount and timing of resources that AstraZeneca devotes to our collaboration, particularly outside of the U.S. If the co-commercialization arrangement for eplontersen is not successful for any reason, eplontersen may not meet our commercial objectives and our revenues for eplontersen may be limited.

In addition, a Joint Steering Committee, or JSC, having equal membership from us and AstraZeneca, and various subcommittees oversee and coordinate the development, manufacturing, commercialization and other exploitation activities for eplontersen in the U.S. by mutual agreement. If any subcommittee cannot reach unanimous agreement on any matter within its respective scope of authority, such matter may be referred to the JSC for resolution. If the JSC cannot come to a mutual agreement on any particular matter, this could delay our ability to develop or commercialize eplontersen.

If we are not successful in expanding our manufacturing capabilities or cannot manufacture our medicines or contract with a third party to manufacture our medicines at costs that allow us to charge competitive prices to buyers, we cannot market our products profitably.*

To successfully commercialize any of our medicines, we need to optimize and manage large-scale commercial manufacturing capabilities either on a standalone basis or through a third-party manufacturer. As our drug development and commercial pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. To that end, in 2022 we entered into a lease agreement ("Lease") with a lessor to construct a new manufacturing facility in Oceanside, California to expand our manufacturing infrastructure. In August 2023, we reached a mutual agreement with the lessor to terminate the Lease. While it remains important to expand our manufacturing infrastructure in the future, we believe our current capabilities and those we obtain through third-party manufacturers will support our manufacturing needs while we secure a suitable alternative for our manufacturing facility. When we do secure a suitable alternative, we will incur substantial expenditures to build the new manufacturing facility and, following its completion, will likely need to hire and train additional staff to operate the facility. If we are not successful in executing this expansion, it could limit our ability to meet our manufacturing requirements and commercial objectives in the future and we will not realize the value of our investment in the expansion.

In addition, we have limited experience manufacturing pharmaceutical products of the chemical class represented by our medicines, called oligonucleotides, on a commercial scale for the systemic administration of a medicine. There are a small number of suppliers for certain capital equipment and raw materials that we use to manufacture our medicines, and some of these suppliers will need to increase their scale of production to meet our projected needs for commercial manufacturing. Further, we must continue to improve our manufacturing processes to allow us to reduce our drug costs. We or our partners may not be able to manufacture our medicines at a cost or in quantities necessary to make commercially successful products.

Manufacturers, including us, must adhere to the FDA's cGMP regulations and similar regulations in foreign countries, which the applicable regulatory authorities enforce through facilities inspection programs. We, our partners and our contract manufacturers may not comply or maintain compliance with cGMP, or similar foreign regulations. Non-compliance could significantly delay or prevent receipt of marketing authorizations for our medicines, including authorizations for QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development, or could result in enforcement action after authorization that might limit the commercial success of our medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, and our medicines in development.

We rely on third-party manufacturers to supply the drug substance and drug product for TEGSEDI and drug product for WAYLIVRA. Any delays or disruption to our own or third-party commercial manufacturing capabilities, including any interruption to our supply chain as a result of the COVID-19 pandemic or the ongoing war between Russia and Ukraine, could limit the commercial success of our medicines.

We are relying on third parties to market, sell and distribute TEGSEDI and WAYLIVRA.*

We have entered into agreements with third parties to commercialize TEGSEDI and WAYLIVRA as follows:

- In April 2021, we entered into a distribution agreement with Sobi to commercialize TEGSEDI in the U.S. and Canada. Effective October 24, 2023, such agreement was terminated;
- In December 2020, we entered into a distribution agreement with Sobi to commercialize TEGSEDI and WAYLIVRA in Europe; and
- In August 2018, we granted PTC the exclusive right to commercialize TEGSEDI and WAYLIVRA in Latin America and certain Caribbean countries.

We are relying on Sobi and PTC to effectively market, sell and distribute TEGSEDI and WAYLIVRA and have less control over sales efforts and may receive less revenue than if we commercialized TEGSEDI or WAYLIVRA by ourselves. If Sobi or PTC does not successfully commercialize TEGSEDI or WAYLIVRA, including as a result of delays or disruption caused by the COVID-19 pandemic, we may receive limited revenue for TEGSEDI or WAYLIVRA in Europe, Latin America or certain Caribbean countries, which could adversely affect our business, prospects, financial condition and results of operations.

Risks Related to the Development and Regulatory Approval of our Medicines

If we or our partners fail to obtain regulatory approval for our medicines and additional approvals for QALSODY, SPINRAZA, TEGSEDI and WAYLIVRA, we or our partners cannot sell them in the applicable markets.

We cannot guarantee that any of our medicines will be considered safe and effective or will be approved for commercialization. In addition, it is possible that QALSODY, SPINRAZA, TEGSEDI and WAYLIVRA may not be approved in additional markets or for additional indications. We and our partners must conduct time-consuming, extensive and costly clinical studies to demonstrate the safety and efficacy of each of our medicines before they can be approved or receive additional approvals for sale. We and our partners must conduct these studies in compliance with FDA regulations and with comparable regulations in other countries.

We and our partners may not obtain necessary regulatory approvals on a timely basis, if at all, for our medicines. It is possible that regulatory agencies will not approve our medicines for marketing or QALSODY, SPINRAZA, TEGSEDI or WAYLIVRA in additional markets or for additional indications. If the FDA or another regulatory agency believes that we or our partners have not sufficiently demonstrated the safety or efficacy of any of our medicines, including QALSODY, SPINRAZA, TEGSEDI and WAYLIVRA, or our medicines in development, the agency will not approve the specific medicine or will require additional studies, which could be time consuming and expensive and delay or harm commercialization of the medicine. For example, in August 2018 we received a complete response letter from the FDA regarding the new drug application for WAYLIVRA in which the FDA determined that the safety concerns identified with WAYLIVRA in our clinical development program outweighed the expected benefits of triglyceride lowering in patients with FCS. We also received a Non-W from Health Canada for WAYLIVRA in November 2018.

The FDA or other comparable foreign regulatory authorities can delay, limit or deny approval of a medicine for many reasons, including:

- such authorities may disagree with the design or implementation of our clinical studies;
- we or our partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a medicine is safe and effective for any indication;
- such authorities may not accept clinical data from studies conducted at clinical facilities that have deficient clinical practices or that are in countries where the standard of care is potentially different from the U.S.;
- we or our partners may be unable to demonstrate that our medicine's clinical and other benefits outweigh its safety risks to support approval;
- such authorities may disagree with the interpretation of data from preclinical or clinical studies;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers who manufacture clinical and commercial supplies for our medicines, or may delay the inspection of such facilities due to restrictions related to the COVID-19 pandemic; and
- the approval policies or regulations of such authorities or their prior guidance to us or our partners during clinical development may significantly change in a manner rendering our clinical data insufficient for approval.

Failure to receive marketing authorization for our medicines, or failure to receive additional marketing authorizations for QALSODY, SPINRAZA, TEGSEDI or WAYLIVRA, or delays in these authorizations, could prevent or delay commercial introduction of the medicine, and, as a result, could negatively impact our ability to generate revenue from product sales.

If the results of clinical testing indicate that any of our medicines are not suitable for commercial use, we may need to abandon one or more of our drug development programs.

Drug discovery and drug development have inherent risks and the historical failure rate for drugs is high. Antisense medicines are a relatively new approach to therapeutics. If we cannot demonstrate that our medicines are safe and effective for human use in the intended indication(s), we may need to abandon one or more of our drug development programs.

Even if our medicines are successful in preclinical and human clinical studies, the medicines may not be successful in late-stage clinical studies.

Successful results in preclinical or initial human clinical studies, including the Phase 2 results for some of our medicines in development, may not predict the results of subsequent clinical studies. If any of our medicines in Phase 3 clinical studies, including the studies of QALSODY, bepirovirsen, donidalorsen, eplontersen, IONIS-FB-L_{Rx}, olezarsen, pelacarsen, ulefnersen and zilganersen, do not show sufficient efficacy in patients with the targeted indication, or if such studies are discontinued for any other reason, it could negatively impact our development and commercialization goals for these medicines and our stock price could decline.

In the past, we have invested in clinical studies of medicines that have not met the primary clinical endpoints in their Phase 3 studies or have been discontinued for other reasons. For example, in October 2021, Biogen reported that QALSODY did not meet the primary clinical endpoint in the Phase 3 VALOR study; however, trends favoring QALSODY were seen across multiple secondary and exploratory measures of disease activity and clinical function. In addition, in March 2021, Roche decided to discontinue dosing in the Phase 3 GENERATION HD1 study of tominersen in patients with manifest Huntington's disease based on the results of a pre-planned review of data from the Phase 3 study conducted by an unblinded Independent Data Monitoring Committee. Similar results could occur in clinical studies for our other medicines, including the studies of QALSODY, bepirovirsen, donidalorsen, eplontersen, IONIS-FB-L_{Rx}, olezarsen, pelacarsen, ulefnersen and zilganersen.

There are a number of factors that could cause a clinical study to fail or be delayed, including:

- the clinical study may produce negative or inconclusive results;
- regulators may require that we hold, suspend or terminate clinical research for noncompliance with regulatory requirements;
- we, our partners, the FDA or foreign regulatory authorities could suspend or terminate a clinical study due to adverse side effects of a medicine on subjects or lack of efficacy in the trial;
- we or our partners may decide, or regulators may require us, to conduct additional preclinical testing or clinical studies;
- enrollment in our clinical studies may be slower than we anticipate;
- we or our partners, including our independent clinical investigators, contract research organizations and other third-party service providers on which we rely, may not identify, recruit and train suitable clinical investigators at a sufficient number of study sites or timely enroll a sufficient number of study subjects in the clinical study;
- the institutional review board for a prospective site might withhold or delay its approval for the study;
- people who enroll in the clinical study may later drop out due to adverse events, a perception they are not benefiting from participating in the study, fatigue with the clinical study process or personal issues;
- a clinical study site may deviate from the protocol for the study;
- the cost of our clinical studies may be greater than we anticipate;
- our partners may decide not to exercise any existing options to license and conduct additional clinical studies for our medicines; and
- the supply or quality of our medicines or other materials necessary to conduct our clinical studies may be insufficient, inadequate or delayed.

The COVID-19 pandemic could make some of these factors more likely to occur.

In addition, our current medicines, including QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen are chemically similar to each other. As a result, a safety observation we encounter with one of our medicines could have, or be perceived by a regulatory authority to have, an impact on a different medicine we are developing. This could cause the FDA or other regulators to ask questions or take actions that could harm or delay our ability to develop and commercialize our medicines or increase our costs. For example, the FDA or other regulatory agencies could request, among other things, additional information or commitments before we can start or continue a clinical study, protocol amendments, increased safety monitoring, additional product labeling information, and post-approval commitments. This happened in connection with the conditional marketing approval for WAYLIVRA in the EU, as the EC is requiring us to conduct a post-authorization safety study to evaluate the safety of WAYLIVRA on thrombocytopenia and bleeding in FCS patients taking WAYLIVRA. We have ongoing post-marketing studies for WAYLIVRA and TEGSEDI and an EAP for WAYLIVRA. Adverse events or results from these studies or the EAPs could negatively impact our pending or future marketing approval applications for WAYLIVRA and TEGSEDI in patients with FCS or ATTRv-PN, respectively, or the commercial opportunity for WAYLIVRA or TEGSEDI.

Any failure or delay in our clinical studies, including the studies of QALSODY, bepirovirsen, donidalorsen, eplontersen, IONIS-FB-$L_{Rx,}$ olezarsen, pelacarsen, ulefnersen and zilganersen, could reduce the commercial potential or viability of our medicines.

We depend on third parties to conduct clinical studies for our medicines and any failure of those parties to fulfill their obligations could adversely affect our development and commercialization plans.

We depend on independent clinical investigators, contract research organizations and other third-party service providers to conduct our clinical studies for our medicines and expect to continue to do so in the future. For example, we use clinical research organizations, such as Icon Clinical Research Limited, Medpace, Inc., Parexel International Corporation, Syneos Health, Inc. and Thermo Fisher Scientific Inc. for the clinical studies for our medicines, including donidalorsen, eplontersen, olezarsen, ulefnersen and zilganersen. We rely heavily on these parties for successful execution of our clinical studies, but do not control many aspects of their activities. For example, the investigators are not our employees, but we are responsible for ensuring that such investigators conduct each of our clinical studies in accordance with the general investigational plan and approved protocols for the study. Third parties may not complete activities on schedule or may not conduct our clinical studies in accordance with regulatory requirements or our stated protocols. For example, some of our key vendors are experiencing labor shortages, which could impact their ability to perform services for us for certain of our clinical trials. The failure of these third parties to carry out their obligations, including as a result of delays or disruptions caused by the COVID-19 pandemic, or a termination of our relationship with such third parties, could delay or prevent the development, marketing authorization and commercialization of our medicines or additional marketing authorizations for TEGSEDI and WAYLIVRA.

In addition, while we do not have any clinical trial sites in Ukraine or Gaza, we do have a limited number of clinical trial sites in Russia and Israel that may be materially impacted by the ongoing war between Russia and Ukraine and recent war between Israel and Hamas, respectively, and could result in difficulties enrolling or completing our clinical trials in such areas on schedule. Furthermore, the U.S. and its European allies have imposed significant sanctions against Russia, including regional embargoes, full blocking sanctions, and other restrictions targeting major Russian financial institutions. The U.S. government has also indicated it will consider imposing additional sanctions and other similar measures in the future. Our ability to conduct clinical trials in Russia may become restricted under applicable sanctions laws, which would require us to identify alternative trial sites, and could increase our costs and delay the clinical development of certain of our medicines.

Since corporate partnering is a significant part of our strategy to fund the advancement and commercialization of our development programs, if any of our collaborative partners fail to fund our collaborative programs, or if we cannot obtain additional partners, we may have to delay or stop progress on our drug development programs.

To date, corporate partnering has played a significant role in our strategy to fund our development programs and to add key development resources. We plan to continue to rely on additional collaborative arrangements to develop and commercialize some of our unpartnered medicines. However, we may not be able to negotiate favorable collaborative arrangements for these drug programs. If we cannot continue to secure additional collaborative partners, our revenues could decrease and the development of our medicines could suffer.

Our corporate partners are developing and funding many of the medicines in our development pipeline. For example, we are relying on:

- AstraZeneca for the joint development and funding of eplontersen;
- Novartis for development and funding of pelacarsen;
- GSK for development and funding of bepirovirsen; and
- Roche for development and funding of IONIS-FB-L_{Rx}.

If any of these pharmaceutical companies stops developing and funding these medicines, our business could suffer and we may not have, or be willing to dedicate, the resources available to develop these medicines on our own. Our collaborators can terminate their relationships with us under certain circumstances, many of which are outside of our control. For example, in 2022, Pfizer and Bayer decided to discontinue the clinical development programs for vupanorsen and fesomersen, respectively.

Even with funding from corporate partners, if our partners do not effectively perform their obligations under our agreements with them, it would delay or stop the progress of our drug development and commercial programs.

In addition to receiving funding, we enter into collaborative arrangements with third parties to:

- conduct clinical studies;
- seek and obtain marketing authorizations; and
- manufacture and commercialize our medicines.

Once we have secured a collaborative arrangement to further develop and commercialize one of our drug development programs, such as our collaborations with AstraZeneca, Biogen, GSK, Novartis and Roche, these collaborations may not continue or result in commercialized medicines, or may not progress as quickly as we anticipated.

For example, a collaborator such as AstraZeneca, Biogen, GSK, Novartis or Roche, could determine that it is in its financial interest to:

- pursue alternative technologies or develop alternative products that may be competitive with the medicine that is part of the collaboration with us;
- pursue higher-priority programs or change the focus of its own development programs; or
- choose to devote fewer resources to our medicines than it does to its own medicines.

If any of these occur, it could affect our partner’s commitment to the collaboration with us and could delay or otherwise negatively affect the commercialization of our medicines, including QALSODY, SPINRAZA, bepirovirsen, eplontersen, IONIS-FB-L_{Rx} and pelacarsen.

We may not be able to benefit from orphan drug designation for our medicines.

In the U.S., under the Orphan Drug Act, the FDA may designate a medicine as an orphan drug if it is intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the U.S. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process, but it can provide financial incentives, such as tax advantages and user-fee waivers, as well as longer regulatory exclusivity periods. The FDA has granted orphan drug designation to donidalorsen for the treatment of patients with HAE, to ulefnersen for the treatment of patients with FUS-ALS, to ION582 for the treatment of patients with Angelman syndrome and to ION356 for the treatment of patients with Pelizaeus-Merzbacher disease. The FDA and EMA have granted orphan drug designation to eplontersen for the treatment of patients with ATTR, to TEGSEDI for the treatment of patients with ATTRv-PN, to WAYLIVRA for the treatment of patients with FCS, and to tominersen for the treatment of patients with HD. In addition, the EMA has granted orphan drug designation to WAYLIVRA for the treatment of patients with FPL. Even if approval is obtained on a medicine that has been designated as an orphan drug, we may lose orphan drug exclusivity if the FDA or EMA determines that the request for designation was materially defective or if we cannot assure sufficient quantity of the applicable medicine to meet the needs of patients with the rare disease or condition, or if a competitor is able to gain approval for the same medicine in a safer or more effective form or that makes a major contribution to patient care. If we lose orphan drug exclusivity on any of our medicines, we may face increased competition and lose market share for such medicine.

Risks Associated with our Businesses as a Whole

Risks related to our financial condition

If we fail to obtain timely funding, we may need to curtail or abandon some of our programs.

Many of our medicines are undergoing clinical studies or are in the early stages of research and development. Most of our programs will require significant additional research, development, manufacturing, preclinical and clinical testing, marketing authorizations, preclinical activities and commitment of significant additional resources prior to their successful commercialization. In addition, as we commercialize more medicines on our own, we will need to invest significant financial resources to continue developing the infrastructure required to successfully commercialize our medicines, including the build-out of a new manufacturing facility. All of these activities will require significant cash. As of September 30, 2023, we had cash, cash equivalents and short-term investments equal to $2.2 billion. If we or our partners do not meet our goals to successfully commercialize our medicines, including QALSODY, SPINRAZA, TEGSEDI and WAYLIVRA, or to license certain medicines and proprietary technologies, we will need additional funding in the future. Our future capital requirements will depend on many factors such as:

- successful commercialization of QALSODY, SPINRAZA, TEGSEDI and WAYLIVRA;
- the profile and launch timing of our medicines, including bepirovirsen, donidalorsen, eplontersen, IONIS-FB-$L_{Rx,}$ olezarsen, pelacarsen, ulefnersen and zilganersen;
- changes in existing collaborative relationships and our ability to establish and maintain additional collaborative arrangements;
- continued scientific progress in our research, drug discovery and development programs;
- the size of our programs and progress with preclinical and clinical studies;
- the time and costs involved in obtaining marketing authorizations;
- competing technological and market developments, including the introduction by others of new therapies that address our markets; and
- our manufacturing requirements and capacity to fulfill such requirements.

If we need additional funds, we may need to raise them through public or private financing. Additional financing may not be available on acceptable terms or at all. If we raise additional funds by issuing equity securities, the shares of existing stockholders will be diluted and the price, as well as the price of our other securities, may decline. If adequate funds are not available or not available on acceptable terms, we may have to cut back on one or more of our research, drug discovery or development programs. Alternatively, we may obtain funds through arrangements with collaborative partners or others, which could require us to give up rights to certain of our technologies or medicines.

We have incurred losses, and our business will suffer if we fail to consistently achieve profitability in the future.

Because drug discovery and development require substantial lead-time and money prior to commercialization, our expenses have generally exceeded our revenue since we were founded in January 1989. As of September 30, 2023, we had an accumulated deficit of approximately $1.8 billion and stockholders' equity of approximately $0.3 billion. Most of our historical losses resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations. Most of our income has historically come from collaborative arrangements, including commercial revenue from royalties and R&D revenue, with additional income from research grants and the sale or licensing of our patents, as well as interest income. We will now and continuing into the foreseeable future need to invest significant financial resources to develop capabilities to commercialize medicines on our own and expect that our income in the future will be driven primarily by commercial sales. If we do not earn substantial revenue from commercial sales, we may incur additional operating losses in the future, which could restrict our ability to successfully develop additional medicines or sustain future profitability.

We may not be entitled to obtain additional milestone payments under our royalty monetization agreement with Royalty Pharma.

In January 2023, we entered into a Royalty Purchase Agreement with Royalty Pharma Investments. In addition to the $500 million we received at closing, this agreement makes available to us up to an additional $625 million in milestone payments. However, these additional milestone payments are subject to satisfaction of certain conditions related to the regulatory approval or commercial sales of pelacarsen, in certain cases by specific deadlines. Should we not satisfy such conditions by the applicable deadlines, or if we fail to meet our obligations or default under this agreement, the actual amount of additional payments to us could be substantially less than the maximum amounts available thereunder.

Risks related to our intellectual property

If we cannot protect our patent rights or our other proprietary rights, others may compete more effectively against us.

Our success depends to a significant degree upon whether we can continue to develop, secure and maintain intellectual property rights to proprietary products and services. However, we may not receive issued patents on any of our pending patent applications in the U.S. or in other countries and we may not be able to obtain, maintain or enforce our patents and other intellectual property rights, any of which could impact our ability to compete effectively. In addition, the scope of any of our issued patents may not be sufficiently broad to provide us with a competitive advantage. Furthermore, other parties may successfully challenge, invalidate or circumvent our issued patents or patents licensed to us so that our patent rights do not create an effective competitive barrier or revenue source.

We cannot be certain that the U.S. Patent and Trademark Office, or U.S. PTO, and courts in the U.S. or the patent offices and courts in foreign countries will consider the claims in our patents and applications covering QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA and eplontersen, or any of our medicines in development as patentable. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products off-label. Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent, even through legal action.

If we or any licensor partner loses or cannot obtain patent protection for QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA or eplontersen, or any of our medicines in development, it could have a material adverse impact on our business.

Intellectual property litigation could be expensive and prevent us from pursuing our programs.

From time to time, we have to defend our intellectual property rights. If we are involved in an intellectual property dispute, we may need to litigate to defend our rights or assert them against others. Disputes can involve arbitration, litigation or proceedings declared by the U.S. PTO or the International Trade Commission or foreign patent authorities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

If a third party claims that our medicines or technology infringe its patents or other intellectual property rights, we may have to discontinue an important product or product line, alter our products and processes, pay license fees or cease certain activities. We may not be able to obtain a license to needed intellectual property on favorable terms, if at all. There are many patents issued or applied for in the biotechnology industry, and we may not be aware of patents or patent applications held by others that relate to our business. This is especially true since patent applications in the U.S. are filed confidentially for the first 18 months. Moreover, the validity and breadth of biotechnology patents involve complex legal and factual questions for which important legal issues remain.

Risks related to product liability

We are exposed to potential product liability claims, and insurance against these claims may not be available to us at a reasonable rate in the future or at all.

Our business exposes us to potential product liability risks that are inherent in the testing, manufacturing, marketing and sale of therapeutic products, including potential product liability claims related to QALSODY, SPINRAZA, TEGSEDI and WAYLIVRA, and our medicines in development. We have clinical study insurance coverage and commercial product liability insurance coverage. However, this insurance coverage may not be adequate to cover claims against us, or be available to us at an acceptable cost, if at all. Regardless of their merit or eventual outcome, product liability claims may result in decreased demand for our medicines, injury to our reputation, withdrawal of clinical study volunteers and loss of revenues. Thus, whether or not we are insured, a product liability claim or product recall may result in losses that could be material.

Risks related to our personnel

The loss of key personnel, or the inability to attract and retain highly skilled personnel, could make it more difficult to run our business and reduce our likelihood of success.

We are dependent on the principal members of our management and scientific staff, and as we move towards commercializing medicines on our own, we will become increasingly dependent on the principal members of our commercial team. We do not have employment agreements with any of our employees that would prevent them from leaving us. The loss of our management, key scientific or commercial employees might slow the achievement of important research and development or commercial goals. It is also critical to our success that we recruit and retain qualified scientific personnel to perform research and development work and that we recruit and retain qualified marketing, sales, market access, distribution, and related personnel to commercialize our medicines. We may not be able to attract and retain skilled and experienced personnel on acceptable terms because of intense competition for experienced personnel among many pharmaceutical and health care companies, universities and non-profit research institutions. In addition, failure to succeed in clinical studies may make it more challenging to recruit and retain qualified personnel.

Risks related to the COVID-19 pandemic and other events

Our business may be adversely affected by pandemics, climate change, extreme weather events, earthquakes, war, civil or political unrest, terrorism or other catastrophic events.

Our business could be adversely affected by health epidemics in regions where we or our partners are commercializing our medicines, have concentrations of clinical trial sites or other business operations, and could cause disruption in the operations of third-party manufacturers and contract research organizations upon whom we rely. For example, some physician and hospital policies that were put in place as a result of the COVID-19 pandemic restricted in-person access by third parties, which in some cases impacted our commercialization efforts for TEGSEDI and WAYLIVRA. In addition, in December 2021, Novartis announced that enrollment for the Phase 3 HORIZON study had been delayed due to the COVID-19 pandemic. The COVID-19 pandemic continues to evolve, and while we believe we have not experienced material adverse effects to our business as a result of the COVID-19 pandemic, the ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain.

In recent years, extreme weather events and changing weather patterns have become more common. As a result, we are potentially exposed to varying natural disaster or extreme weather risks such as hurricanes, tornadoes, fires, droughts, floods, or other events that may result from the impact of climate change on the environment. The potential impacts of climate change may also include increased operating costs associated with additional regulatory requirements and investments in reducing energy, water use and greenhouse gas emissions. In addition, we currently manufacture most of our research and clinical supplies in a manufacturing facility located in Carlsbad, California. We manufacture the finished drug product for TEGSEDI and WAYLIVRA at third-party contract manufacturers. Biogen manufactures the finished drug product for SPINRAZA and QALSODY. The facilities and the equipment we, our partners and our contract manufacturers use to research, develop and manufacture our medicines would be costly to replace and could require substantial lead time to repair or replace. Our facilities or those of our partners or contract manufacturers may be harmed by natural disasters or other events outside our control, such as earthquakes, war, civil or political unrest, deliberate acts of sabotage, terrorism or industrial accidents such as fire and explosion, whether due to human or equipment error, and if such facilities are affected by a disaster or other event, our development and commercialization efforts would be delayed. Although we possess property damage and business interruption insurance coverage, this insurance may not be sufficient to cover all of our potential losses and may not continue to be available to us on acceptable terms, or at all. In addition, our development and commercialization activities could be harmed or delayed by a shutdown of the U.S. government, including the FDA.

Risks related to cybersecurity

We are dependent on information technology systems, infrastructure and data, which exposes us to data security risks.

We are dependent upon our own and third-party information technology systems, infrastructure and data, including mobile technologies, to operate our business. The multitude and complexity of our computer systems may make them vulnerable to service interruption or destruction, disruption of data integrity, malicious intrusion, or random attacks. Likewise, data privacy or security incidents or breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, customers or other business partners may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity, with third-party phishing and social engineering attacks in particular increasing during the COVID-19 pandemic. In addition, the number and frequency of cybersecurity events globally may be heightened during times of geopolitical tension or instability between countries, including, for example, the ongoing war between Russia and Ukraine, as a result of which several companies (not including us) have reported recent cybersecurity events.

Cyber-attacks could include the deployment of harmful malware, denial-of-service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our business partners face similar risks and any security breach of their systems could adversely affect our security posture. A security breach or privacy violation that leads to disclosure or modification of or prevents access to patient information, including personally identifiable information or protected health information, could harm our reputation, compel us to comply with federal and state breach notification laws and foreign law equivalents, subject us to financial penalties and mandatory and costly corrective action, require us to verify the correctness of database contents and otherwise subject us to litigation or other liability under laws and regulations that protect personal data, any of which could disrupt our business and result in increased costs or loss of revenue. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, our efforts may not prevent service interruptions or identify breaches in our systems that could adversely affect our business and operations and result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us.

Risks related to our securities and the global credit markets

If we do not progress in our programs as anticipated, the price of our securities could decrease.

For planning purposes, we estimate and may disclose the timing of a variety of clinical, regulatory and other milestones, such as when we anticipate a certain medicine will enter clinical trials, when we anticipate completing a clinical study, or when we anticipate filing an application for, or obtaining, marketing authorization, or when we or our partners plan to commercially launch a medicine. We base our estimates on present facts and a variety of assumptions, many of which are outside of our control, including the impacts of the COVID-19 pandemic. If we do not achieve milestones in accordance with our or our investors' or securities analysts' expectations, including milestones related to QALSODY, SPINRAZA, TEGSEDI, WAYLIVRA, bepirovirsen, donidalorsen, eplontersen, IONIS-FB-$L_{Rx,}$ olezarsen, pelacarsen, ulefnersen and zilganersen, the price of our securities could decrease.

If the price of our securities continues to be highly volatile, this could make it harder to liquidate your investment and could increase your risk of suffering a loss.

The market price of our common stock, like that of the securities of many other biopharmaceutical companies, has been and is likely to continue to be highly volatile. These fluctuations in our common stock price may significantly affect the trading price of our securities. During the 12 months preceding September 30, 2023, the market price of our common stock ranged from $47.74 to $32.69 per share. Many factors can affect the market price of our securities, including, for example, fluctuations in our operating results, announcements of collaborations, clinical study results, technological innovations or new products being developed by us or our competitors, the commercial success of our approved medicines, governmental regulation, marketing authorizations, changes in payers' reimbursement policies, developments in patent or other proprietary rights and public concern regarding the safety of our medicines.

Broad market factors may materially harm the market price of our common stock irrespective of our operating performance. For example, the COVID-19 pandemic, the ongoing war between Russia and Ukraine and measures taken in response thereto, the recent war between Israel and Hamas and the failure of Silicon Valley Bank have caused disruptions of global financial markets and resulted in increased volatility in the trading price of our common stock. In addition, industry factors may materially harm the market price of our common stock. Nasdaq, and the market for biotechnology companies in particular, have historically experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the particular companies affected. The trading prices and valuations of these stocks, and of ours, may not be predictable. A loss of investor confidence in the market for biotechnology or pharmaceutical stocks or the stocks of other companies that investors perceive to be similar to us, the opportunities in the biotechnology and pharmaceutical market or the stock market in general, could depress our stock price regardless of our business, prospects, financial conditions or results of operations.

Provisions in our certificate of incorporation, convertible notes documents, call spread hedge transaction documents and Delaware law may prevent stockholders from receiving a premium for their shares.*

Our certificate of incorporation provides for classified terms for the members of our board of directors. Our certificate also includes a provision that requires at least 66 2/3 percent of our voting stockholders to approve a merger or certain other business transactions with, or proposed by, any holder of 15 percent or more of our voting stock, except in cases where certain directors approve the transaction or certain minimum price criteria and other procedural requirements are met.

Our certificate of incorporation also requires that any action required or permitted to be taken by our stockholders must be taken at a duly called annual or special meeting of stockholders and may not be taken by written consent. In addition, only our board of directors, chairperson of the board or chief executive officer can call special meetings of our stockholders. We have in the past, and may in the future, implement a stockholders' rights plan, also called a poison pill, which could make it uneconomical for a third party to acquire our company on a hostile basis. In addition, our board of directors has the authority to fix the rights and preferences of, and issue shares of preferred stock, which may have the effect of delaying or preventing a change in control of our company without action by our stockholders.

The provisions of our convertible senior notes could make it more difficult or more expensive for a third party to acquire us. Upon the occurrence of certain transactions constituting a fundamental change, holders of the notes will have the right, at their option, to require us to repurchase all of their notes or a portion of their notes, which may discourage certain types of transactions in which our stockholders might otherwise receive a premium for their shares over the then-current market prices.

In June 2023, we completed a $575 million offering of 1.75% Notes and used a portion of the net proceeds from the issuance of the 1.75% Notes to repurchase $434.1 million of our 0.125% Notes for $420.4 million. In the third quarter of 2023, we repurchased an additional $70.3 million of our 0.125% Notes for $67.8 million. In April 2021, we completed a $632.5 million offering of 0% Notes and used a portion of the net proceeds from the issuance of the 0% Notes to repurchase $247.9 million of our 1% Notes for $257.0 million. In December 2019, we entered into privately negotiated exchange and/or subscription agreements with certain new investors and certain holders of our existing 1% Notes to exchange $375.6 million of our 1% Notes for $439.3 million of our 0.125% Notes, and to issue $109.5 million of our 0.125% Notes. Additionally, in connection with the pricing of our 0% Notes and 0.125% Notes, we entered into call spread transactions in which we purchased note hedges and sold warrants. Terminating or unwinding the call spread transactions could require us to make substantial payments to the counterparties under those agreements or may increase our stock price. The costs or any increase in stock price that may arise from terminating or unwinding such agreements could make an acquisition of our company significantly more expensive to the purchaser.

These provisions, as well as Delaware law, including Section 203 of the Delaware General Corporation Law, and other of our agreements, may discourage certain types of transactions in which our stockholders might otherwise receive a premium for their shares over then-current market prices, and may limit the ability of our stockholders to approve transactions that they think may be in their best interests.

Future sales of our common stock in the public market could adversely affect the trading price of our securities.

Future sales of substantial amounts of our common stock in the public market, or the perception that such sales could occur, could adversely affect trading prices of our securities. For example, we may issue approximately 22.2 million shares of our common stock upon conversion of our 1.75% Notes, 0% Notes and 0.125% Notes, up to 10.9 million shares in connection with the warrant transactions we entered into in connection with the issuance of our 0% Notes, and up to 6.6 million shares in connection with the warrant transactions we entered into in connection with the issuance of our 0.125% Notes, in each case subject to customary anti-dilution adjustments. The addition of any of these shares into the public market may have an adverse effect on the price of our securities.

In addition, pursuant to the call spread transactions we entered into in connection with the pricing of our 0% Notes and 0.125% Notes, the counterparties are likely to modify their hedge positions from time to time at or prior to the conversion or maturity of the notes by purchasing and selling shares of our common stock, other of our securities, or other instruments, including over-the-counter derivative instruments, that they may wish to use in connection with such hedging, which may have a negative effect on the conversion value of those notes and an adverse impact on the trading price of our common stock. The call spread transactions are expected generally to reduce potential dilution to holders of our common stock upon any conversion of our 0% Notes or 0.125% Notes or offset any cash payments we are required to make in excess of the principal amount of the converted 0% Notes or 0.125% Notes, as the case may be. However, the warrant transactions could separately have a dilutive effect to the extent that the market value per share of our common stock exceeds the applicable strike price of the warrants.

Negative conditions in the global credit markets and financial services and other industries may adversely affect our business, financial condition or stock price.*

The global credit and financial markets have experienced extreme volatility and disruptions recently, including as a result of the ongoing COVID-19 pandemic, war between Russia and Ukraine and measures taken in response thereto, and the failure of Silicon Valley Bank. The recent war between Israel and Hamas may also create volatility and disruptions in the global credit markets. These disruptions can result in severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our operations, growth plans, financial performance or stock price. In addition, our insurance carriers and insurance policies covering all aspects of our business may become financially unstable or may not be sufficient to cover any or all of our losses and may not continue to be available to us on acceptable terms, or at all. Furthermore, due to the rapidly rising inflation rate, we may experience significantly increased costs of goods and services for our business.

A variety of risks associated with operating our business and marketing our medicines internationally could adversely affect our business. In addition to our U.S. operations, we are commercializing TEGSEDI in the EU, Canada, Latin America and certain Caribbean countries, and WAYLIVRA in the EU, Latin America and certain Caribbean countries. We face risks associated with our international operations, including possible unfavorable regulatory, pricing and reimbursement, political, tax and labor conditions, which could harm our business. Because we have international operations, we are subject to numerous risks associated with international business activities, including:

- compliance with differing or unexpected regulatory requirements for our medicines and foreign employees;
- complexities associated with managing multiple payer reimbursement regimes, government payers or patient self-pay systems;
- difficulties in staffing and managing foreign operations;
- in certain circumstances, increased dependence on the commercialization efforts and regulatory compliance of third-party distributors or strategic partners;
- foreign government taxes, regulations and permit requirements;
- U.S. and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements;
- anti-corruption laws, including the Foreign Corrupt Practices Act, or the FCPA, and its equivalent in foreign jurisdictions;
- economic weakness, including inflation, natural disasters, war, events of terrorism, political instability or public health issues or pandemics, such as the COVID-19 pandemic, in particular foreign countries or globally;
- fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenue, and other obligations related to doing business in another country;
- compliance with tax, employment, privacy, immigration and labor laws, regulations and restrictions for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.; and
- changes in diplomatic and trade relationships.

Our business activities outside of the U.S. are subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the United Kingdom's Bribery Act 2010. In many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, any dealings with these prescribers and purchasers may be subject to regulation under the FCPA. There is no certainty that all employees and third-party business partners (including our distributors, wholesalers, agents, contractors and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of manufacturers and other third-party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have an adverse impact on our business and financial condition.

Risks related to compliance with laws

Our operations are subject to additional healthcare laws.

Our operations are subject to additional healthcare laws, including federal and state anti-kickback laws, false claims laws, transparency laws, such as the federal Sunshine Act, and health information privacy and security laws, which are subject to change at any time. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Penalties for violations of applicable healthcare laws and regulations may include significant civil, criminal and administrative penalties, damages, disgorgement, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and additional reporting requirements and oversight if we enter into a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws. In addition, violations may also result in reputational harm, diminished profits and future earnings.

Because we use biological materials, hazardous materials, chemicals and radioactive compounds, if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research, development and manufacturing activities involve the use of potentially harmful biological materials as well as materials, chemicals and various radioactive compounds that could be hazardous to human health and safety or the environment. We store most of these materials and various wastes resulting from their use at our facilities in Carlsbad, California pending ultimate use and disposal. We cannot completely eliminate the risk of contamination, which could cause:

- interruption of our research, development and manufacturing efforts;
- injury to our employees and others;
- environmental damage resulting in costly clean up; and
- liabilities under federal, state and local laws and regulations governing health and human safety, as well as the use, storage, handling and disposal of these materials and resultant waste products.

In such an event, we may be held liable for any resulting damages, and any liability could exceed our resources. Although we carry insurance for pollution liability in amounts and types that we consider commercially reasonable, the coverage or coverage limits of our insurance policies may not be adequate. If our losses exceed our insurance coverage, our financial condition would be adversely affected.

Our business is subject to changing regulations for corporate governance and public disclosure that has increased both our costs and the risk of noncompliance.

Each year we are required to evaluate our internal control systems to allow management to report on and our Independent Registered Public Accounting Firm to attest to, our internal controls as required by Section 404 of the Sarbanes-Oxley Act. As a result, we continue to incur additional expenses and divert our management's time to comply with these regulations. In addition, if we cannot continue to comply with the requirements of Section 404 in a timely manner, we might be subject to sanctions or investigation by regulatory authorities, such as the SEC, the Public Company Accounting Oversight Board, or PCAOB, or The Nasdaq Global Select Market. Any such action could adversely affect our financial results and the market price of our common stock.

The SEC and other regulators have continued to adopt new rules and regulations and make additional changes to existing regulations that require our compliance. In July 2010, the Dodd-Frank Wall Street Reform and Protection Act, or the Dodd-Frank Act, was enacted, and in August 2022, the SEC adopted additional rules and regulations under the Dodd-Frank Act related to "say on pay" and proxy access. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which has and may in the future lead to additional compliance costs and impact the manner in which we operate our business.

Risks related to taxes

Our ability to use our net operating loss carryovers and certain other tax attributes may be limited.

Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under the Code, we can carry forward our NOLs to offset our future taxable income, if any, until such NOLs are used or expire. The same is true of other unused tax attributes, such as tax credits.

Under the current U.S. federal income tax law, U.S. federal NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such U.S. federal NOLs is limited to 80 percent of taxable income. It is uncertain if and to what extent various states will conform to current U.S. federal income tax law, and there may be periods during which states suspend or otherwise limit the use of NOLs for state income tax purposes.

In addition, under Sections 382 and 383 of the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage-point cumulative change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our NOL carryforwards or other tax attributes is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. As a result of the Akcea Merger, we are subject to the separate return limitation year, or SRLY, rules. Under the SRLY rules, our utilization of Akcea's pre-merger NOL and tax credit carryforwards is limited to the amount of income that Akcea contributes to our consolidated taxable income. The Akcea pre-merger tax attributes cannot be used to offset any of the income that Ionis contributes to our consolidated taxable income. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Our future taxable income could be impacted by changes in tax laws, regulations and treaties.

A change in tax laws, treaties or regulations, or their interpretation, of any country in which we operate could materially affect us.

We could be subject to additional tax liabilities.

We are subject to U.S. federal, state, local and foreign income taxes, sales taxes in the U.S., withholding taxes and transaction taxes in foreign jurisdictions. Significant judgment is required in evaluating our tax positions and our worldwide provision for taxes. During the ordinary course of business, there are many activities and transactions for which the ultimate tax determination is uncertain. In addition, our tax obligations and effective tax rates could be adversely affected by changes in the relevant tax, accounting and other laws, regulations, principles and interpretations, including those relating to income tax nexus, by recognizing tax losses or lower than anticipated earnings in jurisdictions where we have lower statutory rates and higher than anticipated earnings in jurisdictions where we have higher statutory rates, by changes in foreign currency exchange rates, or by changes in the valuation of our deferred tax assets and liabilities. We may be audited in various jurisdictions, and such jurisdictions may assess additional taxes, sales taxes and value-added taxes against us. Although we believe our tax estimates are reasonable, the final determination of any tax audits or litigation could be materially different from our historical tax provisions and accruals, which could have a material adverse effect on our operating results or cash flows in the period for which a determination is made.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Not applicable.

ITEM 3. DEFAULT UPON SENIOR SECURITIES

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

Trading Plans

During the quarter ended September 30, 2023, our Section 16 officers and directors adopted or terminated contracts, instructions or written plans for the purchase or sale of our securities as noted in the table below.

* Contract, instruction or written plan intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Exchange Act.
** "Non-Rule 10b5-1 trading arrangement" as defined in item 408(c) of Regulation S-K under the Exchange Act.

			Trading Arrangement			
	Action	Date	Rule 10b5-1*	Non-Rule 10b5-1**	Total Shares to Be Sold	Expiration Date
Brett Monia, CEO and Board Member	Termination	July 12, 2023	X		30,023	Upon the execution of all instructions provided in the plan
Brett Monia, CEO and Board Member	Adoption	July 13, 2023	X		54,442	Upon the execution of all instructions provided in the plan
Eric Swayze, EVP, Research	Adoption	July 13, 2023	X		85,614	Upon the execution of all instructions provided in the plan
Spencer Berthelsen, Board Member	Adoption	September 7, 2023	X		16,000	Upon the execution of all instructions provided in the plan
B. Lynne Parshall, Board Member	Adoption	September 27, 2023	X		122,638	Upon the execution of all instructions provided in the plan

ITEM 6. EXHIBITS

a. Exhibits

Exhibit Number	Description of Document
10.1	Collaboration and License Agreement by and between the Registrant and Novartis Pharma AG dated as of August 2, 2023. Portions of this exhibit have been omitted because they are both (i) not material and (ii) the type that the Registrant treats as private or confidential.
10.2	Amended and Restated Lease Agreement between the Registrant and Lots 21 & 22 Owner (DE) LLC dated as of August 21, 2023. Portions of this exhibit have been omitted because they are both (i) not material and (ii) the type that the Registrant treats as private or confidential.
10.3	Research, Development, and License Agreement by and among the Registrant, F. Hoffmann-La Roche Ltd., and Hoffmann-La Roche Inc. dated as of September 26, 2023. Portions of this exhibit have been omitted because they are both (i) not material and (ii) the type that the Registrant treats as private or confidential.
31.1	Certification by Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended.
31.2	Certification by Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended.
32.1*	Certification Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial statements from the Ionis Pharmaceuticals, Inc. Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, formatted in Inline Extensible Business Reporting Language (iXBRL): (i) condensed consolidated balance sheets, (ii) condensed consolidated statements of operations, (iii) condensed consolidated statements of comprehensive income (loss), (iv) condensed consolidated statements of stockholders' equity, (v) condensed consolidated statements of cash flows and (vi) notes to condensed consolidated financial statements (detail tagged).
104	Cover Page Interactive Data File (formatted in iXBRL and included in exhibit 101).

* This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signatures	Title	Date
/s/ BRETT P. MONIA Brett P. Monia, Ph.D.	Director and Chief Executive Officer (Principal executive officer)	November 2, 2023
/s/ ELIZABETH L. HOUGEN Elizabeth L. Hougen	Executive Vice President, Finance and Chief Financial Officer (Principal financial and accounting officer)	November 2, 2023

EXECUTION VERSION

Exhibit 10.1

Certain portions of this exhibit, marked by [***], have been excluded because they are both not material and are the type that the registrant treats as private or confidential.

COLLABORATION AND LICENSE AGREEMENT

BETWEEN

IONIS PHARMACEUTICALS, INC.

AND

NOVARTIS PHARMA AG

COLLABORATION AND LICENSE AGREEMENT

This COLLABORATION AND LICENSE AGREEMENT (the "***Agreement***") is entered into as of August 2, 2023 (the "***Execution Date***") by and between **Ionis Pharmaceuticals, Inc.**, a Delaware corporation, having its principal place of business at 2855 Gazelle Court, Carlsbad CA 92010 USA ("***Ionis***"), and **Novartis Pharma AG**, a company organized under the laws of Switzerland, having its principal place of business at Lichtstrasse 35, CH-4056 Basel, Switzerland ("***Novartis***"). Novartis and Ionis each may be referred to herein individually as a "***Party***" or collectively as the "***Parties***." Capitalized terms used in this Agreement, whether used in the singular or the plural, have the meaning set forth in Appendix 1. All attached appendices, schedules, and exhibits are a part of this Agreement.

RECITALS

WHEREAS, Ionis possesses certain Patent Rights, Know-How, technology and expertise with respect to RNA-targeted antisense drugs, and has novel and valuable capabilities for the research, discovery, identification, development and synthesis of antisense drugs;

WHEREAS, Novartis has expertise in globally researching, developing and commercializing human therapeutics and, in particular, cardio-metabolic lipid drugs;

WHEREAS, the Parties are interested in entering into a collaboration to discover and develop [***] products targeting the RNA encoding APO(a); and

WHEREAS, Novartis desires to receive from Ionis, and Ionis desires to grant to Novartis, an exclusive worldwide license under this Agreement to research, develop, manufacture, and commercialize the Licensed Products under the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the respective covenants, representations, warranties, and agreements set forth herein, the Parties hereto agree as follows:

ARTICLE 1
OVERVIEW

The Parties intend that under this Agreement: the Parties will (a) conduct a research collaboration pursuant to the Research Plan and, under the Research Plan, conduct Research to identify one or more Compounds using Oligonucleotide technology, which may include [***] chemistry, in each case, with the goal of achieving [***] and (b) designate one or more Development Candidates through the JRC and JSC. Following designation of a Development Candidate, as between the Parties, Novartis will be responsible for conducting IND-Enabling Toxicology Studies and all further Development activities for such Development Candidate, at Novartis' cost. Furthermore, following designation of the applicable Development Candidate, Novartis will have the right to Develop Licensed Products containing such Development Candidate under this Agreement and will be responsible for all Development and Commercialization activities for such Licensed Product, at Novartis' cost. The purpose of this Article 1 (Overview) is to provide a high-level overview of the roles and responsibilities and rights and obligations of each Party under this Agreement, and therefore this Article 1 (Overview) is not binding on either Party and is qualified in its entirety by the more detailed provisions of this Agreement set forth below.

ARTICLE 2
RESEARCH PROGRAM

2.1. Research Responsibilities and Research Plan.

2.1.1. **Research Plan**. Prior to the Execution Date, the Parties have agreed upon an initial research plan to identify one or more Development Candidates and to complete IND-Enabling Toxicology Studies for such Development Candidate(s), which initial research plan is attached hereto as SCHEDULE 2.1.1 (Research Plan) (such research plan, as it may be updated in accordance with the terms and conditions of this Agreement, the "***Research Plan***" and the activities to be performed by the Parties thereunder, the "***Research Activities***"). The initial Research Plan includes: (a) all Research and Development activities to be performed by each Party through Completion of IND-Enabling Toxicology Studies for the Development Candidates, (b) the criteria for considering one or more Compounds as Development Candidates set forth in Table 4 thereof (such criteria, the "***Development Candidate Criteria***"), (c) the allocation of responsibilities between the Parties (which allocation will be consistent with Section 2.1.2 (Allocation of Research Activities)) for all Research Activities, (d) the estimated timelines for all Research Activities, and (e) the initial toxicology and study designs for the Licensed Product.

2.1.2. **Allocation of Research Activities**. The Research Plan will include the allocation of responsibilities between the Parties for all Research Activities. Unless otherwise mutually agreed by the Parties and set forth in the Research Plan, the Research Plan will provide that: (a) Ionis will be primarily responsible for all Research Activities to identify the Compounds for the Development Candidate selection process pursuant to Section 2.2 (Development Candidate Selection Process) and (b) Novartis will be responsible for any IND-Enabling Toxicology Studies under the Research Plan.

2.1.3. **Updates to the Research Plan**. At least [***] during the Research Term, or upon either Party's request, the JRC will develop, discuss and determine whether to recommend to the JSC any updates to the Research Plan and the JSC will review, discuss, and determine whether to approve any such recommended updates to the Research Plan. Each such update to the Research Plan will become effective and will supersede the previous Research Plan upon approval thereof by the JSC.

2.2. Development Candidate Selection Process.

2.2.1. **Licensed Compounds; Proposed Development Candidates**. During the Research Term, as part of each Research Report to be submitted to the JRC, each Party will [***] by it as part of the Research Activities conducted by or on behalf of such Party during the most recently completed Calendar Quarter ([***] Compounds identified or evaluated under the Research Activities, collectively, the "***Compound Pool***" and each Compound in the Compound Pool, a "***Licensed Compound***"). In addition, at either Party's request no more than [***], the other Party will provide a reasonably detailed summary of available data with respect to all Licensed Compounds that have been identified or evaluated in [***] as part of the Research Activities conducted by such Party since the last such summary, including, to the extent available, information and data that is sufficiently detailed for the JRC to assess whether such Licensed Compounds satisfy the Development Candidate Criteria. For each Licensed Compound that a Party identifies or evaluates during the Research Term and reasonably believes satisfies the Development Candidate Criteria, such Party will, in addition to any Research Report required pursuant to Section 2.10.2 (Research Reports), submit a Development Candidate Data Package to the JRC for review and discussion in order to determine whether to recommend to the JSC that such Licensed Compound be designated by the JSC as a Development Candidate. If a Party reasonably believes that a Licensed Compound identified or evaluated by the other Party satisfies the Development Candidate Criteria but the evaluating Party did not provide a Development Candidate Data Package for such Licensed Compound, then, at such Party's request during the Research Term, the Party that identified or evaluated such Licensed Compound will submit a Development Candidate Data Package with the information and data that is already in such identifying or evaluating Party's possession to the JRC for review and discussion in order to determine whether to recommend to the JSC that such Licensed Compound be designated by the JSC as a Development Candidate. Any Licensed Compound recommended to the JSC by the JRC in accordance with this Section 2.2.1 (Development Candidate Data Packages) will be a "***Proposed Development Candidate***".

2.2.2. **Carryover Period**. If the JSC does not designate at least one Proposed Development Candidate as a Development Candidate during the Research Term, then for the period beginning upon the expiration of the Research Term and ending on the [***] such expiration (such period, the "***Carryover Period***"), [***] will have the right, but not the obligation, to conduct further Research with respect to the Licensed Compounds or any additional Compounds in order to identify potential Development Candidates pursuant to the terms of this Agreement. During the Carryover Period, if [***] identifies or evaluates a Compound (whether a Licensed Compound or a Compound that is first identified or evaluated after the end of the Research Term) that it reasonably believes satisfies the Development Candidate Criteria (each such Compound, a "***Carryover Candidate***"), then (a) if not already a Licensed Compound, such Carryover Candidate shall be considered a Licensed Compound and be included in the Compound Pool and (b) [***] shall provide to the JSC a Development Candidate Data Package for such Carryover Candidate for the JSC to review, discuss, and determine whether to designate such Carryover Candidate as a Development Candidate pursuant to Section 2.2.4 (Development Candidate Selection Process).

2.2.3. **Novartis Proposed Development Candidate**. At any time after [***] until [***], if Novartis reasonably believes that any Licensed Compound that was not a Proposed Development Candidate or a Carryover Candidate satisfies the Development Candidate Criteria (such Compound, a "***Novartis Proposed Development Candidate***"), then Novartis may provide to the JSC a Development Candidate Data Package for such Novartis Proposed Development Candidate for the JSC to review, discuss, and determine whether to designate such Novartis Proposed Development Candidate as a Development Candidate pursuant to Section 2.2.4 (Development Candidate Selection Process).

2.2.4. **Development Candidate Selection Process**.

(a) Upon the JRC's receipt of a Development Candidate Data Package for a Licensed Compound, the JRC will review and discuss such Development Candidate Data Package and determine whether to submit such Development Candidate Data Package to the JSC for the JSC to determine whether to designate the applicable Proposed Development Candidate as a Development Candidate.

(b) After the JSC's receipt of (i) a Development Candidate Data Package for a Proposed Development Candidate from the JRC, (ii) a Development Candidate Data Package for a Carryover Candidate [***] such Carryover Candidate, or (iii) a Development Candidate Data Package for a Novartis Proposed Development Candidate from Novartis, the JSC will review and discuss such Development Candidate Data Package and determine whether to designate such Proposed Development Candidate, Carryover Candidate, or Novartis Proposed Development Candidate as a Development Candidate.

(c) Upon the JSC's designation of any Proposed Development Candidate, Carryover Candidate, or Novartis Proposed Development Candidate as a Development Candidate pursuant to this Section 2.2.4 (Development Candidate Selection Process) and in accordance with Section 3.3 (Decision Making) (the date of such designation, the "***DC Selection Date***"), (i) Novartis shall make the payment under Section 7.2 (Payments for Development Activities), if [***] under Section 7.2 (Payments for Development Activities), and (ii) as between the Parties, Novartis will be responsible for further Research and Development, including initiating IND-Enabling Toxicology Studies, on such Development Candidate (in the case of a Proposed Development Candidate, in accordance with the Research Plan).

2.3. **Research Term**. The Parties' obligations to perform the Research Activities will commence on the Effective Date and continue until the earlier of (a) Completion of the IND-Enabling Toxicology Studies identified in the then-current Research Plan and (b) [***] (such period, the "***Research Term***"). At the end of the Research Term, unless otherwise agreed in writing by the Parties, neither Ionis nor Novartis will have an obligation to perform any additional Research Activities.

2.4. **Research Costs**. Except as otherwise agreed by the Parties, each Party will be responsible for all costs and expenses incurred by such Party in the performance of Research Activities allocated to such Party under the Research Plan, including, with respect to Novartis, any IND-Enabling Toxicology Study; *provided* that if Novartis requests any changes to the Research Activities allocated to Ionis that would increase Ionis' FTE Costs or Out-of-Pocket Costs compared with the then-current Research Plan, and the JSC approves an amendment to the Research Plan to reflect such change in accordance with Section 3.3 (Decision Making) (such activities that would increase Ionis' FTE Costs or Out-of-Pocket Costs compared with the then-current Research Plan, "***Additional Ionis Research Activities***"), then Novartis will reimburse Ionis for any Material Research Costs incurred by Ionis in conducting such Additional Ionis Research Activities within [***] from the date an Invoice is received by Ionis for such FTE Costs and Out-of-Pocket Costs, except to the extent Novartis disputes such Invoice in good faith (in which case such disputed amount will be paid after resolution of such dispute).

2.5. **Clinical Development Plan**. Within [***] after the DC Selection Date for a Development Candidate, Novartis will provide the JSC with a [***] clinical development plan for such Development Candidate (or, if there is an existing development plan for a Development Candidate, modify such development plan to incorporate such additional Development Candidate) through [***] for such Development Candidate (such plan the "***Clinical Development Plan***") for the JSC to review and discuss. The initial draft of the Clinical Development Plan will include the level of detail that Novartis includes for similarly situated partnered-programs. Thereafter, Novartis will review and update the Clinical Development Plan every [***] and, if requested by Ionis following receipt of any such update, the Parties will meet (in person or virtually) to review such update, which meeting may be held as part of a JSC meeting if the JSC is still in existence. The Parties will mutually determine the location of such meetings. Each Party will be responsible for the costs of its own representatives attending such meetings.

2.6. **IND-Enabling Toxicology Studies**. For each Development Candidate, at least [***] before an IND is filed by or on behalf of Novartis with respect to such Development Candidate or earlier if available and upon Ionis' reasonable request, Novartis will provide Ionis with a Draft Report from an IND-Enabling Toxicology Study for such Development Candidate for Ionis to review. Upon Ionis' reasonable request, the JSC (or, if the JSC has been discontinued, the Parties) will promptly convene a meeting to discuss [***] any comments or concerns raised by Ionis with respect to such Draft Report, which meeting will be convened prior to Novartis filing an IND for such Development Candidate.

2.7. **Manufacturing and Supply**.

2.7.1. **Responsibility During the Research Term**. During the Research Term, Ionis will be responsible for Manufacturing and supplying, at [***] expense, any non-GMP API that is reasonably required to conduct any Research Activities; *provided* that Novartis may assume responsibility for Manufacturing and supplying, at [***] expense, any such non-GMP API by providing written notice to Ionis. If Novartis elects to assume such Manufacturing responsibility, then Ionis will (a) provide any assistance that is reasonably requested by Novartis to facilitate Novartis' ability to Manufacture such non-GMP API and (b) if such non-GMP API requires a Manufacturing process that Novartis does not at such time possess, then the Parties will establish and approve a plan pursuant to which Ionis will perform a technology transfer to Novartis of all Ionis Manufacturing and Analytical Know-How in Ionis' possession that is necessary to Manufacture such non-GMP API solely for use by Novartis, its Affiliates, or a Third Party as permitted under Section 5.3 (Sublicense Rights) in accordance with the licenses granted by Ionis to Novartis pursuant to Section 5.1.1 (License for Research Activities). Novartis will compensate Ionis in accordance with Section 7.10 (Reimbursement for Ionis' Time) for any technology transfer assistance provided by Ionis under this Section 2.7.1 (Responsibility During the Research Term).

2.7.2. **Responsibility After the Research Term**. In addition, if the Parties mutually agree, then Ionis will be responsible for Manufacturing and supplying additional batches of API for use after the Research Term pursuant to a supply agreement between the Parties that is negotiated in good faith and on commercially reasonable terms, including that Novartis will pay for any such API at a price equal to [***]. Except as set forth in this Section 2.7 (Manufacturing and Supply), as between the Parties, Novartis will be responsible for supplying all API and Finished Drug Product in connection with its Development and Commercialization activities under this Agreement.

2.8. Materials Transfer. To facilitate the activities under the Research Plan, each Party shall provide to the other such materials in such quantities as are specified in the Research Plan and, in addition, either Party may provide to the other Party certain materials for use by the other Party in furtherance of the conduct of the activities under the Research Plan. All such materials will be used by the receiving Party in accordance with the terms and conditions of this Agreement solely for purposes of exercising its rights and performing its obligations under this Agreement, and the receiving Party will not transfer such materials to any Third Party unless expressly contemplated by this Agreement or upon the written consent of the supplying Party. THE MATERIALS ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

2.9. Conduct of Research Activities. Each Party will conduct and use Commercially Reasonable Efforts to complete the Research Activities allocated to it under the Research Plan. Each Party will, and will require its Affiliates and subcontractors to, perform its obligations under the Research Plan in compliance with Applicable Law.

2.10. Research Records and Reports.

2.10.1. **Records**. Each Party will maintain, and require its Affiliates and subcontractors to maintain, consistent with its internal policies and Applicable Law, for at least seven years, records and laboratory notebooks, inventory, purchase and invoice records and Manufacturing records, in each case, with respect to the Research Activities and the Licensed Products in sufficient detail and in a good scientific manner appropriate for (a) inclusion in filings with Regulatory Authorities for such Licensed Products and (b) obtaining and maintaining intellectual property rights and protections, including Patent Rights for such Licensed Products. Such records and laboratory notebooks will be complete and accurate in all material respects and will fully and properly reflect all work done, data and developments made, and results achieved. Each Party will allow the other Party, to the extent necessary for such regulatory or intellectual property protection purposes, to inspect or copy such records, subject to reasonable redaction of such Party's Confidential Information to the extent not relevant to the activities under this Agreement.

2.10.2. **Research Reports**. During the Research Term, in advance of each meeting of the JRC (unless otherwise agreed by the JRC), each Party will submit to the JRC for its review and discussion written materials that include a reasonably detailed summary of the Research Activities performed by or on behalf of such Party during the most recently completed Calendar Quarter and the results of such Research Activities as well as the information and data specified in Section 2.2 (Development Candidate Selection Process) (each, a "***Research Report***").

ARTICLE 3
COLLABORATION MANAGEMENT

3.1. Joint Steering Committee.

3.1.1. **Establishment; Meetings**. Within [***] after the Effective Date, the Parties will establish a joint steering committee ("***JSC***"), which JSC will coordinate, oversee and monitor the Parties' activities hereunder in accordance with this Section 3.1 (Joint Steering Committee). The JSC will consist of [***] representatives appointed by Ionis and [***] representatives appointed by Novartis (which may include representative(s) from each Party's Affiliates), and each JSC member will be a senior executive of such Party (or its Affiliate). Each Party will designate one of its representatives who is empowered by such Party to make decisions related to the performance of such Party's obligations under this Agreement to act as the co-chair of the JSC. Unless otherwise agreed by the Parties, the JSC will meet in person, by videoconference, or by teleconference at least [***] each Calendar Quarter during the Research Term, and upon Novartis' request any time after the Research Term prior to [***] for the first Licensed Product if Novartis provides a Development Candidate Data Package for a Novartis Proposed Development Candidate in accordance with Section 2.2.3 (Novartis Proposed Development Candidate), *provided* that in case a Carryover Period applies, the JSC will meet during such Carryover Period to the extent required to review, discuss, and determine whether to designate any Carryover Candidate as a Development Candidate, in each case, on such dates and at such times and places as agreed to by the members of the JSC. The JSC will determine the JSC operating procedures at its first meeting, including the JSC's policies for replacing JSC members, policies for participation by additional representatives or consultants invited to attend JSC meetings, and the location of meetings, which will be codified in the written minutes of the first JSC meeting. Each Party will be responsible for the costs and expenses of its own employees or consultants attending JSC meetings.

3.1.2. **Responsibilities**. The JSC will perform the following functions during the Research Term:

(a) oversee, review, monitor, and coordinate the Parties' activities under this Agreement;

(b) review, discuss, and determine whether to approve any updates to the Research Plan as proposed by the JRC, as described in Section 2.1.3 (Updates to the Research Plan)

(c) review, discuss, and determine whether to designate any Proposed Development Candidate as a Development Candidate, as described in Section 2.2.4 (Development Candidate Selection Process);

(d) review and discuss the Clinical Development Plan, as described in Section 2.5 (Clinical Development Plan);

(e) at Ionis' reasonable request, review and discuss a Draft Report for an IND-Enabling Toxicology Study, as described in Section 2.6 (IND-Enabling Toxicology Studies);

(f) oversee each Technology Transfer Plan, as described in Section 5.9.1 (Licensed Know-How – Generally);

(g) oversee each Manufacturing Technology Transfer Plan, as described in Section 5.9.2 (Ionis Manufacturing and Analytical Know-How) and, as applicable, Section 2.7.1 (Responsibility During the Research Term);

(h) review and discuss any safety concerns regarding the Licensed Compounds or Licensed Products raised by either Party;

(i) establish and oversee joint subcommittees, including the JRC, as it deems necessary or advisable to further the purpose of this Agreement;

(j) perform such other review and advisory responsibilities as may be assigned to the JSC by mutual agreement of the Parties pursuant to this Agreement; and

(k) resolve any disputes at the JRC or any other subcommittee.

Subject to Section 3.1.3 (Obligations to Participate in JSC) and Section 3.1.4 (Discontinuation of JSC), after the end of the Research Term, the JSC will perform the following functions:

(a) review, discuss, and determine whether to designate any Carryover Candidate or Novartis Proposed Development Candidate as a Development Candidate, as described in Section 2.2.4 (Development Candidate Selection Process);

(b) oversee each Technology Transfer Plan, as described in Section 5.9.1 (Licensed Know-How – Generally) with respect to any such Development Candidate; and

(c) oversee each Manufacturing Technology Transfer Plan, as described in Section 5.9.2 (Ionis Manufacturing and Analytical Know-How) with respect to any such Development Candidate.

3.1.3. **Obligation to Participate in JSC**. Ionis' obligation to participate in the JSC will terminate upon the JSC's designation of the first Compound as a Development Candidate in accordance with Section 2.2.4 (Development Candidate Selection Process).

3.1.4. **Discontinuation of JSC**. The JSC shall continue to exist until the first to occur of (a) the Parties mutually agreeing to disband the JSC or (b) [***] for the first Licensed Product.

3.2. Joint Research Committee.

3.2.1. **Establishment**. Within [***] after the Effective Date, the Parties will establish a joint research committee ("***JRC***"), which JRC will coordinate, oversee, and monitor the Parties' activities hereunder in accordance with this Section 3.2 (Joint Research Committee). The JRC will comprise an equal number of at most [***] members from each Party. The JRC will meet as often as agreed by them (and at least on [***] basis during the Research Term), to discuss matters arising out of the activities set forth in this Section 3.2 (Joint Research Committee). The JRC will determine the JRC operating procedures at its first meeting, including the JRC's policies for replacement of JRC members, and the location of meetings, which will be codified in the written minutes of the first JRC meeting. The Parties may escalate issues to the JSC for input and resolution. Each Party's representatives on the JRC will consider comments and suggestions made by the other in good faith. Each Party will bear their own cost of participation on the JRC.

3.2.2. **Responsibilities**. The JRC will perform the following functions during the Research Term:

(a) review and discuss the Research Reports and any Development Candidate Data Package submitted to it by a Party;

(b) coordinate the Research Activities and facilitate communications between the Parties with respect to the Research Activities;

(c) prepare and submit any updates to the Research Plan to the JSC for the JSC to review, discuss, and determine whether to approve;

(d) discuss each Party's performance under the Research Plan and the anticipated timeline for initiating and completing the activities set forth therein;

(e) (i) review, discuss, and determine whether any Compounds satisfy the Development Candidate Criteria, (ii) review, discuss, and determine whether to submit a Development Candidate Data Package to the JSC for the JSC to consider designating such Compound as a Development Candidate, and (iii) recommend Proposed Development Candidate(s), if any, for the JSC's designation as Development Candidate(s); and

(f) perform such other functions as may be appropriate to further the purposes of this Agreement with respect to the research of the Licensed Products, as directed by the JSC.

3.2.3. **Discontinuation of JRC**. The JRC shall continue to exist until the first to occur of (a) the Parties mutually agreeing to disband the JRC or (b) the end of the Research Term.

3.3. Decision Making.

3.3.1. **Committee Decisions**. Each Party's representatives on the JSC and the JRC will, collectively, have one vote (the "***Party Vote***") on all matters brought before the JSC or JRC for a decision by consensus. Except as otherwise expressly set forth in this Agreement, the phrase "determine," "designate," "confirm," "approve," or "determine whether to approve" by the JSC or JRC and similar phrases used in this Agreement will mean approval in accordance with this Section 3.3 (Decision Making). The JSC and JRC will make decisions as to matters within their jurisdiction by unanimous Party Vote, which Party Vote may either be reflected in the minutes of the committee meeting or by an action by written consent signed by a representative of each Party. No vote will be binding on either Party unless each Party has at least one representative in attendance.

3.3.2. **Scope of Committee Authority**. For the avoidance of doubt, matters that are specified in this Article 3 (Collaboration Management) only to be reviewed and discussed (as opposed to reviewed, discussed, and approved) or where a committee is to oversee certain activities do not require any agreement or decision by either Party and are not subject to the voting and decision-making procedures set forth in this Section 3.3 (Decision Making).

3.3.3. **Escalation**. If the JRC is unable to reach agreement as to a particular matter within its jurisdiction within [***] (or a later date mutually agreed to by the Parties) after such matter has been brought to the JRC for resolution, then such disagreement will be referred to the JSC for resolution. If the representatives of Novartis and Ionis are unable to agree on or resolve any matter requiring the approval of the JSC (including any disagreements referred from the JRC to the JSC) after the use of good faith efforts, then, at the election of either Party, such Party may refer such matter to the Party's respective Executives. The Executives will use good faith efforts to resolve any such disagreement so referred to them as soon as practicable, and any final decision that the Executives agree to in writing will be conclusive and binding on the Parties. If the Executives are unable to resolve any disagreement so referred within a period of [***] after such matter is referred to them (or such longer period as the Executives may agree upon), then:

(a) **Novartis Final Decision-Making Authority**. Except for the matters set out in Section 3.3.3(b) (Ionis Final Decision-Making Authority), Novartis will have the right to make the final decision regarding [***], *provided, however*, that:

(i) [***];

(ii) [***];

(iii) [***]; and

(iv) [***].

(b) **Ionis Final Decision-Making Authority**. Ionis will have the right to make the final decision regarding [***].

3.4. Day-to-Day Responsibilities. Each Party will: (a) be responsible for day-to-day implementation and conduct of the activities hereunder for which it has or is otherwise assigned responsibility under this Agreement, *provided* that such implementation is consistent with the express terms of this Agreement and the decisions of the JSC that are within the scope of its authority as provided herein; and (b) provide the other Party with information about material events related to the progress of such activities, as may be reasonably requested by the other Party from time to time.

3.5. Limitations on Authority. Each Party shall retain the rights, powers, and discretion granted to it under this Agreement and no such rights, powers, or discretion shall be delegated to or vested in the JSC or JRC unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties expressly so agree in writing. The JSC and JRC shall not have the power to: (a) amend, modify, or waive compliance with this Agreement or any term or condition of this Agreement; (b) make any determination that any Party is in breach of this Agreement, (c) impose additional material financial obligations on a Party beyond those provided in this Agreement, or (d) make any decisions in a manner that would require a Party to perform any act that would cause such Party to violate any Applicable Law or the requirements of any Regulatory Authority, or otherwise breach any of its obligations hereunder.

3.6. Alliance Managers. Each Party shall appoint a representative to act as its alliance manager under this Agreement (each, an "***Alliance Manager***"). The Alliance Managers shall be responsible for: (a) facilitating the flow of information and otherwise promoting communication, coordination, and collaboration between the Parties under this Agreement, (b) providing support and guidance to the JSC and the JRC, (c) developing a mutually agreed launch plan covering any activities and systems the Parties need to implement within 100 days after the Effective Date, (d) coordinating proper approval of press releases, publications, and public disclosures prior to submission in accordance with Section 12.4 (Press Release; Publications; Disclosure of Agreement), and (e) organizing JSC and JRC meetings, including agendas, drafting minutes, publishing final minutes and facilitating dispute resolution as necessary. The Alliance Managers shall have the right to attend all meetings of the JSC and the JRC as non-voting members, and shall bring matters to the attention of the relevant committee if the Alliance Manager reasonably believes that such matter warrants such attention. Each Party may replace its Alliance Manager at any time upon written notice to the other Party.

ARTICLE 4
EXCLUSIVITY

4.1. Exclusivity Covenants. Except as expressly set forth in this Article 4 (Exclusivity), neither Party nor its Affiliates will (independently or with a Third Party) Develop or Commercialize any Competitive Compound until the earlier of (a) [***] or (b) [***]. For clarity, the exclusivity obligations in this Section 4.1 (Exclusivity Covenants) will not survive expiration or termination of this Agreement.

4.2. Limitations and Exceptions to the Parties' Exclusivity Covenants. Notwithstanding anything to the contrary in Section 4.1 (Exclusivity Covenants), either Party or its Affiliates may perform the following activities:

(a) With regard to such Party and its Affiliates:

(i) all activities permitted or contemplated under this Agreement, including Exploiting a Licensed Product in accordance with this Agreement and those activities contained in Section 4.3 (Acquisition of a Competitive Compound), Section 4.4 (Change of Control), and Section 4.5 (Effect of Exclusivity on Indications); and

(ii) all activities permitted or contemplated under the Akcea-Novartis Collaboration Agreement.

(b) With regard to Ionis and its Affiliates:

(i) activities conducted pursuant to the Prior Agreements [***] in Appendix 3 (License Conditions; Limitations); and

(ii) the granting of, or performance of obligations under, Permitted Licenses.

4.3. Acquisition of a Competitive Compound. The Parties acknowledge that after the Effective Date a Party or any of its Affiliates may in-license or otherwise acquire rights (including through any merger or business combination but excluding through a Change of Control Event) to Develop or Commercialize a Competitive Compound (such Competitive Compound, an "***Acquired Compound***"). In the case of such a transaction where a Party acquires rights to Develop or Commercialize an Acquired Compound and, on the date of closing of such transaction, such Acquired Compound is being Developed or Commercialized and such activities would violate Section 4.1 (Exclusivity Covenants), then, (a) such Party must notify the other Party within [***] of closing of such transaction and (b) notwithstanding anything to the contrary in this Agreement, within [***] after such acquisition (such period, the "***Evaluation Period***"), such Party (or its Affiliate) or such Third Party must (i) [***], or (ii) [***]. Novartis will have the right to extend the Evaluation Period for an additional [***] by providing written notice to Ionis prior to the expiration of the [***] period and paying Ionis a one-time fee of $[***]. Following receipt of such notice, Ionis will promptly provide Novartis with an Invoice for such fee and Novartis shall pay such fee within [***] after receipt by Novartis of such Invoice. [***]. During the period between the closing of a transaction to acquire rights to an Acquired Compound and the date that the applicable Party completes the steps set forth in clause (b)(i) or (b)(ii) above, such Party must (1) establish and enforce internal processes, policies, procedures and systems to segregate information relating to any such Acquired Compound from any Confidential Information related to the Development Candidates and Licensed Products under this Agreement, (2) not use, directly or indirectly, any Patent Rights, Know-How or Confidential Information licensed or acquired from the other Party under this Agreement in the Exploitation of such Acquired Compound, and (3) segregate all activities relating to the Acquired Compound from the Exploitation of the Development Candidates and Licensed Products under this Agreement.

4.4. **Change of Control**. If there is a Change of Control Event involving a Party (where such Party or its parent is the acquired entity), then the obligations of Section 4.1 (Exclusivity Covenants) will not apply to any product that (a) is controlled by the relevant acquirer or its Affiliates and (b) exists prior to the closing of such Change of Control Event or is subsequently developed by the relevant acquirer or any of its Affiliates existing immediately prior to the effective date of such Change of Control Event (such product, a "***Competitive Product***"); *provided* that (i) the acquired Party and the acquirer and its Affiliates existing immediately prior to the effective date of such Change of Control Event establish and enforce internal processes, policies, procedures and systems to segregate information relating to any such Competitive Product from any Confidential Information related to the Development Candidates and Licensed Products under this Agreement, (ii) the acquirer and its Affiliates existing immediately prior to the effective date of such Change of Control Event do not use, directly or indirectly, any Patent Rights, Know-How or Confidential Information of the acquired Party (including any Patent Rights, Know-How or Confidential Information licensed or acquired from the other Party under this Agreement) in the Exploitation of such Competitive Product, and (iii) the acquired Party and the acquirer will segregate all activities relating to the Competitive Product from the Exploitation of the Development Candidates and Licensed Products under this Agreement.

4.5. **Effect of Exclusivity on Indications**. While Ionis and Novartis are subject to certain restrictive covenants under Section 4.1 (Exclusivity Covenants), the Parties acknowledge and agree that, for clarity, each Party (on its own or with a Third Party) may continue to Develop and Commercialize any therapeutic compound that is designed to directly modulate a gene other than APO(a) for any indication, even if such therapeutic compound is designed to treat the same indication as a Licensed Product.

ARTICLE 5
LICENSE GRANTS; TECHNOLOGY TRANSFER AND SUPPORT

5.1. **License Grants to Novartis**.

5.1.1. **License for Research Activities**. Subject to the terms of this Agreement, Ionis hereby grants to Novartis a worldwide, non-exclusive, sublicensable (in accordance with Section 5.3 (Sublicense Rights)) license under (a) the Ionis Research Activities Technology and the Licensed Technology, in each case, to (i) during the Research Term, perform the Research Activities allocated to Novartis under the Research Plan, (ii) during the Carryover Period or during the period after [***] until [***], conduct Research to identify a Compound that satisfies the Development Candidate Criteria and (iii) conduct internal Research utilizing any Licensed Compound solely to the extent such Research is in connection with the Exploitation of a Licensed Product or the Licensed Compound included in such Licensed Product; *provided* that, for clarity, such license to conduct internal Research shall not include a license to Develop or Commercialize such Licensed Compound or any product containing such Licensed Compound and will not be sublicensable to any Third Parties, and (b) the Ionis Manufacturing and Analytical Patents and Ionis Manufacturing and Analytical Know-How to Manufacture non-GMP API for the Research Activities solely if Novartis elects to assume responsibility for Manufacturing and supplying such non-GMP API in accordance with Section 2.7 (Manufacturing and Supply).

5.1.2. **Licensed Product License**. Subject to the terms and conditions of this Agreement, including Section 5.11 (HSR Matters), on a Development Candidate-by-Development Candidate basis, effective upon the DC Selection Date for such Development Candidate in accordance with Section 2.2.4 (Development Candidate Selection Process), Ionis hereby grants to Novartis an exclusive (even as to Ionis), royalty-bearing, sublicensable (in accordance with Section 5.3 (Sublicense Rights)) license under the Licensed Technology to Exploit such Development Candidate and Licensed Products containing such Development Candidate in the Field in the Territory (such license, a "***Licensed Product License***").

5.2. **Research License Grant to Ionis**. Subject to the terms of this Agreement, Novartis hereby grants to Ionis a worldwide, non-exclusive license, with the right to grant sublicenses only to its Affiliates and to subcontractors set forth in the Research Plan, under the Novartis Research Activities Technology to perform the Research Activities allocated to Ionis under the Research Plan or, as applicable, to conduct Research to identify a Compound that satisfies the Development Candidate Criteria during the Carryover Period.

5.3. **Sublicense Rights**. Novartis will have the right to grant sublicenses under the licenses granted to Novartis in Section 5.1 (License Grants to Novartis) as expressly permitted by this Section 5.3 (Sublicense Rights).

5.3.1. **Right to Grant Sublicenses**. Notwithstanding anything to the contrary but subject to this Section 5.3 (Sublicense Rights), Novartis will have the right to grant sublicenses (through multiple tiers) under the licenses granted under Section 5.1 (License Grants to Novartis) to its Affiliates and Third Parties, *provided*, that:

(a) any sublicense under the Ionis Manufacturing and Analytical Patents and Ionis Manufacturing and Analytical Know-How shall be subject to Section 5.4.2 (Novartis' CMOs); and

(b) any [***] shall require Ionis' prior written consent (which consent will not be unreasonably withheld, conditioned or delayed).

5.3.2. **Sublicensing Requirements**. Each sublicense granted by either Party will be consistent with and subject to the applicable terms and conditions of this Agreement and the Party granting such sublicense will remain responsible to the other Party for the compliance of each such sublicensee with such terms and conditions. Novartis will, within [***] following the grant of a sublicense pursuant to Section 5.3.1 (Right to Grant Sublicenses) other than [***], notify Ionis of its grant of any sublicense pursuant to Section 5.3.1 (Right to Grant Sublicenses), including the identity of the relevant Sublicensee as well as a [***]. [***], Novartis will promptly provide Ionis with a true and complete copy of any sublicense agreement for, or that includes, such country that is (a) granted to a CMO under Section 5.4.2 (Novartis' CMOs) or (b) for a grant of all or substantially all of Novartis' or its Affiliates' rights to Commercialize a Licensed Product in such country to a Third Party; *provided*, *however*, that Novartis will have the right to redact any financial terms and other technical or business information from such copy of the sublicense agreement if Novartis determines in good faith that such redactions are necessary to protect any of its or its Sublicensee's confidential or proprietary information unrelated to Novartis' obligations under this Agreement.

5.3.3. **Enforcement of Sublicense Agreements**. In the event of a material breach of any sublicense granted by Novartis pursuant to Section 5.3.1 (Right to Grant Sublicenses), [***], Novartis will inform Ionis promptly after becoming aware of such breach. If such breach is [***], then Ionis may request Novartis to enforce the terms of the breached provision(s) of such sublicense. If Novartis fails to take any action to enforce such terms within [***] after Ionis' request, then, [***], Ionis may enforce such terms on Novartis' behalf and, in such case, Novartis will cooperate with Ionis, upon Ionis' reasonable request, in connection with enforcing such terms. Notwithstanding the foregoing, Ionis shall not have the right to amend or otherwise modify the terms of any such sublicense or impose any obligations on Novartis in connection with such enforcement. For clarity, this Section 5.3.3 (Enforcement of Sublicense Agreements) will not limit or modify Novartis' obligation to remain responsible to Ionis for Novartis' sublicensees' compliance with the terms and conditions of this Agreement.

5.3.4. **Effect of Termination on Sublicenses**. If this Agreement terminates for any reason, any Sublicensee that has been granted a sublicense pursuant to Section 5.3.1 (Right to Grant Sublicenses), other than [***], and that is not, at the time of termination, in material breach of its sublicense agreement with Novartis, will, from the effective date of such termination, automatically become a direct licensee of Ionis with respect to the rights sublicensed to the Sublicensee by Novartis; so long as (a) such Sublicensee agrees in writing to comply with all of the terms of this Agreement to the extent applicable to the rights originally sublicensed to it by Novartis, (b) such Sublicensee agrees to pay directly to Ionis such Sublicensee's payments under this Agreement to the extent applicable to the rights sublicensed to it by Novartis, and (c) in no event will Ionis have any greater obligations to any such Sublicensee than it has to Novartis under this Agreement. Upon Ionis' written request after such termination of this Agreement, Novartis will [***] deliver to Ionis within [***] a copy of any such sublicense with such Sublicensee; *provided* that Novartis may redact any information in such sublicense that does not relate to the Licensed Products.

5.4. Subcontracting.

5.4.1. **General**. Subject to the terms of Section 5.2 (Research License Grant to Ionis), Section 5.3.1 (Right to Grant Sublicenses), and this Section 5.4 (Subcontracting), each Party will have the right to engage Third Party subcontractors to perform certain of its obligations under this Agreement. Any subcontractor to be engaged by a Party to perform a Party's obligations set forth in this Agreement will meet the qualifications typically required by such Party for the performance of work similar in scope and complexity to the subcontracted activity and will be bound by written obligations of confidentiality and non-use consistent with this Agreement. Any Party engaging a subcontractor hereunder will remain responsible and obligated for such activities and will not grant rights to such subcontractor that interfere with the rights of the other Party under this Agreement. As between the Parties, each Party will be responsible for any income or non-income taxes that arise as a result of such Party's use of any Third Party subcontractors hereunder, including payroll, income, withholding, sales and use, VAT, customs, duties excise or property taxes, and such taxes will not be reimbursable expenditures.

5.4.2. **Novartis' CMOs**.

(a) Ionis agrees that, where Novartis wishes to (sub)contract with a Third Party to Manufacture API or Licensed Products in accordance with Section 5.3.1(a) (Right to Grant Sublicenses), Ionis will, within [***] of any request by Novartis, provide Novartis with a letter of authorization as necessary for Novartis to be able to contract with such Third Party in accordance with the terms of this Agreement if such Third Party already has a valid license granted by Ionis or its Affiliates; *provided* that if Ionis has not provided the necessary letter of authorization to Novartis within such [***] period, then the required authorization shall be deemed granted by Ionis. If such Third Party does not have a valid license under the Ionis Manufacturing and Analytical Patents and Ionis Manufacturing and Analytical Know-How, then Ionis will, within [***] (or such other period as mutually agreed between the Parties) of any request by Novartis, grant such license to such Third Party to Manufacture API or Licensed Products in a manufacturing facility owned or operated by such Third Party on reasonable terms consistent with the terms of the relevant Prior Agreements with CMOs, *provided* that if Ionis has not granted the required license to the Third Party within such [***] period (or such other period as mutually agreed between the Parties), then [***].

(b) Ionis furthermore agrees to [***], grant such Third Party the required license [***] with respect to the Manufacture of API or Licensed Products for Novartis or its Affiliates or Sublicensees.

(c) Novartis will use Commercially Reasonable Efforts to ensure that any CMOs Novartis may use to conduct any such Manufacturing activities will be obligated to assign to Novartis all right, title, and interest in and to any inventions developed by such (sub)contractors in the performance of such activities. In addition, Novartis will [***]. [***] will have final decision-making authority with regard to the selection of CMOs (*provided* that such CMO is engaged in accordance with Section 5.3.1(a)(Right to Grant Sublicenses) and this Section 5.4 (Subcontracting)) and the terms of any such CMO Agreement.

5.5. Consequence of Natural Expiration of this Agreement. If this Agreement naturally expires in accordance with Section 11.1.1 (Agreement Term; Expiration) or Section 11.1.2 (Agreement Term; Expiration), then with respect to any Licensed Product that is the subject of such expiration for which Novartis has a license under Section 5.1.2 (Licensed Product License) at such time, Ionis grants to Novartis a perpetual, non-exclusive, worldwide, royalty-free and sublicensable (through multiple tiers) license under Ionis Manufacturing and Analytical Patents and the Licensed Know-How to Develop, Manufacture, have Manufactured and Commercialize such Licensed Product.

5.6. No Implied Licenses. All rights in and to Licensed Technology not expressly licensed to Novartis under this Agreement are hereby retained by Ionis and its Affiliates. All rights in and to Novartis Technology not expressly licensed to Ionis under this Agreement are hereby retained by Novartis and its Affiliates. Except as expressly provided in this Agreement, no Party will be deemed by estoppel or implication to have granted the other Party any license or other right with respect to any intellectual property.

5.7. License Conditions; Limitations. The licenses granted under Section 5.1 (License Grants to Novartis), and the sublicense rights under Section 5.3 (Sublicense Rights) are subject to (a) [***] the Prior Agreements disclosed in APPENDIX 3 (License Conditions; Limitations), (b) the Ionis In-License Agreements, and (c) in-licenses to [***] included in the license granted to Novartis under Section 5.1 (License Grants to Novartis) pursuant to Section 7.9.2 (New In-License Agreements).

5.8. Trademark and Domain Names.

5.8.1. As between the Parties, Novartis will be solely responsible for selecting, registering and maintaining the Trademarks used to Commercialize Licensed Products. As between the Parties, Novartis will own and control the Trademarks and pay all relevant costs related thereto.

5.8.2. As between the Parties, only Novartis will be authorized to initiate at its own discretion legal Proceedings against any infringement or threatened infringement of the Trademarks.

5.8.3. As between the Parties, Novartis will be responsible for registering, hosting, maintaining and defending the Domain Names under all generic Top Level Domains (gTLDs) and under all relevant country code Top Level Domains (ccTLD). For the avoidance of doubt, Novartis may register such Domain Names in its own name, to host on its own servers, maintain and defend the Domain Names and use them for websites.

5.9. Technology and Information Transfer.

5.9.1. **Licensed Know-How – Generally**. On a Development Candidate-by-Development Candidate basis, within [***] after the DC Selection Date for a Development Candidate, the Parties will establish and mutually agree on a plan ([***]) pursuant to which Ionis will perform a technology transfer to Novartis of all Licensed Know-How (other than the Ionis Manufacturing and Analytical Know-How) related to such Development Candidate to the extent that such Licensed Know-How is in Ionis' possession and has not previously been provided hereunder and for use solely in accordance with the licenses granted by Ionis to Novartis hereunder (with respect to each Development Candidate, the "***Technology Transfer Plan***"). The Technology Transfer Plan for a Development Candidate will set forth the type, name and quantity of any Know-How transferred and the anticipated timelines for completing such transfer.

5.9.2. **Ionis Manufacturing and Analytical Know-How**. On a Development Candidate-by-Development Candidate basis, within [***] after the DC Selection Date for a Development Candidate, the Parties will establish and mutually agree on a plan ([***]) pursuant to which Ionis will perform a technology transfer to Novartis of all Ionis Manufacturing and Analytical Know-How related to such Development Candidate and in Ionis' possession that has not previously been provided hereunder solely for use by Novartis, its Affiliates or a Third Party as permitted under Section 5.3 (Sublicense Rights) in accordance with the licenses granted by Ionis to Novartis hereunder (with respect to each Development Candidate, the "***Manufacturing Technology Transfer Plan***"). The Manufacturing Technology Transfer Plan for a Development Candidate will set forth the type, name and quantity of any Know-How transferred and the anticipated timelines for completing such transfer.

5.9.3. **Ionis Assistance**. If requested by Novartis, Ionis will provide Novartis with a timely and reasonable level of assistance and cooperation in connection with such Licensed Know-How under Section 5.9.1 (Licensed Know-How – Generally) and such Ionis Manufacturing and Analytical Know-How under Section 5.9.2 (Ionis Manufacturing and Analytical Know-How). Novartis will compensate Ionis in accordance with Section 7.10 (Reimbursement for Ionis' Time), for Ionis' and its Affiliates' activities conducted under Section 5.9.1 (Licensed Know-How – Generally) and Section 5.9.2 (Ionis Manufacturing and Analytical Know-How).

5.10. Cross-Licenses under Program Technology.

5.10.1. **Enabling Patent License from Novartis to Ionis**. Subject to the terms and conditions of this Agreement (including Ionis' exclusivity obligations under Section 4.1 (Exclusivity Covenants) and without limiting the license(s) granted to Novartis under Section 5.1 (License Grants to Novartis)), Novartis hereby grants Ionis a fully-paid, royalty-free, irrevocable, worldwide, non-exclusive, sublicensable (through multiple tiers) license under any Novartis Program Technology ([***]), to Develop, manufacture, have manufactured, and Commercialize products that include an Oligonucleotide as an active pharmaceutical ingredient (other than a Licensed Product that is being Developed or Commercialized by Novartis, its Affiliates or Sublicensees under this Agreement).

5.10.2. **Enabling Patent License from Ionis to Novartis**. Subject to the terms and conditions of this Agreement (including Novartis' exclusivity obligations under Section 4.1 (Exclusivity Covenants) and without limiting the license(s) granted to Novartis under Section 5.1 (License Grants to Novartis)), Ionis hereby grants Novartis a fully-paid, royalty-free, irrevocable, worldwide, non-exclusive, sublicensable (through multiple tiers) license under any Ionis Program Technology (excluding any Product-Specific Patents) to the extent it was discovered, invented, or created during the Research Term to Develop, manufacture, have manufactured, and Commercialize products that do not include an Oligonucleotide as an active pharmaceutical ingredient; *provided*, *however*, if [***].

5.11. HSR Matters.

5.11.1. **Effectiveness of the Agreement**. Except for the Parties' rights and obligations under this Section 5.11 (HSR Matters), Article 9 (Representations, Warranties and Covenants), Article 12 (Confidentiality), and Article 13 (Miscellaneous), which will be effective as of the Execution Date, this Agreement will not become effective until the applicable waiting period (and any extensions thereof, including any timing agreement entered into with the United States Federal Trade Commission ("***FTC***") or the Antitrust Division of the United States Department of Justice ("***DOJ***")) under the HSR Act shall have expired or terminated (the "***Effective Date***"). Novartis will provide written notice to Ionis of such Effective Date. As of the Effective Date, all other provisions of this Agreement will become effective automatically without the need for further action by the Parties. Notwithstanding any other provisions of this Agreement to the contrary, if the Effective Date has not occurred on or before the date that is [***] after the Execution Date (the "***Outside Date***"), then either Party, by written notice to the other, may terminate this Agreement, which will then become void and of no further effect as of such notice, *provided* that the Outside Date may be extended upon written notice from either Party to the other Party prior to the then-applicable Outside Date expiring up to [***] times for a period of [***] each if the Effective Date has not occurred within such [***] period or such initial [***] period, as applicable; *provided* that such requesting Party is not in material breach of its obligations under this Section 5.11 (HSR Matters).

5.11.2. **HSR Filing**.

(a) Ionis and Novartis will, as promptly as practicable (but no later than [***] after the Execution Date), prepare and file with the FTC and DOJ, the Notification and Report Form for Certain Mergers and Acquisitions (as that term is defined in the HSR Act) required for the transactions contemplated hereby, together with all required documentary attachments thereto (the "***HSR Filings***"). Notwithstanding the foregoing, the Parties may, upon mutual agreement, delay the filing of any of the HSR Filings if they reasonably believe that such delay would result in obtaining any clearance required under the HSR Act for the consummation of this Agreement and the transactions contemplated hereby more expeditiously. Each of Ionis and Novartis will cooperate in the antitrust clearance process, including by furnishing to each other's counsel such necessary information and reasonable assistance as the other may reasonably request in connection with its preparation of any filing or submission that is necessary under the HSR Act and to furnish promptly with the FTC and DOJ any information reasonably requested by them in connection with such filings. Each Party will be responsible for its own fees, costs and expenses associated with any HSR Filings or in connection with its obligations pursuant to this Section 5.11.2 (HSR Filing).

(b) Ionis and Novartis will each use commercially reasonable efforts to promptly obtain the expiration or termination of the HSR waiting period as it relates to this Agreement and the transactions contemplated hereby and will keep each other apprised of the status of any communications with, and any inquiries or requests for additional information from, the FTC or DOJ and will comply promptly with any such inquiry or request. Commercially reasonable efforts as used in this Section 5.11.2 (HSR Filing) will not include, and will not require, proposing, negotiating, committing to or effecting, by consent decree, hold separate order, or otherwise, (i) the sale, divestiture, disposition, licensing or sublicensing of any of a Party's or its Affiliates' assets, properties or businesses, (ii) behavioral limitations, conduct restrictions or commitments with respect to such assets, properties or business, or of any of the rights or obligations of a Party under this Agreement, or (iii) defending through litigation any claim asserted in court by any Third Party that would restrain, prevent or delay the Effective Date.

(c) The Parties will instruct their respective counsel to cooperate with each other and use commercially reasonable efforts to facilitate and expedite the identification and resolution of any issues arising under the HSR Act at the earliest practicable dates. Such commercially reasonable efforts and cooperation include counsel's undertaking to (i) keep each other informed of communications, inquiries and requests from and to personnel of the FTC or DOJ, including by providing copies thereof to the other Party (subject to reasonable redactions for privilege or confidentiality concerns), and (ii) confer with each other regarding appropriate contacts with and response to such personnel of the FTC or DOJ and the content of any such contacts or presentations. Each of Ionis and Novartis will consult with the other Party, to the extent practicable, in advance of participating in any substantive meeting or discussion with the FTC or DOJ with respect to any such filings, applications, investigation, or other inquiry and, to the extent permitted by the DOJ or FTC, give the other Party the opportunity to attend and participate in such meeting or discussion. Ionis and Novartis will each give the other Party the opportunity to review in advance, and will consider in good faith the other Party's reasonable comments in connection with, the content of any presentations, white papers or other written materials to be submitted to the FTC or DOJ. Notwithstanding any of the preceding, the final determination as to the appropriate course of action shall be made by [***]. For clarity, the Parties' rights and obligations hereunder apply only in so far as they relate to this Agreement and to the transactions contemplated under this Agreement.

(d) Prior to designating a Development Candidate, Novartis will determine whether HSR Filings or any other antitrust or merger control filings are required in connection with the grant of the Licensed Product License for such Development Candidate. If Novartis reasonably determines that an HSR Filing is required, Novartis shall notify Ionis thereof, and the Parties will comply with the provisions of this Section 5.11.2 (HSR Filing), which will apply *mutatis mutandis* with respect to such HSR Filing. If Novartis reasonably determines that any other antitrust or merger control filings or submissions are required in connection with the grant of such Licensed Product License, the Parties will cooperate to effect such filing or submission and use commercially reasonable efforts to cause such Licensed Product License to go into effect as expeditiously as possible. If HSR Filings or any other antitrust or merger control filings are required in connection with the grant of the Licensed Product License for a Development Candidate, the Licensed Product License for such Development Candidate will not be effective until the applicable waiting period (and any extensions thereof, including any timing agreement entered into with the FTC or the DOJ under the HSR Act) shall have expired or terminated.

ARTICLE 6
DEVELOPMENT, REGULATORY, AND COMMERCIALIZATION

6.1. **Development**. Subject to the terms and conditions of this Agreement, from and after the expiration of the Research Term, (a) as between the Parties, Novartis will have sole and exclusive control over the Development of any Licensed Products and (b) Novartis shall itself, or through its Affiliates or Sublicensees, use Commercially Reasonable Efforts to Develop and seek Regulatory Approval for [***]. For clarity, (i) Novartis' application of Commercially Reasonable Efforts shall not require Novartis to [***] and (ii) such obligation to use Commercially Reasonable Efforts shall [***].

6.2. **The Strategic Plan for Licensed Product(s)**.

6.2.1. **Scope**. Novartis will adopt a [***] global strategic development and commercialization plan to Develop and Commercialize the Licensed Products (the "***Strategic Plan***"). The Strategic Plan will cover both the long-term global strategy for each Licensed Product and, on a rolling [***] basis, the material Development and Commercialization activities Novartis plans to perform over the course of the next [***].

6.2.2. **Initial Strategic Plan**. Novartis will deliver the initial Strategic Plan for the Licensed Products to Ionis within [***] after expiration of the Research Term, or if a Development Candidate has not been designated at such time, within [***] following [***] for the first Development Candidate designated thereafter. Ionis may review and comment on such plan and Novartis will consider such comments in good faith.

6.2.3. **Updating the Strategic Plan**. Novartis will review and update the Strategic Plan every [***] and, if requested by Ionis following receipt of such update, the Parties will meet (in person or virtually) to review such update, which meeting may be held as part of a JSC meeting if the JSC is still in existence. The Parties will mutually determine the location of such meetings. Each Party will be responsible for the costs of its own representatives attending such meetings.

6.2.4. **Ad Hoc Meetings**. At either Party's reasonable request, the Parties may as mutually agreed on an ad-hoc basis meet or hold a telephone conference to address any urgent matters that arise with respect to the Licensed Products.

6.3. **Commercialization**. As between the Parties, Novartis will be solely responsible for all aspects of Commercialization of the Licensed Products, including planning and implementation, distribution, booking of sales, and pricing and reimbursement. Novartis shall itself, or through its Affiliates or Sublicensees, use Commercially Reasonable Efforts to Commercialize [***]. For clarity, (i) Novartis' application of Commercially Reasonable Efforts shall not require Novartis to [***] and (ii) such obligation to use Commercially Reasonable Efforts shall [***].

6.4. **Regulatory Interactions**.

6.4.1. **Regulatory Responsibility; Major Regulatory Submissions**. As between the Parties, Novartis will be responsible for (i) determining the regulatory plans and strategies for the Licensed Products, (ii) (either itself or through its Affiliates or Sublicensees) making all regulatory filings with respect to the Licensed Products, and (iii) obtaining and maintaining Regulatory Approvals in the name of Novartis or its Affiliates or Sublicensees. [***], Novartis will provide Ionis with any Major Regulatory Submissions to any Regulatory Authority in each Major Market for such Licensed Product in advance of providing such submission to the applicable Regulatory Authority for Ionis to provide any comments on the contents thereof. If Ionis does not provide comments within [***] from receipt (or shorter notice as reasonably indicated by Novartis), then Novartis will be entitled to submit such submissions. Novartis will consider in good faith any such comments provided on a timely basis by Ionis. [***], Novartis will also provide Ionis with a copy of all final Major Regulatory Submissions without undue delay after providing such submission to the relevant Regulatory Authority and all Major Regulatory Communications without undue delay after receiving such correspondence from a Regulatory Authority. For the avoidance of doubt, Ionis' performance under this Section 6.4.1 (Regulatory Responsibilities; Major Regulatory Submissions) shall be at no cost to Novartis.

6.4.2. **Ionis Cooperation**. If requested by Novartis, Ionis shall cooperate with and provide reasonable assistance to Novartis in connection with filings or submission to any Regulatory Authority relating to the Licensed Products, including by executing any required documents, providing access to personnel and providing Novartis with copies of all reasonably required documentation and supporting data. Novartis will compensate Ionis in accordance with Section 7.10 (Invoices) for Ionis' and its Affiliates' activities conducted under this Section 6.4.2 (Ionis Cooperation). To the extent required to submit a regulatory filing or submission to a Regulatory Authority, Ionis shall grant or cause to be granted to Novartis and its Affiliates or Sublicensees cross-reference rights to any relevant drug master files and other filings Controlled by Ionis or its Affiliates and submitted with any Regulatory Authority.

6.4.3. **Class Generic Claims; Investigator's Brochure**. To the extent Novartis intends to make any claims in a Licensed Product label or regulatory filing that are class generic to Oligonucleotides, Ionis' or its Affiliate's chemistry platform(s), Conjugate Technology, or any other Ionis technology included in a Licensed Product, Novartis will provide such claims and regulatory filings to Ionis in advance and will consider in good faith any proposals and comments made by Ionis (or its Affiliates). Novartis will provide Ionis updated versions of the investigator's brochure [***].

6.5. **Compliance**. Each Party will perform its activities pursuant to this Agreement (and will use reasonable efforts to require Third Parties to perform any such activities) in compliance with Applicable Law, including good laboratory practices (GLP), good clinical practices (GCP), and good manufacturing practices (GMP), in each case as applicable under the laws and regulations of the country and the state and local government wherein such activities are conducted or which are otherwise affected.

6.6. **Pharmacovigilance and Ionis Internal Oligonucleotide Safety Database**.

6.6.1. **Pharmacovigilance Agreement**. If, at any time during the Agreement Term, the Parties agree that it is necessary to enter into a separate pharmacovigilance agreement in order to fulfill their respective local and international regulatory reporting obligations to Regulatory Authorities and other Applicable Law, then the Parties will negotiate in good faith a pharmacovigilance agreement which is consistent with such reporting obligations and such other Applicable Law.

6.6.2. **Ionis Internal Oligonucleotide Safety Database.**

(a) Ionis maintains an internal database that includes information regarding the tolerability of its drug compounds, individually and as a class, including information discovered during non-clinical and clinical development (the "***Ionis Internal Oligonucleotide Safety Database***"). To the extent identified and collected by Novartis or its Affiliates, Novartis will [***] promptly provide Ionis with all material information concerning toxicology, pharmacokinetics, safety pharmacology study(ies) and adverse events directly related to the Licensed Products. Novartis may elect to provide such information in the form in which Novartis maintains such information for internal purposes. In addition, with respect to the Licensed Products, Novartis will provide Ionis with copies of Annual safety updates filed with each IND (*e.g.*, DSURs or IND annual reports) and the safety sections of any final Clinical Study reports within [***] following the date such information is submitted to the applicable Regulatory Authority, as applicable. Furthermore, Novartis will answer in a timely manner any follow-up questions reasonably requested by Ionis or its Affiliates to the extent such data and answers are reasonably available to Novartis. In addition, so long as Ionis does not disclose the identity of a Licensed Product or the identity of Novartis, its Affiliates or its Sublicensees, Ionis may disclose any such information to (i) Ionis' other partners pursuant to Section 6.6.2(b) (Ionis Internal Oligonucleotide Safety Database) below if such information is regarding class generic properties of Oligonucleotides, (ii) any other Third Party (other than a Regulatory Authority) that contributes to the populating of the Ionis Internal Oligonucleotide Safety Database, or (iii) a Regulatory Authority. Novartis will deliver all such information to Ionis for the Ionis Internal Oligonucleotide Safety Database to Ionis at 2855 Gazelle Court, Carlsbad, California 92010, Attention: Chief Medical Officer (or to such other address/contact designated in writing by Ionis). Novartis will [***] cause its Sublicensees to comply with this Section 6.6.2 (Ionis Internal Oligonucleotide Safety Database). At either Party's request, the Alliance Managers will use good faith efforts to establish mutually acceptable specific time periods for the provision of information under this Section 6.6.2 (Ionis Internal Oligonucleotide Safety Database).

(b) From time to time, Ionis utilizes the information in the Ionis Internal Oligonucleotide Safety Database to conduct analyses to keep Ionis and its partners informed regarding class generic properties of Oligonucleotides, including with respect to safety. As such, if and when Ionis identifies safety or other related issues that may be relevant to a Licensed Product (including any potential class-related toxicity), Ionis will inform Novartis in a timely manner of such issues and, if requested, allow Novartis to review such issues and conclusions and allow Novartis the opportunity to review and align on safety statement and health authority submissions in a timely manner before release.

(c) During the Agreement Term, Novartis may submit written requests to Ionis for Ionis to have queries run of the Ionis Internal Oligonucleotide Safety Database relevant to the Licensed Products, and Ionis will [***] promptly cause such queries to be run and deliver to Novartis the results of such queries. Any information disclosed by a Party to the other Party under this Section 6.6.2 (Ionis Internal Oligonucleotide Safety Database) will be treated as Confidential Information of such Party in accordance with Article 12 (Confidentiality).

(d) To the extent any information required to be disclosed by Novartis to Ionis under this Section 6.6.2 (Ionis Internal Oligonucleotide Safety Database) is disclosed pursuant to a pharmacovigilance agreement entered into pursuant to Section 6.6.1 (Pharmacovigilance Agreement), such disclosure shall be deemed to satisfy the corresponding obligation under this Section 6.6.2 (Ionis Internal Oligonucleotide Safety Database).

ARTICLE 7
FINANCIAL PROVISIONS

7.1. **Upfront Fee**. In consideration of the licenses and rights granted to Novartis hereunder, Novartis will pay Ionis a non-refundable, non-creditable upfront payment of $60,000,000 no later than [***] (the "***Upfront Fee***").

7.2. **Payments for Development Activities**. Upon the designation of each of the [***] Development Candidates in accordance with Section 2.2.4 (Development Candidate Selection Process), Novartis will pay Ionis $[***]. Each payment is due within [***] after receipt by Novartis of an Invoice from Ionis for such amount, *provided* that such Invoice may not be provided earlier than the DC Selection Date for such Development Candidate. For clarity, the maximum amount payable under this Section 7.2 (Payments for Development Activities) is $[***].

7.3. **Milestone Payments for Achievement of Early Development Milestone Events**. In further consideration of the licenses and rights granted to Novartis hereunder, Novartis will pay Ionis each of the milestone payments set forth in TABLE 1 below upon the achievement of the corresponding development milestone event listed in TABLE 1 for [***] Licensed Products to achieve such milestone events:

TABLE 1	
Early Development Milestone Event	**Milestone Event Payment**
1. [***]	US$[***]
2. [***]	US$[***]

Each milestone payment set forth in TABLE 1 above will be paid [***] upon the achievement of the milestone event by [***] Licensed Product regardless of how many Licensed Products achieve such milestone event or how many times such Licensed Products achieve such milestone event. For clarity, the maximum aggregate milestone payments payable under TABLE 1 above if each early development milestone event is achieved [***] is $[***].

7.4. **Milestone Payments for First Achievement of Development Milestone Events**. In further consideration of the licenses and rights granted to Novartis hereunder, Novartis will pay Ionis each of the milestone payments set forth in TABLE 2 below upon the achievement of the corresponding development milestone event listed in TABLE 2 for a Licensed Product:

TABLE 2	
Development Milestone Event	**Milestone Event Payment**
1. [***]	US$[***]
2. (a) [***] or (b) [***]	US$[***]
3. [***]	US$[***]
4. [***]	US$[***]
5. [***]	US$[***]
6. [***]	US$[***]

Each milestone payment set forth in Table 2 above will be paid only once upon the first achievement of the milestone event by the applicable Licensed Product regardless of how many Licensed Products achieve such milestone event or how many times such Licensed Product achieves such milestone event. For clarity, the maximum aggregate milestone payments payable under Table 2 above if each development milestone event is achieved is $[***].

7.5. Milestone Payments for First Achievement of Sales Milestone Events. In further consideration of the licenses and rights granted to Novartis hereunder, on a Licensed Product-by-Licensed Product basis, Novartis will pay Ionis each of the sales milestone payments set forth in Table 3 below upon the achievement of the corresponding sales milestone event listed in Table 3 for a Licensed Product:

Table 3	
Annual Worldwide Net Sales Levels	**Milestone Payment**
Exceeding US$[***] in Annual Net Sales for a Licensed Product	US$[***]
Exceeding US$[***] in Annual Net Sales for a Licensed Product	US$[***]
Exceeding US$[***] in Annual Net Sales for a Licensed Product	US$[***]
Exceeding US$[***] in Annual Net Sales for a Licensed Product	US$[***]
Exceeding US$[***] in Annual Net Sales for a Licensed Product	US$[***]

Each milestone payment set forth in Table 3 above will be paid only once upon the first achievement of the milestone event by the applicable Licensed Product regardless of how many Licensed Products achieve such milestone event or how many times such Licensed Product achieves such milestone event. For clarity, the maximum aggregate milestone payments payable under Table 3 above if each sales milestone event is achieved is $[***].

7.6. Skipped Milestone Payments; Notice and Payment.

7.6.1. Except with respect to (a) the [***] milestone event in Table 2 above which is addressed in Section 7.6.2 and (b) the [***] milestone event in Table 2 above which [***], if a particular milestone event in Table 2 is not achieved by a Licensed Product, then upon achievement of a later milestone event in Table 2 by a Licensed Product, the milestone event payment applicable to such earlier milestone event will also be due. For example, if [***] without achieving the "[***]," then upon achieving the "[***]" milestone event, both the "[***]" and "[***]" milestone event payments are due.

7.6.2. If the [***] milestone event in Table 2 above is not achieved by a Licensed Product, but the [***] milestone event in Table 2 above is achieved by a Licensed Product with a [***], then, upon achievement of the [***] milestone event, the applicable payments for the [***] and [***] milestone events in Table 2 will both be due.

7.6.3. Each time a milestone event other than a sales milestone event set forth in Table 3 above is achieved under this Article 7 (Financial Provisions), Novartis will send Ionis a written notice thereof within [***] following the date of achievement of such milestone event and the applicable milestone payment is due within [***] after receipt by Novartis of an Invoice from Ionis for such amount, *provided* that such Invoice may not be provided before such notice. With respect to the achievement of any sales milestone event set forth in Table 3 above, Novartis will notify Ionis thereof concurrently with the provision of the Royalty Report for the relevant Calendar Quarter in which such sales milestone event was achieved, and the applicable milestone payment is due within [***] after receipt by Novartis of an Invoice from Ionis for such amount, *provided* that such Invoice may not be provided before receipt of such notice by Ionis.

7.7. Royalty Payments.

7.7.1. **Royalty**. In further consideration of the licenses and rights granted to Novartis hereunder, subject to the provisions of this Section 7.7.1 (Royalty) and Section 7.7.2 (Application of Royalty Rates), Novartis will pay to Ionis royalties on Annual worldwide Net Sales of Licensed Products sold by Novartis, its Affiliates or Sublicensees, on a country-by-country and Licensed Product-by-Licensed Product basis, in each case in the amounts as follows in Table 4 below:

	Table 4	
Royalty Tier	**Annual Worldwide Net Sales of such Licensed Product**	**Royalty Rate**
1	For the portion of Annual Worldwide Net Sales ≤ US$[***]	[***]%
2	For the portion of Annual Worldwide Net Sales > US$[***] but ≤ US$[***]	[***]%
3	For the portion of Annual Worldwide Net Sales > US$[***] but ≤ US$[***]	[***]%
4	For the portion of Annual Worldwide Net Sales > US$[***] but ≤ US$[***]	[***]%
5	For the portion of Annual Worldwide Net Sales > US$[***] but ≤ US$[***]	[***]%
6	For the portion of Annual Worldwide Net Sales > US$[***]	[***]%

Annual worldwide Net Sales will be calculated by taking the aggregate sum of Net Sales of a Licensed Product for all countries worldwide.

No royalties are due on Net Sales of Licensed Products arising from compassionate use and other programs providing for the delivery of a Licensed Product at or below cost. The sales of Licensed Products arising from named patient, compassionate use, or other similar programs will not be considered a First Commercial Sale for purposes of calculating the Royalty Term.

7.7.2. **Application of Royalty Rates**. All royalties set forth under Section 7.7.1 (Royalty) are subject to the provisions of this Section 7.7.2 (Application of Royalty Rates), and are payable as follows:

(a) **Royalty Term**. Novartis' obligation to pay Ionis the royalties pursuant to Section 7.7.1 (Royalty) above with respect to a Licensed Product will continue on a country-by-country and Licensed Product-by-Licensed Product basis from the date of First Commercial Sale of such Licensed Product in such country until the later of the date of expiration of (i) the last Valid Claim of a Licensed Patent, Jointly-Owned Program Patent, or Novartis Royalty Bearing Patent Covering the sale of such Licensed Product in such country, (ii) any Regulatory Exclusivity Period conferred by the applicable Regulatory Authority in such country with respect to such Licensed Product, and (iii) the [***] anniversary of the First Commercial Sale of such Licensed Product in such country (such royalty period, the "***Royalty Term***").

(b) **Know-How Royalty**. If a Licensed Product is sold in a country during the applicable Royalty Term at a time when there is no Valid Claim of a Licensed Patent, Jointly-Owned Program Patent, or Novartis Royalty Bearing Patent in such country that Covers the sale of such Licensed Product, then [***].

(c) **Generic Competition During the Royalty Term**. On a country-by-country and Licensed Product-by-Licensed Product basis, if at any time during the Royalty Term a Generic Product is sold in such country and the aggregate Net Sales of such Licensed Product in such country in any Calendar Quarter thereafter are at least [***]% lower as compared to the average quarterly Net Sales of such Licensed Product in such country during the last [***] Calendar Quarters immediately preceding the Calendar Quarter in which the Generic Product was first sold, then, following such reduction in Net Sales, the Net Sales of such Licensed Product in such country used for calculation of royalties pursuant to Section 7.7.1 (Royalty) shall be [***].

7.7.3. **Limitation on Aggregate Reduction for Novartis Royalties**. In no event will the aggregate royalty reductions under Section 7.7.2 (Application of Royalty Rates) and Section 7.9.4 (Right to Offset), alone or together, reduce the royalties payable to Ionis on Net Sales of a Licensed Product in any given Calendar Quarter by more than [***] of the applicable royalties that would otherwise be owed on such Net Sales in such Calendar Quarter without the reductions under Section 7.7.2 (Application of Royalty Rates) and Section 7.9.4 (Right to Offset). If Novartis would, but for the restriction set forth in this Section 7.7.3 (Limitation on Aggregate Reduction for Novartis Royalties), have the right to reduce the royalties due to Ionis for a Licensed Product in a Calendar Quarter by more than [***], then such unused reduction that may otherwise have been taken pursuant to Section 7.9.4 (Right to Offset) may be carried forward and used as a credit against royalties due to Ionis in one or more future Calendar Quarter(s) until such reduction is fully realized.

7.8. [***]. [***].

7.9. In-License Agreements.

7.9.1. **Existing In-License Agreements**. On a Licensed Product-by-Licensed Product basis, certain of the Licensed Technology Controlled by Ionis as of the Execution Date that may be licensed to Novartis under Section 5.1 (License Grants to Novartis) are in-licensed or were acquired by Ionis or its Affiliates under the agreements with Third Party licensors or sellers listed on Appendix 2 (Ionis In-License Agreements) (such license or purchase agreements being the "***Ionis In-License Agreements***"), and the payments set out on Appendix 2 (Ionis In-License Agreements) may become payable by Ionis or its Affiliates to such Third Parties under the Ionis In-License Agreements based on the Research, Development, or Commercialization of a Licensed Product by Novartis, its Affiliates or Sublicensees. Any such payment obligations set out on Appendix 2 (Ionis In-License Agreements) will be [***].

7.9.2. **New In-License Agreements**. Either Party will promptly provide written notice to the other Party of any Patent Rights or Know-How of a Third Party that it has identified and believes are [***] to Exploit a Development Candidate or Licensed Product, including in the case of Ionis, notice of any such Patent Rights or Know-How that it has identified and believes would constitute Necessary Platform IP (such Patent Rights and Know-How, "***Identified Rights***"). Ionis or its Affiliates will have the first right, but not the obligation, to negotiate with, and obtain a license from the Third Party Controlling Identified Rights that would have been considered Ionis Core Technology Patents, Ionis Manufacturing and Analytical Know-How, or Ionis Manufacturing and Analytical Patents had Ionis Controlled such Identified Rights on the Execution Date. If, however, Ionis and its Affiliates elect not to obtain such Identified Rights, Ionis will so notify Novartis within [***], and Novartis may obtain such Identified Rights. Novartis or its Affiliates will have the first right, but not the obligation, to negotiate with, and obtain a license from the Third Party Controlling Identified Rights other than those that would have been considered Ionis Core Technology Patents, Ionis Manufacturing and Analytical Know-How, or Ionis Manufacturing and Analytical Patents had Ionis Controlled such Identified Rights on the Execution Date. If, however, Novartis and its Affiliates elect not to obtain such Identified Rights, Novartis will so notify Novartis within [***], and Ionis may obtain such Identified Rights.

7.9.3. **Ionis In-License Agreements**.

(a) **New Necessary Platform IP**. If (i) Ionis obtains Identified Rights that would have been considered Ionis Core Technology Patents, Ionis Manufacturing and Analytical Know-How, or Ionis Manufacturing and Analytical Patents had Ionis Controlled such Identified Rights on the Execution Date and (ii) such Identified Rights are [***] (such Identified Rights, "***Necessary Platform IP***"), then such Necessary Platform IP will be included in the license granted to Novartis under Section 5.1 (License Grants to Novartis) and any and all costs arising under such Third Party agreement as they apply to a Licensed Product will be [***].

(b) **Other Identified Rights**. If Ionis obtains Identified Rights that are not Necessary Platform IP, then Ionis will include such Identified Rights in the license granted to Novartis under Section 5.1 (License Grants to Novartis) only [***] such Identified Right (or that, prior to the applicable transaction with Ionis or its Affiliates, [***]) to license or acquire such Identified Rights; *provided* that, if the applicable Identified Rights relate to both a Licensed Compound or Licensed Product and one or more other programs of Ionis or its Affiliates ("***Shared Ionis Identified Rights***"), then any such [***] will be [***], and Novartis will [***].

7.9.4. **Right to Offset**. If Novartis obtains a license or other rights to any Identified Rights for a Development Candidate or Licensed Product or [***] for obtaining such Identified Rights pursuant to Section 7.9.3(b) (Other Identified Rights) and such rights are necessary to Exploit a Development Candidate or Licensed Product, then Novartis may offset against any royalties payable to Ionis pursuant to Section 7.7.1 (Royalty) for the Exploitation of such Licensed Product in a Calendar Quarter an amount equal to [***]% of any amounts paid to such Third Party or Ionis, as applicable, with respect to the Identified Rights; *provided* that, if the applicable Identified Rights relate to both a Development Candidate or Licensed Product and one or more other programs of Novartis or its Affiliates ("***Shared Novartis Identified Rights***"), then [***], and Novartis will only be allowed to exercise the offset set forth in this Section 7.9.4 (Right to Offset) for the amount that is allocated to the applicable Development Candidate or Licensed Products. Any reductions pursuant to this Section 7.9.4 (Royalty Offset) will be [***] pursuant to Section 7.7.2 (Application of Royalty Rates).

7.9.5. **Third Party IP Dispute**. If Ionis does not agree that certain intellectual property acquired by Novartis constitutes Identified Rights that Novartis has the right to offset costs for in accordance with Section 7.9.4 (Right to Offset) or if the Parties do not agree on whether Identified Rights obtained by Ionis are Necessary Platform IP or the allocation of [***] payable in respect of Shared Ionis Identified Rights or the Shared Novartis Identified Rights, then, in any such case, the disputing Party will send written notice to such effect to the other Party and the Parties will engage a mutually agreed upon independent Third Party intellectual property lawyer with expertise in the patenting of Oligonucleotides, and appropriate professional credentials in the relevant jurisdiction, or other applicable expertise, to resolve such dispute. The determination of the Third Party expert engaged under the preceding sentence will be binding on the Parties solely for purposes of, as applicable, determining (a) [***], (b) [***] or (c) [***]. The costs of any Third Party expert engaged under this Section 7.9.5 (Right to Offset) will be paid by the Party against whose position the Third Party lawyer's determination is made.

7.10. Reimbursement for Ionis' Time. After the first [***] hours of Ionis' time for any (a) technology transfer assistance provided by Ionis in accordance with Section 2.7.1 (Responsibility During the Research Term) and Section 5.9 (Technology and Information Transfer), and (b) any regulatory assistance provided in accordance with Section 6.4.1 (Regulatory Responsibilities; Major Regulatory Submissions), then Novartis will reimburse Ionis for the FTE Costs [***] within [***] from the date an Invoice is received by Novartis [***]; *provided* that before Ionis commences work for which it intends to invoice Novartis, Novartis and Ionis will agree to the scope of Ionis' work and a budget for such work that will include Ionis' good faith estimate of the [***].

7.11. Payments.

7.11.1. **Royalty Reports and Payment**.

(a) Beginning with the Calendar Quarter in which the First Commercial Sale for a Licensed Product is made and for each Calendar Quarter thereafter during the Royalty Term, Novartis will provide Ionis with a report summarizing Net Sales in USD and local currency for Licensed Products during the relevant Calendar Quarter and the calculation of royalties and sales milestones (if applicable) due thereon, including country and units, within [***] following the end of each such Calendar Quarter (each a "***Royalty Report***"). If no royalties are payable in respect of a given Calendar Quarter, Novartis will nevertheless submit a Royalty Report to Ionis so indicating together with an explanation as to why no such royalties are payable. After its receipt of such Royalty Report, Ionis will submit an Invoice to Novartis for the corresponding royalty payment. Novartis will pay to Ionis such amount within [***] after receipt by Novartis of such Invoice. For the avoidance of doubt, Royalty Reports and any feedback provided by Novartis pursuant to paragraph (b) are Novartis' Confidential Information subject to the terms and conditions of this Agreement.

(b) Beginning with the Calendar Quarter in which the First Commercial Sale for a Licensed Product is made and for each Calendar Quarter thereafter during the Royalty Term, [***].

7.11.2. **Mode of Payment**. All payments under this Agreement will be (a) payable in full in U.S. dollars, regardless of the country(ies) in which sales are made, (b) made by wire transfer of immediately available funds to an account designated by Ionis in writing, and (c) non-creditable (except (i) as otherwise provided in Section 4.3 (Acquisition of a Competitive Compound) or Section 7.12 (Audits) and (ii) [***]. All payments under this Agreement shall be made in US Dollars. Any sales incurred in a currency other than US Dollars shall be converted to the US Dollar equivalent using [***] for the conversion of foreign currency sales into US Dollars. [***]. In addition, an Invoice will be deemed duly delivered by a Party to the other Party under this Agreement when delivered electronically to such other Party and, if so delivered electronically, will be promptly followed by delivery of a paper copy of such Invoice.

7.11.3. **Records Retention**. Commencing with the First Commercial Sale of a Licensed Product, Novartis will keep complete and accurate records pertaining to the Net Sales of Licensed Products for the [***] in accordance with Novartis' Accounting Standards.

7.12. Audits.

7.12.1. During the Agreement Term and for a period of [***] thereafter, at [***] expense and upon written notice to Novartis, Novartis will permit an independent accounting firm of internationally recognized standing (the "***Auditor***") appointed by Ionis and reasonably acceptable to Novartis, at reasonable times and upon reasonable notice, but in no case more than [***] per Calendar Year and not more frequently than [***] with respect to records covering any specific period of time, to examine such records as may be necessary for the sole purpose of verifying the accrual of any milestone payments, the calculation and reporting of Net Sales, and the correctness of any milestone or royalty payment made under this Agreement; *provided* that the Auditor shall only be entitled to audit Novartis' records from the [***] prior to the Calendar Year in which the audit request is made.

7.12.2. As a condition to and prior to examining any of Novartis' records, such Auditor will sign a nondisclosure agreement reasonably acceptable to Novartis in form and substance. Any and all of Novartis' records examined by such independent certified public accountant will be deemed Novartis' Confidential Information. Novartis and its Affiliates shall make their records available for inspection by such Auditor during regular business hours at such place or places where such records are customarily kept, upon receipt of reasonable advance notice from Ionis.

7.12.3. Upon completion of the audit, the Auditor will provide both Novartis and Ionis with a written audit report disclosing whether the milestone or royalty payments made by Novartis are correct ("***Audit Report***"). The Auditor shall have the right to disclose to Ionis only its conclusions regarding any payments owed under this Agreement and all information received and all information learned in the course of any audit or inspection will be deemed Novartis' Confidential Information. Before it is considered final, Novartis shall have the right to [***] following receipt of such Audit Report. Novartis will provide Ionis and the Auditor with [***].

7.12.4. If, as a result of any inspection of Novartis' books and records, it is [***] that Novartis' payments under this Agreement were more or less than the milestone or royalty amount which should have been paid, then the relevant Party will make all payments required to be made by paying the other Party the difference between such amounts to eliminate any discrepancy revealed by said inspection within [***] of receiving the final Audit Report, with interest calculated in accordance with Section 7.14 (Interest) solely in the event the paying Party is responsible for the discrepancy; *provided*, *however*, that any such payment by Ionis to Novartis will be [***]. Ionis will pay for such audit, except that if Novartis is found to have underpaid Ionis by more than [***]% of the amount that should have been paid for the audited period, Novartis will reimburse Ionis [***] charged by the Auditor for the audit.

7.13. Taxes.

7.13.1. **Taxes on Income**. Each Party alone will be solely responsible for paying any and all taxes (other than withholding taxes required by Applicable Law to be paid by Novartis or Ionis (as the case may be)) levied on account of, or measured in whole or in part by reference to, the income of such Party.

7.13.2. **Indirect Taxes**. All amounts mentioned in this Agreement are exclusive of Indirect Taxes. If any Indirect Taxes are chargeable in respect of any payments, the paying Party will pay such Indirect Taxes at the applicable rate in respect of such payments following receipt, where applicable, of an Indirect Taxes invoice in the appropriate form issued by the receiving Party in respect of those payments. The Parties will issue invoices for all amounts payable under this Agreement consistent with Indirect Tax requirements and irrespective of whether the sums may be netted for settlement purposes. The Parties agree to reasonably cooperate to provide any information required by the Party pursuing a refund of Indirect Taxes paid.

7.13.3. **Withholding Tax**. To the extent the paying Party is required to deduct and withhold taxes on any payment under Applicable Law, including extra-territorial taxation, the paying Party will be authorized to deduct the withholding tax from such payments and will pay the amounts of such taxes to the proper Governmental Authority for the account of the receiving Party and remit the net amount to the receiving Party in a timely manner. The paying Party will promptly furnish the receiving Party with proof of payment of such taxes. If documentation is necessary in order to secure an exemption from, or a reduction in, any withholding taxes, the Parties will provide such documentation to the extent they are entitled to do so. The Parties will make all reasonable efforts to obtain relief or reduction of all withholding taxes under Applicable Law, including applicable tax treaties and including but not limited to the submission or issuance of requisite forms and information. If a special procedure is required for treaty relief by Applicable Law, such treaty relief will only be taken into account if the non-paying Party submits an exemption certificate requested by the paying Party to the paying Party in accordance with the requirements of Applicable Law on or prior to the time of the payment to the non-paying Party. If no withholding tax deduction has been made on the payments to the non-paying Party under this Agreement, but a Governmental Authority subsequently takes the position that a withholding tax deduction should have been made, including extra-territorial taxation, the non-paying Party shall provide, at its own expense, all reasonable support to the paying Party to obtain relief or reduction of the withholding taxes under the Applicable Law, including applicable tax treaties and including but not limited to the submission or issuance of requisite forms and information, and the Parties will bear such liability (and reimburse one another as necessary) in a manner consistent with that which would have resulted had the tax been originally withheld. Any refunds of withholding taxes that are granted to the non-paying Party by the relevant Governmental Authority and which would cause the non-paying Party to receive payments in excess of that which the paying Party would owe under this Agreement, including with interest calculated in accordance with Section 7.14 (Interest), shall be paid to the paying Party by the non-paying Party.

7.13.4. **Tax Cooperation**. To the extent that the paying Party is required to deduct and withhold taxes on any payments under this Agreement, the paying Party will pay the amounts of such taxes to the proper Governmental Authority in a timely manner and promptly transmit to the non-paying Party an official tax certificate or other evidence of such withholding sufficient to enable the non-paying Party to claim such payments of taxes. The paying Party will request from the non-paying Party any tax forms that may be reasonably necessary in order for the paying Party not to withhold tax or will withhold tax at a reduced rate under an applicable bilateral income tax treaty, if appropriate under the Applicable Law. Each Party will provide the other with reasonable assistance to enable the recovery, as permitted by Applicable Law, of withholding taxes resulting from payments made under this Agreement, such recovery to be for the benefit of the Party who would have been entitled to receive the money but for the application of withholding tax under this Section 7.13 (Taxes).

The provisions of this Section 7.13 (Taxes) are to be read in conjunction with the provisions of Section 13.4 (Assignment and Successors) below.

7.14. **Interest**. Any undisputed payments to be made hereunder that are not paid on or before the date such payments are due under this Agreement, and any payments that are pending resolution of any dispute unless the dispute is ruled in favor of the paying Party, will bear interest at a rate per annum equal to the lesser of (a) [***]% above the six-month CME Term Secured Overnight Financing Rate (USD SOFR) from the date on which such payment would have been first due until the date of payment or (b) the maximum rate permissible under Applicable Law.

7.15. **No Estimate, Projection, Representation or Warranty**. Novartis and Ionis acknowledge and agree that nothing in this Agreement shall be construed as representing an estimate or projection of anticipated achievement of any milestone events with respect to or sales of any Licensed Product, and that the milestones and Net Sales levels set forth above are only intended to define the milestone payment and royalty obligations to Ionis in the event such milestones or Net Sales levels are achieved. Neither Ionis nor Novartis makes any representation or warranty, either express or implied, that it will be able to successfully Research, Develop or Commercialize any Licensed Product or, if Commercialized, that any particular Net Sales of such Licensed Product will be achieved.

ARTICLE 8
INTELLECTUAL PROPERTY

8.1. **Joint Patent Committee**.

8.1.1. No later than [***] after the Effective Date, the Parties will establish a "***Joint Patent Committee***" or "***JPC***". The JPC will serve as the primary contact and forum for discussion between the Parties with respect to intellectual property matters arising under this Agreement, and will cooperate with respect to the activities set forth in this Section 8.1 (Joint Patent Committee). If the JPC dissolves, each Party may designate a patent attorney who will be responsible for intellectual property matters under this Agreement. A strategy will be discussed with regard to (a) prosecution and maintenance, defense and enforcement of Ionis Product-Specific Patents that are licensed to Novartis under Section 5.1 (License Grants to Novartis) and Novartis Product-Specific Patents, including strategies in relation to the Unified Patent Court and Unitary Patent in Europe, such as but not limited to the filing or withdrawing of an opt-out of the respective European patents and validating as a Unitary Patent or a classical European Patent, (b) defense against allegations of infringement of Third Party Patent Rights, (c) licenses to Third Party Patent Rights or Know-How, and (d) the timing and subject matter of any potential publications regarding a Licensed Product, in each case to the extent such matter would be reasonably likely to have a material impact on this Agreement or the licenses granted hereunder, which strategy will be considered in good faith by the Party entitled to prosecute, enforce and defend such Patent Rights, as applicable, hereunder, but will not be binding on such Party. Upon expiration of the Research Term, each Party will no longer have the obligation, but will continue to have the right, to participate in the JPC, *provided* that, if requested by Novartis, Ionis shall consider in good faith and not unreasonably refuse to participate in the JPC.

8.1.2. The JPC will comprise an equal number of at most three members from each Party. The JPC will meet as often as agreed by them (and at least semi-Annually), to discuss matters arising out of the activities set forth in this Section 8.1 (Joint Patent Committee). The JPC will determine the JPC operating procedures at its first meeting, including the JPC's policies for replacement of JPC members, and the location of meetings, which will be codified in the written minutes of the first JPC meeting. The Parties may escalate issues to the Executives for input and resolution pursuant to Section 13.1 (Dispute Resolution). Each Party's representatives on the JPC will consider comments and suggestions made by the other in good faith. Each Party will bear their own cost of participation on the JPC.

8.2. **Ownership**.

8.2.1. **Licensed Technology and Novartis Technology**. As between the Parties, Ionis will own and retain all of its rights, title and interest in and to the Licensed Know-How and Licensed Patents and Novartis will own and retain all of its rights, title and interest in and to the Novartis Know-How and Novartis Patents, subject to any rights or licenses expressly granted by one Party to the other Party under this Agreement.

8.2.2. **Program Technology**.

(a) **Allocation of Ownership**. As between the Parties, Novartis is the sole owner of any Know-How discovered, invented or created solely by or on behalf of Novartis or its Affiliates under or in connection with this Agreement ("***Novartis Program Know-How***") and any Patent Rights that claim or cover Novartis Program Know-How ("***Novartis Program Patents***" and together with the Novartis Program Know-How, the "***Novartis Program Technology***"), and will retain all of its rights, title and interest thereto, subject to any rights or licenses expressly granted by Novartis to Ionis under this Agreement. As between the Parties, Ionis is the sole owner of any Know-How discovered, invented or created solely by or on behalf of Ionis or its Affiliates under or in connection with this Agreement ("***Ionis Program Know-How***") and any Patent Rights that claim or cover such Know-How ("***Ionis Program Patents***" and together with the Ionis Program Know-How, the "***Ionis Program Technology***"), and will retain all of its rights, title and interest thereto, subject to any rights or licenses expressly granted by Ionis to Novartis under this Agreement. Any Know-How discovered, invented or created jointly under or in connection with this Agreement by or on behalf of both Parties or their respective Affiliates or Third Parties acting on their behalf ("***Jointly-Owned Program Know-How***"), and any Patent Rights that claim or cover such Jointly-Owned Program Know-How ("***Jointly-Owned Program Patents***", and together with the Jointly-Owned Program Know-How, the "***Jointly-Owned Program Technology***"), are owned jointly by Novartis and Ionis on an equal and undivided basis, including all rights, title and interest thereto, subject to any rights or licenses expressly granted by one Party to the other Party under this Agreement.

(b) **Practice of the Jointly-Owned Program Technology**. Except as expressly provided in this Agreement, neither Party will have any obligation to account to the other for profits with respect to, or to obtain any consent of the other Party to license or Exploit, the Jointly-Owned Program Technology by reason of joint ownership thereof, and each Party hereby waives any right it may have under the laws of any jurisdiction to require any such consent or accounting. The Parties acknowledge and agree that either Party may, subject to the exclusivity covenants in Section 4.1 (Exclusivity Covenants), freely utilize or otherwise Exploit any Jointly-Owned Program Technology without recourse, accounting or any other obligations to the other Party, except as expressly set out in this Agreement.

(c) **Disclosure**. Each Party will promptly disclose to the other Party in writing, and will cause its Affiliates to so disclose, the discovery, invention or creation of any Novartis Program Technology, Ionis Program Technology or Jointly-Owned Program Technology. The Novartis Program Patents, Ionis Program Patents and Jointly-Owned Program Patents are collectively referred to herein as the "***Program Patents***," the Novartis Program Know-How, Ionis Program Know-How and Jointly-Owned Program Know-How are collectively referred to herein as the "***Program Know-How***," and Novartis Program Technology, Ionis Program Technology and Jointly-Owned Program Technology are collectively referred to herein as "***Program Technology***."

8.2.3. **Inventorship**. Determination of inventorship will be made by the JPC in accordance with US patent laws. In case of a dispute in the JPC (or otherwise between Ionis and Novartis) over inventorship of any Program Patents, if the JPC (or the Parties' respective patent representatives if no JPC exists) cannot resolve such dispute, such dispute will be resolved by independent patent counsel not engaged or regularly employed in the past [***] years by either Party (or its Affiliates) and reasonably acceptable to both Parties. The decision of such independent patent counsel will be binding on the Parties. Expenses of such patent counsel will be shared equally by the Parties.

8.3. Filing, Prosecution and Maintenance of Patents.

8.3.1. **General Principles**.

(a) **Ionis Core Technology Patents and Ionis Manufacturing and Analytical Patents**. Ionis will control and be responsible for Prosecuting and Maintaining (i) the Ionis Core Technology Patents, and (ii) the Ionis Manufacturing and Analytical Patents, including any Jointly-Owned Program Patents in (i) or (ii).

(b) **Product-Specific Patents**. Novartis will control and be responsible for Prosecuting and Maintaining all Product-Specific Patents (including any Jointly-Owned Program Patents, Ionis Program Patents, and Novartis Program Patents, in each case, that are Product-Specific Patents).

(c) **Other Jointly-Owned Program Patents**. The Parties will decide through the JPC the appropriate Party to control and be responsible for Prosecuting and Maintaining all other Jointly-Owned Program Patents not provided for above.

(d) **Other Program Patents**. (i) Novartis will control and be responsible for Prosecuting and Maintaining all Novartis Program Patents and (ii) Ionis will control and be responsible for Prosecuting and Maintaining all Ionis Program Patents, in each case ((i) and (ii)) other than Product-Specific Patents.

8.3.2. **Other Matters Pertaining to Prosecution and Maintenance of Patents**.

(a) Each Party will keep the other Party informed through the JPC as to material developments with respect to the Prosecution and Maintenance of the Product-Specific Patents or Jointly-Owned Program Patents for which such Party has responsibility for Prosecution and Maintenance pursuant to Section 8.3.1 (General Principles) or this Section 8.3.2 (Other Matters Pertaining to Prosecution and Maintenance of Patents), including by providing copies of any office actions or office action responses or other correspondence that such Party provides to or receives from any patent office, including notice of all interferences, reissues, re-examinations, inter partes reviews, post-grant reviews, oppositions or requests for patent term extensions, and all patent-related filings, and by providing the other Party the timely opportunity to have reasonable input into the strategic aspects of such Prosecution and Maintenance.

(b) Each Party will fully cooperate with the other in connection, as necessary, in Prosecuting and Maintaining the Product-Specific Patents or Jointly-Owned Program Patents for which such Party has responsibility pursuant to Section 8.3.1 (General Principles) or this Section 8.3.2 (Other Matters Pertaining to Prosecution and Maintenance of Patents), in relation to the Unified Patent Court and Unitary Patent in Europe, including by providing access to relevant persons and executing all documentation reasonably requested by a Party within the timeframe reasonably requested by the Party.

(c) If Novartis elects (i) not to file and prosecute patent applications for a Patent Right Novartis is responsible for Prosecuting and Maintaining under Section 8.3.1(b) (Product-Specific Patents) above ("***Novartis-Prosecuted Patents***") in a particular country, (ii) not to continue the prosecution (including any interferences, oppositions, reissue Proceedings, re-examinations, and patent term extensions, adjustments, and restorations) or maintenance of any Novartis-Prosecuted Patent in a particular country, or (iii) not to file and prosecute patent applications for the Novartis-Prosecuted Patent in a particular country following a written request from Ionis to file and prosecute in such country, then Novartis will so notify Ionis promptly in writing of its intention (including a reasonably detailed rationale for doing so) with sufficient time to enable Ionis to meet any deadlines by which an action must be taken to establish or preserve any such Patent Right in such country; and Ionis will have the right, but not the obligation, to file, prosecute, maintain, enforce or otherwise pursue such Novartis-Prosecuted Patent in the applicable country at its own expense with counsel of its own choice. In such case, Novartis will cooperate with Ionis to file for, or continue to Prosecute and Maintain or enforce, or otherwise pursue such Novartis-Prosecuted Patent in such country in Ionis' own name, but only to the extent that Novartis is not required to take any position with respect to such abandoned Novartis-Prosecuted Patent that would be reasonably likely to adversely affect the scope, validity or enforceability of any of the other Patent Rights being prosecuted and maintained by Novartis under this Agreement. Notwithstanding anything to the contrary in this Agreement, if Ionis assumes responsibility for the Prosecution and Maintenance of any such Novartis-Prosecuted Patent under this Section 8.3.2(b) (Other Matters Pertaining to Prosecution and Maintenance of Patents), Ionis will have no obligation to notify Novartis if Ionis intends to abandon such Novartis-Prosecuted Patent.

(d) The Parties, through the JPC, will cooperate in good faith to determine if and when any divisional or continuation applications will be filed with respect to any Jointly-Owned Program Patents or Product-Specific Patents, and where a divisional or continuation patent application filing would be practical and reasonable, then such a divisional or continuation filing will be made.

(e) If the Party responsible for Prosecution and Maintenance pursuant to Section 8.3.1 (General Principles) intends to abandon a Jointly-Owned Program Patent (other than a Jointly-Owned Program Patent that is Novartis-Prosecuted Patent, which is covered under Section 8.3.2(b) (Other Matters Pertaining to Prosecution and Maintenance of Patents) above) without first filing a continuation or substitution, then such Party will notify the other Party of such intention at least [***] before such Jointly-Owned Program Patent will become abandoned, and such other Party will have the right, but not the obligation, to assume responsibility for the Prosecution and Maintenance thereof at its own expense (subject to Section 8.4 (Patent Costs)) with counsel of its own choice, in which case the abandoning Party will, and will cause its Affiliates to, assign to the other Party (or, if such assignment is not possible, grant a fully-paid exclusive license in) all of their rights, title and interest in and to such Jointly-Owned Program Patents. If a Party assumes responsibility for the Prosecution and Maintenance of any such Jointly-Owned Program Patents under this Section 8.3.2(e) (Other Matters Pertaining to Prosecution and Maintenance of Patents), such Party will have no obligation to notify the other Party of any intention of such Party to abandon such Jointly-Owned Program Patents.

8.4. Patent Costs. Except as set forth in Section 8.3.2 (Other Matters Pertaining to Prosecution and Maintenance of Patents) and this Section 8.4 (Patent Costs), each Party will be responsible for all Patent Costs incurred by such Party prior to and after the Effective Date in all countries designated by it in the Prosecution and Maintenance of Patent Rights for which such Party is responsible under Article 8 (Intellectual Property). Unless the Parties agree otherwise, Ionis and Novartis will [***] ([***]) the Patent Costs associated with the Prosecution and Maintenance of Jointly-Owned Program Patents; *provided* that, either Party may decline to pay its share of costs for filing, prosecuting and maintaining any Jointly-Owned Program Patents in a particular country or particular countries, in which case the declining Party will, and will cause its Affiliates to, assign to the other Party (or, if such assignment is not possible, grant a fully-paid exclusive license in) all of their rights, titles and interests in and to such Jointly-Owned Program Patents (as applicable) and, if Novartis' is the declining Party, then such Patent Right will no longer be a Licensed Patent under this Agreement.

8.5. Defense of Claims Brought by Third Parties; Oppositions.

8.5.1. **Defense of Third Party Claims**. If a Third Party initiates a Proceeding claiming a Patent Right owned by or licensed to such Third Party is infringed by the Development, Manufacture or Commercialization of any Licensed Product, then, subject to Section 10.4.1 (Control of the Defense), Novartis will have the first right, but not the obligation, to defend against any such Proceeding at its sole cost and expense. If Novartis elects to defend against such Proceeding, then Novartis will have the sole right to direct the defense and to elect whether to settle such claim (but only with the prior written consent of Ionis, not to be unreasonably withheld, conditioned, or delayed). Ionis will reasonably assist Novartis in defending such Proceeding. Novartis will keep Ionis apprised of the progress of such Proceeding. If Novartis elects not to defend against a Proceeding, then Novartis will so notify Ionis in writing within [***] after Novartis first receives written notice of the initiation of such Proceeding, and Ionis will have the right, but not the obligation, to defend against such a Proceeding at its sole cost and expense and thereafter Ionis will have the sole right to direct the defense thereof, including the right to settle such claim (but only with the prior written consent of Novartis, which consent will not be unreasonably withheld, delayed or conditioned). In any event, the Parties will reasonably assist each other and cooperate in any such Proceedings at the other Party's request and expense. Each Party may at its own expense and with its own counsel join any defense initiated or directed by the other Party under this Section 8.5 (Defense of Claims Brought by Third Parties; Oppositions). Each Party will provide the other Party with prompt written notice of the commencement of any such Proceeding under this Section 8.5 (Defense of Claims Brought by Third Parties; Oppositions), and such Party will promptly furnish the other Party with a copy of each communication relating to the alleged infringement that is received by such Party.

8.5.2. **Interferences, Reissues, Re-Examinations and Oppositions**. If a Third Party initiates a Proceeding related to an interference, reissue, re-examination, inter partes review, post-grant review or opposition of any Ionis Product-Specific Patent, then Novartis will, at Novartis' expense, by written notice to Ionis either (a) control the defense of such Proceeding (including the right to elect whether to settle such Proceeding), or (b) have Ionis control the defense of such Proceeding. If Novartis makes no such election within [***], then Ionis will have the right, but not the obligation, to control the defense of such Proceeding and Ionis and Novartis will [***]. The Party not defending such Proceeding will reasonably assist the other Party and cooperate in any such litigation at the defending Party's request and expense. Each Party may at its own expense and with its own counsel join any defense initiated or directed by the other Party under this Section 8.5 (Defense of Claims Brought by Third Parties; Oppositions). Each Party will provide the other Party with prompt written notice of the commencement of any such Proceeding under this Section 8.5 (Defense of Claims Brought by Third Parties; Oppositions), and such Party will promptly furnish the other Party with a copy of each communication relating to the alleged infringement that is received by such Party.

8.6. Enforcement of Patents Against Competitive Infringement. With respect to infringement, unauthorized use, or threatened infringement or such other activity by a Third Party of any Product-Specific Patents, Jointly-Owned Program Patents, or Ionis Core Technology Patents by reason of the development, manufacture, use or commercialization of a product that is designed to bind to the RNA encoding APO(a) ("***Competitive Infringement***"), the Parties will handle such Competitive Infringement in accordance with this Section 8.6 (Enforcement of Patents Against Competitive Infringement).

8.6.1. **Duty to Notify of Competitive Infringement**. If either Party learns of a Competitive Infringement by a Third Party, such Party will promptly notify the other Party in writing and will provide such other Party with available evidence of such Competitive Infringement; *provided, however*, that for cases of Competitive Infringement under Section 8.6.6 (35 USC 271(e)(2) Infringement) below, such written notice will be given within 10 calendar days.

8.6.2. **Control of Competitive Infringement Proceedings**. For any Competitive Infringement, Novartis will have the first right, but not the obligation, to institute, prosecute, and control a Proceeding to enforce any (a) Product-Specific Patents, (b) Jointly-Owned Program Patents, or (c) Ionis Core Technology Patents, in each case ((a)-(c)), with respect thereto by counsel of its own choice at its own expense, and Ionis will have the right, at its own expense, to be represented in that action by counsel of its own choice (but, for clarity, Novartis will have the right to control such litigation), including deciding on any litigation strategy and selecting the Licensed Patent(s) and jurisdictions for enforcement of such Licensed Patent(s), *provided*, that, in the case of a Competitive Infringement of Ionis Core Technology Patents, Novartis shall only have such first right to institute, prosecute, and control a Proceeding to enforce such Ionis Core Technology Patents so long as Novartis also enforces Patent Rights Controlled by Novartis that Cover the relevant Licensed Product, if any. If Novartis fails to initiate a Proceeding (i) within a period of [***] after receipt of written notice of such Competitive Infringement (subject to a [***] extension to conclude negotiations, if Novartis has commenced good faith negotiations with an alleged infringer for elimination of such Competitive Infringement within such [***] period), or (ii) prior to [***] before the time limit, if any, set forth in the appropriate Laws and regulations for the filing of such actions, whichever comes first, then, unless [***], Ionis will have the right to initiate and control a Proceeding with respect to such Competitive Infringement by counsel of its own choice, and Novartis will have the right to be represented in any such action by counsel of its own choice at its own expense (but, for clarity, Ionis will have the right to control such litigation); *provided*, *however*, that if Novartis notifies Ionis in writing prior to [***] before such time limit for the filing of any such action that Novartis intends to file such action before the time limit, then Novartis shall be obligated to file such action before the time limit, and Ionis will not have the right to bring and control such action.

8.6.3. **Joinder; Cooperation**.

(a) If a Party initiates a Proceeding in accordance with this Section 8.6 (Enforcement of Patents Against Competitive Infringement), the other Party agrees to be joined as a party plaintiff where necessary and to give the first Party reasonable assistance and authority to file and prosecute the Proceeding. Subject to Section 8.6.4 (Share of Recoveries), each Party will bear the costs and expenses it incurred pursuant to this Section 8.6.3(a) (Joinder; Cooperation); *provided* that Novartis will only be requested to join such a Proceeding if such Proceeding relates to a Patent Right or Licensed Product licensed to Novartis under Section 5.1 (License Grants to Novartis).

(b) If one Party initiates a Proceeding in accordance with this Section 8.6.3 (Joinder; Cooperation), the other Party may join such Proceeding as a party plaintiff where necessary for such other Party to seek lost profits with respect to such infringement.

8.6.4. **Share of Recoveries**. Any damages or other monetary awards recovered with respect to a Proceeding brought pursuant to Section 8.5 (Defense of Claims Brought by Third Parties; Oppositions) or this Section 8.6 (Enforcement of Patents Against Competitive Infringement) will be shared as follows:

(a) the amount of such recovery will first be applied to the Parties' reasonable Out-of-Pocket costs incurred in connection with such Proceeding (which amounts will be allocated *pro rata* if insufficient to cover the totality of such expenses); then

(b) any remaining proceeds will be allocated as follows: (i) if Novartis initiates or controls the defense of the Proceeding pursuant to Section 8.5.1 (Defense of Third Party Claims) or Section 8.6.2 (Control of Competitive Infringement Proceedings), [***], or (ii) if Ionis initiates or controls the defense of the Proceeding, [***].

8.6.5. **Settlement**. Notwithstanding anything to the contrary in this Article 8 (Intellectual Property), neither Party may enter a settlement, consent judgment or other voluntary final disposition of a suit under this Article 8 (Intellectual Property) that disclaims, limits the scope of, admits the invalidity or unenforceability of, or grants a license, covenant not to sue or similar immunity under a Patent Right Controlled by the other Party without first obtaining the written consent of the Party that Controls the relevant Patent Right.

8.6.6. **35 USC 271(e)(2) Infringement**. Notwithstanding anything to the contrary in this Section 8.6 (Enforcement of Patents Against Competitive Infringement), for a Competitive Infringement under 35 USC 271(e)(2), the time period set forth in Section 8.6.2 (Control of Competitive Infringement Proceedings) during which a Party will have the initial right to bring a Proceeding will be shortened to a total of 25 calendar days, so that, to the extent the other Party has the right, pursuant to such Section to initiate a Proceeding if the first Party does not initiate a Proceeding, such other Party will have such right if the first Party does not initiate a Proceeding within 25 calendar days after such first Party's receipt of written notice of such Competitive Infringement.

8.7. Other Infringement – Jointly-Owned Program Patents. With respect to the infringement of a Jointly-Owned Program Patent which is not a Competitive Infringement, the Parties will cooperate in good faith to bring suit together against such infringing party or the Parties may decide to permit one Party to solely bring suit. Any damages or other monetary awards recovered with respect to a Proceeding brought pursuant to this Section 8.7 (Other Infringement – Jointly-Owned Program Patents) will be shared as follows: (a) the amount of such recovery will first be applied to the Parties' reasonable Out-of-Pocket costs incurred in connection with such Proceeding (which amounts will be allocated *pro rata* if insufficient to cover the totality of such expenses); (b) (i) if the Parties jointly initiate a Proceeding pursuant to this Section 8.7 (Other Infringement – Jointly-Owned Program Patents), [***]; and (ii) if only one Party initiates the Proceeding pursuant to this Section 8.7 (Other Infringement – Jointly-Owned Program Patents), [***]. Notwithstanding the provision of Section 8.6.4 (Share of Recoveries) the remaining proceeds contemplated under this Section 8.7 (Other Infringement – Jointly-Owned Program Patents), [***].

8.8. Patent Listing. Novartis will promptly, accurately and completely list, with the applicable Regulatory Authorities during the Agreement Term, all applicable Patent Rights for a Licensed Product that such Party intends to, or has begun to Commercialize, and that have become the subject of a Regulatory Approval, such listings include all so-called Orange Book listings required under the Hatch Waxman Act and all so-called "Patent Register" listings as required in Canada. Prior to such listings, the Parties will meet, through the JPC, to evaluate and identify all applicable Patent Rights, and Novartis will have the right to review, where reasonable, original records relating to any invention for which Patent Rights are being considered by the JPC for any such listing. Notwithstanding the preceding sentence, Novartis will retain final decision-making authority as to the listing of all applicable Orange Book Patents for a Licensed Product that are not Ionis Core Technology Patents or Ionis Manufacturing and Analytical Patents, regardless of which Party owns such Orange Book Patent.

8.9. Joint Research Agreement under the Leahy-Smith America Invents Act. If a Party intends to invoke its rights under 35 U.S.C. § 102(c) of the Leahy-Smith America Invents Act, it will notify the other Party and neither Party will make an election under such provision when exercising its rights under this Article 8 (Intellectual Property) without the prior written consent of the other Party (such consent not to be unreasonably withheld, conditioned or delayed), and the Parties will use reasonable efforts to cooperate and coordinate their activities with respect to any submissions, filings or other activities in support thereof. The Parties acknowledge and agree that this Agreement is a "*joint research agreement*" as defined in 35 U.S.C. § 100(h).

8.10. Obligations to Third Parties. Notwithstanding any of the foregoing, each Party's rights and obligations with respect to Licensed Technology under this Article 8 (Intellectual Property) will be subject to the restrictions set forth in Section 5.7 (License Conditions; Limitations), *provided*, *however*, that, to the extent that Ionis has a non-transferable right to prosecute, maintain or enforce any Patent Rights licensed to Novartis hereunder and, this Agreement purports to grant any such rights to Novartis, Ionis will use reasonable efforts to act in such regard with respect to such Patent Rights at Novartis' reasonable direction and expense.

8.11. **Additional Rights and Exceptions**. Other than as set forth in this Article 8 (Intellectual Property), Ionis retains the sole right to Prosecute and Maintain Ionis Core Technology Patents and Ionis Manufacturing and Analytical Patents during the Agreement Term and to control any enforcement of Ionis Core Technology Patents and Ionis Manufacturing and Analytical Patents, and will take the lead on such enforcement solely to the extent that the scope or validity of any Patent Rights Controlled by Ionis and Covering the Ionis Core Technology Patents or Ionis Manufacturing and Analytical Patents is at risk.

8.12. **Patent Term Extension**. If requested by Novartis, Ionis will cooperate in obtaining patent term restoration (including under the Drug Price Competition and Patent Term Restoration Act), supplemental protection certificates or their equivalents, and patent term extensions wherever applicable to a Licensed Product. Ionis will provide all reasonable assistance requested by Novartis, including permitting Novartis to proceed with applications for such in the name of Ionis, if deemed appropriate by Novartis, and executing documentation and providing any relevant information to Novartis. Novartis will in its sole discretion determine which Ionis Product-Specific Patents will be extended.

ARTICLE 9
REPRESENTATIONS, WARRANTIES AND COVENANTS

9.1. **Representations and Warranties of Both Parties**. Each Party hereby represents and warrants as of the Execution Date (and covenants as applicable) to the other Party that:

9.1.1. it is a corporation duly organized, validly existing, and in good standing under the laws of its jurisdiction of incorporation;

9.1.2. it has the power and authority and the legal right to enter into this Agreement and perform its obligations hereunder, and that it has taken all necessary action on its part required to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder;

9.1.3. this Agreement has been duly executed and delivered on behalf of such Party and constitutes a legal, valid and binding obligation of such Party and is enforceable against it in accordance with its terms subject to the effects of bankruptcy, insolvency or other laws of general application affecting the enforcement of creditor rights and judicial principles affecting the availability of specific performance and general principles of equity, whether enforceability is considered a Proceeding at law or equity;

9.1.4. all necessary consents, approvals and authorizations of all Regulatory Authorities and other parties required to be obtained by such Party in connection with the execution and delivery of this Agreement and the performance of its obligations hereunder have been obtained;

9.1.5. the execution and delivery of this Agreement and the performance of such Party's obligations hereunder (a) do not conflict with or violate any requirement of Applicable Law or any provision of the certificate of incorporation, bylaws or any similar instrument of such Party, as applicable, and (b) do not conflict with, violate, or breach or constitute a default or require any consent not already obtained under, any contractual obligation or court or administrative order by which such Party is bound;

9.1.6. all employees, consultants, or (sub)contractors (except academic collaborators or Third Parties under material transfer agreements) of such Party or Affiliates performing development activities hereunder on behalf of such Party will be obligated to assign all right, title and interest in and to any inventions developed by them, whether or not patentable, to such Party or Affiliate, respectively, as the sole owner thereof;

9.1.7. (a) neither such Party nor, to the actual knowledge of such Party, any employee, agent or subcontractor of such Party involved or to be involved in the Development or Research of the Licensed Products has been debarred under Subsection (a) or (b) of Section 306 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 335a) or under comparable Applicable Law; (b) no Person who is known by such Party to have been debarred under Subsection (a) or (b) of Section 306 of said Act or under comparable Applicable Law will be employed by such Party in the performance of any activities hereunder; (c) to the actual knowledge of such Party, no Person on any of the FDA clinical investigator enforcement lists (including, but not limited to, the (1) Disqualified/Totally Restricted List, (2) Restricted List and (3) Adequate Assurances List) will participate in the performance of any activities hereunder and (d) if either Party becomes aware of the debarment or threatened debarment of any person or entity providing services to such Party, including the Party itself and its Affiliates, which directly or indirectly relate to activities under this Agreement, the other Party will be immediately notified in writing;

9.1.8. Ionis has taken and each Party will take reasonable precautions to preserve the confidentiality of the Licensed Know-How, including requiring each Person having access to the Licensed Know-How to be subject to confidentiality, non-use, and non-disclosure obligations protecting the Licensed Know-How as the confidential, proprietary materials and information of Ionis;

9.1.9. there are no claims pending or, to each Party's Knowledge, threatened against such Party or any of its Affiliates, nor is such Party or any of its Affiliates a party to any judgment or settlement, that would be reasonably expected to adversely affect or restrict the ability of such Party to consummate any of the transactions contemplated under this Agreement or to perform any of its obligations under this Agreement, or which would affect any of the Licensed Technology, including the Licensed Patents, or Ionis's Control thereof, or any Licensed Product;

9.1.10. all non-Clinical and Clinical studies and trials conducted by a Party for a Licensed Product will be conducted in accordance with Applicable Law including, as applicable, GLP and GCP; and

9.1.11. each Party and its Affiliates have conducted and will conduct their business in compliance with the Foreign Corrupt Practices Act of 1977, the UK Bribery Act of 2010 and any other applicable anti-corruption Laws.

9.2. Representations, Warranties and Covenants of Ionis. As of the Execution Date [***] (unless otherwise noted below), Ionis represents, warrants and, as applicable, covenants to Novartis that, except as set forth on SCHEDULE 9.2 (Ionis Disclosure Schedule) (which schedule may be updated with respect to [***]):

9.2.1. Ionis is the sole and exclusive owner or exclusive licensee of, and has the right to grant all rights and licenses it purports to grant to Novartis with respect to, the Warranty Technology, free and clear of all liens, claims, security interests or other encumbrances of any kind (including prior license grants other than under the Ionis In-License Agreements) that would interfere, or the exercise of which would interfere, with Novartis' exercise of any license or right granted, or that may be granted, hereunder;

9.2.2. Ionis is listed in the records of the appropriate governmental agencies as the sole and exclusive owner of record or exclusive licensee for each registration, grant and application included in the Warranty Patents;

9.2.3. the Warranty Technology owned by Ionis and, to Ionis's Knowledge, the Warranty Technology licensed by Ionis was not and will not be funded by the U.S. federal government or otherwise subject to any rights of the U.S. federal government under the Bayh-Dole Act;

9.2.4. all Warranty Patents have been filed, prosecuted and maintained properly and correctly in all material respects;

9.2.5. neither Ionis nor any of its Affiliates has previously entered into, or during the term of this Agreement will enter into, any agreement, whether written or oral, with respect to, or has otherwise assigned, transferred, licensed, conveyed or otherwise encumbered, or during the term of this Agreement will otherwise assign, transfer, license, convey or otherwise encumber, any portion of its right, title or interest in or to, the Warranty Technology (including by granting any covenant not to sue with respect thereto) in such a way as to make the representation set forth in Section 9.2.1 (Representations, Warranties and Covenants of Ionis) not true;

9.2.6. each Ionis Product-Specific Patent and, to Ionis' Knowledge, each of the other Warranty Patents properly identifies each and every inventor of the claims thereof as determined in accordance with the laws of the jurisdiction in which such Patent Right is issued or such application is pending;

9.2.7. to Ionis' Knowledge, the issued patents in the Warranty Patents are valid and enforceable without any claims, challenges, oppositions, nullity actions, interferences, inter-partes reexaminations, inter-partes reviews, post-grant reviews, derivation Proceedings or other Proceedings pending or threatened;

9.2.8. to Ionis' Knowledge, neither Ionis nor any of its Affiliates has committed any act, or omitted to commit any act, that may cause the Warranty Patents to expire prematurely or be declared invalid or unenforceable;

9.2.9. all application, registration, maintenance and renewal fees in respect of the Warranty Patents existing as of the Execution Date have been paid and all necessary documents and certificates have been filed with the relevant agencies for the purpose of maintaining such Warranty Patents;

9.2.10. neither Ionis nor any of its Affiliates has received any written claim alleging that any of the Warranty Technology is invalid or unenforceable;

9.2.11. where Ionis' or its Affiliates' ownership of any of the Warranty Technology is based upon or depends on a sequence of historical transfers of title to any of the Warranty Technology (*i.e.*, chain of title to the applicable Warranty Technology) being valid, effective and free from defects and other problems, if at any time there is a potential defect with the validity or effectiveness in such transfers or other problems in such chain of title, then Ionis and its Affiliates shall, at their expense, with urgency and diligence, use reasonable efforts to make any and all corrections and clarifications, including preparing any documents and obtaining any necessary Third Party signatures and consents, as may be necessary, including filing such documents in any patent office as appropriate, to remedy any such problems and to restore such chain of title;

9.2.12. (a) the Ionis In-License Agreements are set forth on Appendix 2 (Ionis In-License Agreements), (b) the licenses granted to Ionis under the Ionis In-License Agreements are in full force and effect, (c) Ionis has not received any written notice, and is not aware, of any breach by any party to the Ionis In-License Agreements, and (d) Ionis' performance of its obligations under this Agreement (including the Research Plan as it exists on the Execution Date) will not constitute a breach of Ionis' obligations under the Ionis In-License Agreements or the licenses granted to Ionis thereunder;

9.2.13. to Ionis' Knowledge, in respect of the pending United States patent applications included in the Warranty Patents, Ionis or its Affiliates have submitted all material prior art of which it or they are aware in accordance with the requirements of the United States Patent and Trademark Office;

9.2.14. to Ionis' Knowledge, there are no rights of any Person that may be infringed, misappropriated or violated by any of the activities specifically anticipated by Ionis as of the Execution Date to be performed under this Agreement; *provided* that Novartis cannot assert a claim against Ionis for breach of this Section 9.2.14 (Representations, Warranties and Covenants of Ionis) related to any Third Party Patent Rights Novartis has Knowledge of as of the Execution Date;

9.2.15. as of the Execution Date, neither Ionis nor any of its Affiliates has initiated or been involved in any claim in which it has alleged that any Third Party is or was infringing or misappropriating any Warranty Technology, nor has any such claim been threatened by Ionis or any of its Affiliates, nor do Ionis or any of its Affiliates know of any valid basis for any such claim;

9.2.16. except for the Ionis In-License Agreements, there are no agreements between Ionis or any of its Affiliates and any Third Party pursuant to which Ionis or its Affiliate has in-licensed or otherwise acquired Control of any of the Warranty Technology;

9.2.17. to Ionis' Knowledge, no officer, employee or consultant of Ionis or any of its Affiliates is, or during the term of this Agreement will be, subject to any agreement that requires such individual to assign any interest in any Warranty Technology to any Third Party;

9.2.18. the Patent Rights listed in APPENDICES 5 (Ionis Core Technology Patents), 6 (Ionis Manufacturing and Analytical Patents) and 7 (Ionis Product-Specific Patents) are a complete and correct listing of the relevant Ionis Core Technology Patents, Ionis Manufacturing and Analytical Patents, and Ionis Product-Specific Patents which are owned or otherwise Controlled by Ionis;

9.2.19. other than the Ionis Core Technology Patents, Ionis Manufacturing and Analytical Patents and Ionis Product-Specific Patents, no other Patent Rights are owned by or licensed to Ionis or any of its Affiliates as of the Execution Date that are necessary or reasonably useful for the Research Activities;

9.2.20. except as otherwise expressly provided in this Agreement, Ionis or its Affiliate shall be and remain solely responsible for fulfilling and performing at its cost and expense, any and all obligations under each Ionis In-License Agreement, including timely, full and complete payment of any and all amounts due thereunder or in connection therewith to the other parties thereto;

9.2.21. Ionis shall not, and shall cause its Affiliates not to, incur or permit to exist, with respect to any Licensed Technology, any lien, encumbrance, charge, security interest, mortgage, liability, assignment, grant of license or other obligation that is or would be inconsistent with the licenses and other rights granted to, or that may be granted to, Novartis under this Agreement;

9.2.22. Ionis shall not enter into any amendment to any Ionis In-License Agreement that adversely affects any rights granted to, or that may be granted to, Novartis hereunder without the prior written consent of Novartis;

9.2.23. Ionis will promptly furnish Novartis with true and complete copies of all amendments to the Ionis In-License Agreements arising after the Execution Date;

9.2.24. Ionis will remain, and cause its Affiliates to remain, in compliance in all material respects with all Ionis In-License Agreements; and

9.2.25. Ionis will furnish Novartis with copies of all notices received by it or any of its Affiliates relating to any alleged breach or default by Ionis or any of its Affiliates under any Ionis In-License Agreement within [***] after receipt thereof and thereafter furnish Novartis with copies of all correspondence and summaries of material discussions between the applicable parties to the Ionis In-License Agreement relating to the alleged breach, including any proposed resolution of the matter.

9.3. Novartis Covenant. During the Agreement Term, neither Novartis nor its Affiliates will (independently or with a Third Party) Exploit any Licensed Compounds except as Development Candidates or as included in Licensed Products under this Agreement; *provided*, that the foregoing restriction will not prohibit Novartis from (a) outside of the activities conducted under this Agreement, Exploiting any Novartis Compound that (i) targets and modulates another target other than APO(a) as its primary mechanism of action and (ii) does not modulate APO(a) or (b) Researching any Licensed Compound in accordance with the license grant under Section 5.1.1(a)(iii) (License for Research Activities).

9.4. DISCLAIMER OF WARRANTY. EXCEPT FOR THE EXPRESS WARRANTIES SET FORTH IN THIS ARTICLE 9 (REPRESENTATIONS, WARRANTIES AND COVENANTS), NOVARTIS AND IONIS MAKE NO REPRESENTATIONS AND GRANT NO WARRANTIES, EXPRESS OR IMPLIED, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND NOVARTIS AND IONIS EACH SPECIFICALLY DISCLAIM ANY WARRANTIES, WHETHER WRITTEN OR ORAL, OR EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF QUALITY, MERCHANTABILITY OR FITNESS FOR A PARTICULAR USE OR PURPOSE OR ANY WARRANTY AS TO THE VALIDITY OF ANY PATENT RIGHTS OR THE NON-INFRINGEMENT OF ANY INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES.

ARTICLE 10
INDEMNIFICATION; INSURANCE

10.1. Indemnification by Novartis. Novartis agrees to defend Ionis, its Affiliates and their respective directors, officers, employees and their respective successors, heirs and assigns (collectively, the "***Ionis Indemnitees***"), and will indemnify and hold harmless the Ionis Indemnitees, from and against any liabilities, losses, costs, damages, fees or expenses payable to a Third Party, and reasonable attorneys' fees and other legal expenses with respect thereto (collectively, "***Losses***") arising out of any claim, action, lawsuit or other Proceeding by a Third Party (collectively, "***Third Party Claims***") brought against any Ionis Indemnitee and resulting from or occurring as a result of: (a) any activities conducted by a Novartis employee, consultant, Affiliate, Sublicensee, or (sub)contractor in the performance of the activities Novartis agrees to perform under this Agreement, including, the Manufacture, Research, Development or Commercialization of any Licensed Product, or (b) any breach by Novartis of any of its representations, warranties or covenants pursuant to this Agreement; except in any such case to the extent such Losses result from: (i) the negligence or willful misconduct of any Ionis Indemnitee, (ii) any breach by Ionis of any of its representations, warranties, covenants or obligations pursuant to this Agreement, or (iii) any breach of Applicable Law by any Ionis Indemnitee, and *provided* that Novartis shall not be obliged to so indemnify, defend and hold harmless the Ionis Indemnitees for any claims for which Ionis has an obligation to indemnify Novartis Indemnitees pursuant to Section 10.2 (Indemnification by Ionis).

10.2. Indemnification by Ionis. Ionis agrees to defend Novartis, its Affiliates and their respective directors, officers, employees and their respective successors, heirs and assigns (collectively, the "***Novartis Indemnitees***"), and will indemnify and hold harmless the Novartis Indemnitees, from and against any Losses arising out of Third Party Claims brought against any Novartis Indemnitee and resulting from or occurring as a result of: (a) any activities that an Ionis employee, consultant, Affiliate, Sublicensee, or (sub)contractor has undertaken in respect of Licensed Products either outside the scope of this Agreement, or in the performance of the activities Ionis agreed to perform under this Agreement, including the Manufacture, Research, Development or Commercialization of any Licensed Product or Terminated Product, or (b) any breach by Ionis of any of its representations, warranties or covenants pursuant to this Agreement; except in any such case to the extent such Losses result from: (i) the negligence or willful misconduct of any Novartis Indemnitee, (ii) any breach by Novartis of any of its representations, warranties, covenants or obligations pursuant to this Agreement, or (iii) any breach of Applicable Law by any Novartis Indemnitee, and *provided* that Ionis shall not be obliged to so indemnify, defend and hold harmless the Novartis Indemnitees for any claims for which Novartis has an obligation to indemnify Ionis Indemnitees pursuant to Section 10.1 (Indemnification by Novartis).

10.3. Notice of Claim. If an Ionis Indemnitee or Novartis Indemnitee seeks indemnification (as applicable) (such Party, the "***Indemnified Party***"), then the Indemnified Party will give the indemnifying Party prompt written notice (an "***Indemnification Claim Notice***") of any Losses or the discovery of any fact upon which the Indemnified Party intends to base a request for indemnification under Section 10.1 (Indemnification by Novartis) or Section 10.2 (Indemnification by Ionis), but in no event will the indemnifying Party be liable for any Losses to the extent such Losses result from any delay in providing such notice. The failure or delay to so notify the Indemnified Party shall not relieve the indemnifying Party of any obligation or liability to the Indemnified Party, except to the extent that the indemnifying Party demonstrates that its ability to defend or resolve such claim is adversely affected as a result of such failure or delay. Each Indemnification Claim Notice must contain a description of the claim and the nature and amount of such Loss (to the extent that the nature and amount of such Loss is known at such time). The Indemnified Party will furnish promptly to the indemnifying Party copies of all papers and official documents received or sent in respect of any Losses and Third Party Claims.

10.4. Defense, Settlement, Cooperation and Expenses.

10.4.1. **Control of the Defense**. At its option, the indemnifying Party may assume the defense and handling of any Third Party Claim by giving written notice to the Indemnified Party within 30 calendar days after the indemnifying Party's receipt of an Indemnification Claim Notice. The assumption and handling of the defense of a Third Party Claim by the indemnifying Party shall not be construed as an acknowledgment that the indemnifying Party is liable to indemnify the Indemnified Party in respect of the Third Party Claim, nor shall it constitute a waiver by the indemnifying Party of any defenses it may assert against the Indemnified Party's claim for indemnification. Upon assuming the defense of a Third Party Claim, the indemnifying Party may appoint as lead counsel in the defense of the Third Party Claim any legal counsel selected by the indemnifying Party. If the indemnifying Party assumes the defense of a Third Party Claim, the Indemnified Party will as soon as is reasonably possible deliver to the indemnifying Party all original notices and documents (including court papers) received or sent by the Indemnified Party in connection with the Third Party Claim. Should the indemnifying Party assume the defense of a Third Party Claim, except as provided in this Section 10.4.1 (Control of the Defense), the Indemnified Party will be responsible for the legal costs or expenses subsequently incurred by such Indemnified Party in connection with the analysis, defense or settlement of the Third Party Claim.

10.4.2. **Right to Participate in Defense**. Without limiting Section 10.4.1 (Control of the Defense), any Indemnified Party will be entitled to participate in, but not control, the defense of such Third Party Claim and to employ counsel of its choice for such purpose; *provided*, *however*, that such employment will be at the Indemnified Party's own cost and expense unless (a) the employment thereof has been specifically authorized by the indemnifying Party in writing, (b) the indemnifying Party has failed to assume the defense and employ counsel in accordance with Section 10.4.1 (Control of the Defense) (in which case the Indemnified Party will control the defense), or (c) the interests of the Indemnified Party and the indemnifying Party with respect to such Third Party Claim are sufficiently adverse to prohibit the representation by the same counsel of both Parties under Applicable Law, ethical rules or equitable principles in which case the indemnifying Party will be responsible for any such costs and expenses of counsel for the Indemnified Party.

10.4.3. **Settlement**. With respect to any Third Party Claims relating solely to the payment of money damages in connection with a Third Party Claim and that will not admit liability or violation of Law on the part of the Indemnified Party or result in the Indemnified Party's becoming subject to injunctive or other relief or otherwise adversely affecting the business of the Indemnified Party in any manner (such as granting a license or admitting the invalidity of a Patent Right Controlled by an Indemnified Party), and as to which the indemnifying Party will have acknowledged in writing the obligation to indemnify the Indemnified Party hereunder, the indemnifying Party will have the sole right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss, on such terms as the indemnifying Party, in its sole discretion, will deem appropriate. With respect to all other Losses in connection with Third Party Claims, where the indemnifying Party has assumed the defense of the Third Party Claim in accordance with Section 10.4.1 (Control of the Defense), the indemnifying Party will have authority to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss provided it obtains the prior written consent of the Indemnified Party (which consent will not be unreasonably withheld, delayed or conditioned). The indemnifying Party will not be liable for any settlement, consent to entry of judgment, or other disposition of a Loss by an Indemnified Party that is reached without the written consent of the indemnifying Party. Regardless of whether the indemnifying Party chooses to defend or prosecute any Third Party Claim, no Indemnified Party will admit any liability with respect to or settle, compromise or discharge, any Third Party Claim without the prior written consent of the indemnifying Party, such consent not to be unreasonably withheld, delayed or conditioned.

10.4.4. **Cooperation**. Regardless of whether the indemnifying Party chooses to defend or prosecute any Third Party Claim, the Indemnified Party will, and will cause each other Indemnified Party to, cooperate in the defense or prosecution thereof and will furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery Proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith. Such cooperation will include access during normal business hours afforded to indemnifying Party to, and reasonable retention by the Indemnified Party of, records and information that are reasonably relevant to such Third Party Claim, and making Indemnified Parties and other employees and agents available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder, and the indemnifying Party will reimburse the Indemnified Party for all its reasonable out-of-pocket costs and expenses in connection therewith.

10.4.5. **Costs and Expenses**. Except as provided above in this Section 10.4 (Defense, Settlement, Cooperation and Expenses), the costs and expenses, including attorneys' fees and expenses, incurred by the Indemnified Party in connection with any claim will be reimbursed on a Calendar Quarter basis by the indemnifying Party, without prejudice to the indemnifying Party's right to contest the Indemnified Party's right to indemnification and subject to refund in the event the indemnifying Party is ultimately held not to be obligated to indemnify the Indemnified Party.

10.5. Insurance.

10.5.1. **Ionis' Insurance Obligations**. Ionis will maintain, at its cost, reasonable insurance against liability and other risks associated with its activities contemplated by this Agreement, including its indemnification obligations herein, in such amounts and on such terms as are customary for prudent practices for biotech companies of similar size and with similar resources in the pharmaceutical industry for the activities to be conducted by it under this Agreement taking into account the scope of development of Licensed Products. Any deductibles associated with Ionis' insurance programs are the responsibility of Ionis and may not be passed on to Novartis. Such insurance will not be construed to create a limit of Ionis' liability with respect to its indemnification obligations under this Article 10 (Indemnification).

10.5.2. **Novartis' Insurance Obligations**. Novartis will maintain, at its cost, reasonable insurance against liability and other risks associated with its activities contemplated by this Agreement (including product liability), including its indemnification obligations herein, in such amounts and on such terms as are customary for prudent practices for large companies in the pharmaceutical industry for the activities to be conducted by Novartis under this Agreement; *provided*, that Ionis hereby acknowledges and agrees that such obligation may be satisfied by a program of self-insurance that is consistently applied across Novartis' other programs. Any deductibles associated with Novartis' insurance programs are the responsibility of Novartis and shall not be passed on to Ionis. Such insurance will not be construed to create a limit of Novartis' liability with respect to its indemnification obligations under this Article 10 (Indemnification).

10.6. LIMITATION OF CONSEQUENTIAL DAMAGES. EXCEPT FOR (A) THIRD PARTY CLAIMS THAT ARE SUBJECT TO INDEMNIFICATION UNDER THIS ARTICLE 10 (INDEMNIFICATION; INSURANCE), (B) CLAIMS ARISING OUT OF A PARTY'S WILLFUL MISCONDUCT OR FRAUD UNDER THIS AGREEMENT, (C) A PARTY'S BREACH OF ARTICLE 4 (EXCLUSIVITY), OR (D) CLAIMS ARISING OUT OF A PARTY'S BREACH OF ITS CONFIDENTIALITY OBLIGATIONS UNDER THIS AGREEMENT, NEITHER PARTY NOR ANY OF ITS AFFILIATES WILL BE LIABLE TO THE OTHER PARTY TO THIS AGREEMENT OR ITS AFFILIATES FOR ANY INCIDENTAL, CONSEQUENTIAL, SPECIAL, PUNITIVE OR OTHER INDIRECT DAMAGES OR LOST OR IMPUTED PROFITS OR ROYALTIES, WHETHER LIABILITY IS ASSERTED IN CONTRACT, TORT (INCLUDING NEGLIGENCE AND STRICT PRODUCT LIABILITY), INDEMNITY OR CONTRIBUTION, AND IRRESPECTIVE OF WHETHER THAT PARTY OR ANY REPRESENTATIVE OF THAT PARTY HAS BEEN ADVISED OF, OR OTHERWISE MIGHT HAVE ANTICIPATED THE POSSIBILITY OF, ANY SUCH LOSS OR DAMAGE.

ARTICLE 11
TERM; TERMINATION

11.1. Agreement Term; Expiration. Except as otherwise set forth in Section 5.11 (HSR Matters), this Agreement is effective as of the Effective Date and, unless earlier terminated pursuant to the other provisions of this Article 11 (Term; Termination), will continue in full force and effect until this Agreement expires as follows:

11.1.1. on a country-by-country and Licensed Product-by-Licensed Product basis, on the date of expiration of all payment obligations by Novartis under this Agreement with respect to such Licensed Product in such country;

11.1.2. in its entirety upon the expiration of all payment obligations by Novartis under this Agreement with respect to the last Licensed Product in all countries pursuant to Section 11.1.1 (Agreement Term; Expiration); or

11.1.3. in its entirety if, by the end of the Carryover Period, the JSC has not designated a Development Candidate (or no Licensed Product License for a Development Candidate has become effective in accordance with Section 5.11.2(d)), *provided*, that if Novartis has identified a Licensed Compound that it reasonably believes satisfies the Development Candidate Criteria and has started the internal processes for approval to have the JSC designate such Licensed Compound as a Development Candidate, the Agreement will be extended by up to 60 calendar days to allow for such approval.

The period from the Effective Date until the date of expiration of this Agreement pursuant to this Section 11.1 (Agreement Term; Expiration) or earlier termination of this Agreement pursuant to Section 11.2 (Termination of the Agreement), is the "***Agreement Term***."

11.2. Termination of the Agreement.

11.2.1. **Novartis' Termination for Convenience**. At any time after the Effective Date following payment by Novartis of the Upfront Fee under Section 7.1 (Upfront Fee), subject to Section 11.3 (Consequences of Expiration or Termination of this Agreement) below, Novartis will be entitled to, in its sole discretion, terminate this Agreement in its entirety or in part on a Licensed Product-by-Licensed Product basis for convenience by providing [***] written notice to Ionis of such termination.

11.2.2. **Termination for Material Breach**.

(a) **Novartis' Right to Terminate**. Subject to Section 11.2.3(b) (Remedies for Failure to Use Commercially Reasonable Efforts), if Novartis has reason to believe that Ionis is in material breach of this Agreement, then Novartis may deliver notice of such material breach to Ionis. Ionis will have [***] to cure such breach (except to the extent such breach involves the failure to make a payment when due, which breach must be cured within [***] following such notice). If Ionis fails to cure such breach within such [***] or [***] period, as applicable, then Novartis may terminate this Agreement in its entirety if such breach relates to this Agreement in its entirety, or in relevant part on a Licensed Product-by-Licensed Product basis if such breach does not relate to this Agreement in its entirety, by providing written notice to Ionis.

(b) **Ionis' Right to Terminate**. Subject to Section 11.2.3(a) (Remedies for Failure to Use Commercially Reasonable Efforts), if Ionis has reason to believe that Novartis is in material breach of this Agreement, then Ionis may deliver notice of such material breach to Novartis. Novartis will have [***] to cure such breach (except to the extent such breach involves the failure to make a payment when due, which breach must be cured within [***] following such notice). If Novartis fails to cure such breach within such [***] or [***] period, as applicable, Ionis may terminate this Agreement in its entirety if such breach relates to this Agreement in its entirety, or in relevant part on a Licensed Product-by-Licensed Product basis if such breach does not relate to this Agreement in its entirety, by providing written notice to Novartis.

11.2.3. **Remedies for Failure to Use Commercially Reasonable Efforts**.

(a) If Ionis fails to use Commercially Reasonable Efforts as contemplated in Section 2.9 (Conduct of Research Activities) in material breach of this Agreement, Novartis may notify Ionis and, within [***] thereafter, Ionis and Novartis will meet through the JSC (or directly if the JSC has been dissolved) and attempt to resolve the matter in good faith, and to devise a mutually agreeable plan to address any outstanding issues related to Ionis's use of Commercially Reasonable Efforts in Section 2.9 (Conduct of Research Activities). Following such a meeting, if Ionis fails to use Commercially Reasonable Efforts as contemplated in Section 2.9 (Conduct of Research Activities) and such failure constitutes a material breach of this Agreement, then subject to Section 11.2.4 (Disputes Regarding Material Breach) below, Novartis will have the right, at its sole discretion, to terminate this Agreement in whole or in part on a Licensed Product-by-Licensed Product basis or elect the alternative remedy in lieu of terminating this Agreement, in each case pursuant to the terms (including the cure period) of Section 11.2.2 (Termination for Material Breach).

(b) If Novartis fails to use Commercially Reasonable Efforts as contemplated in Section 2.9 (Conduct of Research Activities), Section 6.1 (Development) or Section 6.3 (Commercialization) in material breach of this Agreement, Ionis may notify Novartis and, within [***] thereafter, Ionis and Novartis will meet and confer to discuss and resolve the matter in good faith, and attempt to devise a mutually agreeable plan to address any outstanding issues related to Novartis' use of Commercially Reasonable Efforts in Section 2.9 (Conduct of Research Activities), Section 6.1 (Development) or Section 6.3 (Commercialization). Following such a meeting, if Novartis fails to use Commercially Reasonable Efforts as contemplated in Section 2.9 (Conduct of Research Activities), Section 6.1 (Development) or Section 6.3 (Commercialization), and such failure constitutes a material breach of this Agreement then subject to Section 11.2.4 (Disputes Regarding Material Breach) below, Ionis will have the right, at its sole discretion, to terminate this Agreement in part on a Licensed Product-by-Licensed Product basis pursuant to the terms (including the cure period) of Section 11.2.2 (Termination for Material Breach).

11.2.4. **Disputes Regarding Material Breach**. Notwithstanding the foregoing, if the Breaching Party in Section 11.2.2 (Termination for Material Breach) or Section 11.2.3 (Remedies for Failure to Use Commercially Reasonable Efforts) disputes in good faith the existence, materiality, or failure to cure any such breach and provides notice to the Non-Breaching Party or, as applicable, terminating Party of such dispute within such [***] or [***] cure period, as applicable, the Non-Breaching Party will not have the right to terminate this Agreement in accordance with Section 11.2.2 (Termination for Material Breach), or Section 11.2.3 (Remedies for Failure to Use Commercially Reasonable Efforts), unless and until it has been determined in accordance with Section 13.1 (Arbitration) that this Agreement was materially breached by the Breaching Party and the Breaching Party fails to cure such breach within [***] or [***], as applicable, following such determination. It is understood and acknowledged that during the pendency of such dispute, all the terms and conditions of this Agreement will remain in effect and the Parties will continue to perform all of their respective obligations hereunder, including satisfying any payment obligations.

11.2.5. **Termination for Insolvency**.

(a) Either Party may terminate this Agreement if, at any time, the other Party files in any court or agency pursuant to any statute or regulation of any state or country a petition in bankruptcy or insolvency or for the appointment of a receiver or trustee of the Party or of substantially all of its assets; or if the other Party proposes a written agreement of composition or extension of substantially all of its debts; or if the other Party will be served with an involuntary petition against it, filed in any insolvency Proceeding, and such petition will not be dismissed within 90 calendar days after the filing thereof; or if the other Party will propose or be a party to any dissolution or liquidation; or if the other Party will make an assignment of substantially all of its assets for the benefit of creditors.

(b) All rights and licenses granted under or pursuant to any section of this Agreement are and will otherwise be deemed to be for purposes of Section 365(n) of Title 11, United States Code (the "***Bankruptcy Code***") or analogous provisions of Applicable Law outside the U.S. licenses of rights to "intellectual property" as defined in Section 101(56) of the Bankruptcy Code or analogous provisions of Applicable Law outside the U.S. The Parties will retain and may fully exercise all of their respective rights and elections under the Bankruptcy Code or analogous provisions of Applicable Law outside the U.S. Upon the commencement of a bankruptcy Proceeding of any Party, the non-bankrupt Party will further be entitled to a complete duplicate of, or complete access to, any such intellectual property, and all embodiments which, if not already in its possession, will be promptly delivered to the non-bankrupt Party upon written request.

11.2.6. **Termination for Safety Issue**. Novartis shall have the right to terminate this Agreement with respect to a Licensed Product, upon [***] written notice to Ionis, without any further obligations or liabilities towards Ionis (other than the consequences of termination set forth in Section 11.5 (Consequences of Expiration or Termination of this Agreement) below), to the extent applicable, if, during the Agreement Term, Novartis, based on applicable data, determines reasonably and in good faith that the continued Development or Commercialization of such Licensed Product presents safety concerns that pose a material risk or threat of harm in humans that, in Novartis' reasonable and good faith determination are unable to be resolved through reasonable additional Development activities. Such determination shall be [***].

11.3. Remedy for Patent Challenge. If Novartis or its Affiliates disputes, or assists any Third Party to dispute, the validity of any Licensed Patent, in a patent re-examination, inter partes review, post grant or other patent-office Proceeding, opposition, litigation, or other court Proceeding and, within 60 calendar days from written notice from Ionis, Novartis fails to rescind any and all of such actions, Ionis may [***] by providing written notice of such [***] to Novartis, *provided however* that, nothing in this clause prevents Novartis or its Affiliates from taking any of the actions referred to in this clause and *provided further* that Ionis will not have the right to [***] if Novartis or its Affiliates (a) asserts invalidity as a defense in any court Proceeding brought by Ionis or its Affiliates asserting infringement of a Licensed Patent; or (b) acquires a Third Party that has an existing challenge, whether in a court or administrative Proceeding, against a Licensed Patent.

11.4. Alternative Remedy in Lieu of Termination. If Novartis has the right to terminate this Agreement in its entirety pursuant to Section 11.2.2(a) (Novartis' Right to Terminate) (after giving effect to the applicable cure period under Section 11.2.2(a) (Novartis' Right to Terminate)) for any material breach of this Agreement other than a payment breach, then in lieu of Novartis' terminating this Agreement pursuant to Section 11.2.2(a) (Novartis' Right to Terminate), Novartis will have the right to elect (in its sole discretion) by written notice to Ionis to have this Agreement continue in full force and effect, except that [***]; *provided* that such right, if exercised, will be Novartis' sole and exclusive remedy with respect to the events giving rise to Novartis' termination right. Novartis must provide Ionis with written notice that it is electing to exercise the alternative remedy set forth in this Section 11.4 (Alternative Remedy in Lieu of Termination) within [***] after expiration of the applicable cure period (as tolled pursuant to Section 11.2.4 (Disputes Regarding Material Breaches)) and, in any event, prior to initiating the damages phase of any arbitration proceeding with respect to such breach pursuant to Section 13.1 (Arbitration).

11.5. Consequences of Expiration or Termination of this Agreement.

11.5.1. **Consequence of Termination of this Agreement**. If this Agreement expires in accordance with Section 11.1.3 or is terminated by a Party in accordance with Section 11.2 (Termination of the Agreement) in its entirety or on a Licensed Product-by-Licensed Product basis at any time and for any reason, the following terms will apply to any such expiration or termination, but only to the extent of any such termination (*i.e.*, with respect to any Terminated Product or in its entirety):

(a) **Licenses and Compounds**. Any license granted by Ionis to Novartis under Section 5.1 (License Grants to Novartis) will terminate. Novartis and its Affiliates and, subject to Section 5.3.4 (Effect of Termination on Sublicenses), its Sublicensees will cease selling Terminated Products under such licenses; *provided*, that (i) Novartis and its Affiliates and Sublicensees will have the right to sell any remaining inventory of Terminated Product over a period of no greater than [***] after the effective date of such termination and Novartis will pay Ionis royalties in accordance with Section 7.7 (Royalty Payments) on the Net Sales of such inventory of such Terminated Products, to the extent not already paid; and (ii) if there are any Clinical Studies being conducted at the date of termination, Novartis shall be entitled to continue Developing and Manufacturing Terminated Products to the extent and for the period necessary to effect an orderly transfer or wind down of such Clinical Studies in a timely manner and in accordance with all Applicable Law. In addition, Novartis and its Affiliates will not (independently or with a Third Party) Exploit any Licensed Compounds or any product containing any Licensed Compound after the effective date of termination, *provided* that the foregoing restriction will not prohibit Novartis from (A) Exploiting any Novartis Compound that (1) targets and modulates another target other than APO(a) as its primary mechanism of action and (2) does not modulate APO(a) or (B) solely in the event of termination after designation of a Development Candidate, Researching or Manufacturing any Novartis Compound other than a Novartis Compound that was designated as a Development Candidate.

(b) **Exclusivity**. If this Agreement is terminated in its entirety, then neither Party will have any further obligations under Article 4 (Exclusivity) of this Agreement.

(c) **Research Plan**. Neither Party will have any further obligations with respect to the Terminated Product under the Research Plan.

(d) **Return of Information and Materials**. The Parties will return (or destroy) all data, files, records and other materials containing or comprising the other Party's Confidential Information to which it does not retain rights under the surviving provisions of this Agreement. Notwithstanding the foregoing, the Parties will be permitted to retain one copy of such data, files, records, and other materials for archival and legal compliance purposes. Each Party will also be permitted to retain such additional copies of or any computer records or files containing the other Party's Confidential Information that have been created solely by automatic archiving and back-up procedures, to the extent created and retained in a manner consistent with the retaining Party's standard archiving and back-up procedures, but not for any other use or purpose. All Confidential Information shall continue to be subject to the terms of this Agreement for the period set forth in Article 12 (Confidentiality).

(e) **Accrued Rights**. Termination of this Agreement for any reason will be without prejudice to any rights or financial compensation that have accrued to the benefit of a Party prior to such termination. Such termination will not relieve a Party from obligations that are expressly indicated to survive the termination of this Agreement. For purposes of clarification, milestone payments under Article 7 (Financial Provisions) accrue as of the date the applicable milestone event is achieved even if the payment is not due at the time of termination and royalty payments under Article 7 (Financial Provisions) accrue as of the date the applicable Net Sale even if the payment is not due at the time of termination.

11.5.2. **Survival**. In addition to the expiration or termination consequences set forth in this Section 11.5 (Consequences of Expiration or Termination of this Agreement), the following provisions of this Agreement will survive the expiration of this Agreement pursuant to Section 11.1 (Agreement Term; Expiration) or earlier termination of this Agreement pursuant to Section 11.2 (Termination of this Agreement): Section 2.4 (Research Costs) (with respect to any costs accrued prior to expiration or the date of the notice of termination), Section 2.10.1 (Records), Section 5.1.2 (Licensed Product License) ((1) in the event of expiration, solely in accordance with Section 5.5 (Consequence of Natural Expiration of this Agreement) and (2) in the event of termination, solely as set forth and pursuant to the terms of Section 11.5.1(a) (Consequence of Termination of this Agreement)), Section 5.5 (Consequence of Natural Expiration of this Agreement), Section 5.10 (Cross-Licenses under Program Technology), Section 7.7.2 (Application of Royalty Rates), Section 7.7.3 (Limitation on Aggregate Reduction for Novartis Royalties), and Section 7.9.4 (Right to Offset) (in each case solely with respect to any financial compensation that has accrued prior to expiry or termination in accordance with Section 11.5.1(e) (Accrued Rights)), Section 7.11 (Payments) through Section 7.14 (Interest) (in each case with respect to any financial compensation that has accrued prior to expiry or termination in accordance with Section 11.5.1(e) (Accrued Rights)), Section 8.2 (Ownership), Section 8.5 (Defense of Claims Brought by Third Parties; Oppositions) through Section 8.7 (Other Infringement - Jointly Owned Program Patents) (with respect to any action initiated prior to the effective date of expiration or termination), Section 9.4 (Disclaimer of Warranty), Section 10.1 (Indemnification by Novartis) through Section 10.4 (Defense, Settlement, Cooperation and Expenses), Section 10.6 (Limitation of Consequential Damages), Section 11.5 (Consequences of Expiration or Termination of this Agreement), Article 12 (Confidentiality), Article 13 (Miscellaneous) and Appendix 1 (Definitions) (to the extent definitions are embodied in the foregoing listed Articles and Section).

11.5.3. **Ionis: Special Consequences of Certain Terminations**. If (A) Novartis terminates this Agreement under [***], (B) Ionis terminates this Agreement under Section 11.2.2(b) (Ionis' Right to Terminate), Section 11.2.3(b) (Remedies for Failure to Use Commercially Reasonable Efforts), or Section 11.2.5 (Termination for Insolvency), or (C) this Agreement expires in accordance with Section 11.1.3, then, in addition to the terms set forth in Section 11.5.1 (Consequence of Termination of this Agreement), the following additional terms will also apply but only with respect to any Terminated Products:

(a) **Reversion License**.

(i) **License Grant**. Subject to Section [***], Novartis will and hereby does grant to Ionis:

(1) a sublicensable, worldwide, exclusive royalty-bearing license or sublicense, as the case may be, under all Novartis Technology (excluding Novartis Background Technology and Trademarks) Controlled by Novartis as of the effective date of such termination that is necessary for or Actually Used in the Development, Manufacture, or Commercialization of a Terminated Product as of the effective date of termination;

(2) a sublicensable, worldwide, non-exclusive royalty-bearing license or sublicense, as the case may be, under all Novartis Background Technology (excluding Trademarks) Controlled by Novartis as of the effective date of such termination that is necessary for or Actually Used in the Development, Manufacture, or Commercialization of a Terminated Product as of the effective date of termination; *provided*, *however*, that [***]; and

(3) a sublicensable, worldwide, exclusive license under any Trademarks that are solely related to a Terminated Products (excluding any Novartis corporate names and logos); in each case of (1), (2) and (3) solely to Exploit the Terminated Product (the licenses set forth in clauses (1), (2), and (3), collectively, the "***Reversion License***"); *provided*, that if Ionis determines that any Antitrust Filings are required in connection with the grant of the Reversion License, such license shall not become effective unless and until the applicable waiting period (and any extensions thereof, including any timing agreement entered into with the DOJ or FTC) under the HSR Act shall have expired or been terminated and any other required clearances under Antitrust Laws shall have been obtained.

(ii) **Reversion License Economics**. Promptly following notice of termination, the Parties will negotiate and agree in good faith on a reasonable compensation to be paid by Ionis to Novartis in consideration of the Reversion License, taking into account, among other things, (i) the stage of Development or Commercialization of the Terminated Products at the time of termination, (ii) the nature of the Reversion License granted to Ionis (*i.e.*, the scope of the Patent Rights, Know-How and Trademarks included in the Reversion License and if the Reversion License includes rights to any other active pharmaceutical ingredient that is not a Licensed Compound), (iii) the reason for termination, and (iv) the relative value of the Patent Rights and Know-How licensed under the Reversion License. If the Parties cannot agree on the applicable compensation for the Reversion License within [***] of initiating good faith negotiations (a "***Reversion License Dispute***"), then such Reversion License Dispute shall be finally settled [***] pursuant to terms set forth in Schedule 11.5.3. For the purpose of this Section 11.5.3(a) (Ionis: Special Consequences for Certain Terminations), the term "Control" shall not include any Novartis Technology or Novartis Background Technology for which Novartis or its relevant Affiliate or Sublicensee would be obligated to pay any additional royalties, milestones or other consideration or amounts in connection with granting the Reversion License or the Exploitation of the Terminated Products by Ionis, its Affiliates or sublicensees, unless Ionis agrees in writing to pay Novartis for any and all out-of-pocket costs, including upfront payments, purchase price, milestones, royalties, any license fees, option fees, option exercise fees, and other payments paid or payable by Novartis or its Affiliates to a Third Party that owns or controls such rights to license or acquire such rights; *provided* that, if the applicable rights relate to both a Terminated Product and one or more other programs of Novartis or its Affiliates, then any such out-of-pocket costs that are not specific to the Exploitation of a Terminated Product (e.g., upfront payments, purchase price, etc.) will be equitably allocated by Novartis among the applicable Terminated Product and such other programs, and Ionis will only be required to reimburse Novartis for the amount that is allocated to the applicable Terminated Product.

(iii) **[***]**. Notwithstanding any other provision of this Agreement, if a Terminated Product [***], then [***] (such [***]), unless the Parties [***] pursuant to this Section 11.5.3(a)(iii) ([***]). If Ionis [***], then Ionis shall [***]. If Ionis [***], the Parties will [***]; *provided* that Ionis may [***]. If Ionis does not [***], or Ionis [***] but the Parties [***], then Novartis [***]. Notwithstanding any other provision in this Agreement, in no event shall [***] except as set forth in this Section 11.5.3(a)(iii) ([***]).

(iv) **Acquisition of Alternative Technologies**. As part of the negotiations for the reasonable compensation to be paid by Ionis to Novartis in consideration of the Reversion License pursuant to Section 11.5.3(a)(ii) (Reversion License Economics), the Parties will discuss whether any of the Novartis Technology that is Actually Used but not necessary for the Exploitation of the Terminated Product (or a suitable alternative) [***].

(b) Within [***] following the date of termination, Novartis will deliver to Ionis for use with respect to the Research, Development, and Commercialization of the Terminated Product, any material Know-How, data, results (to the extent such Know-How, data, and results are included in the Reversion License), regulatory information, health economic study information, communications with payors, regulatory filings, or copies thereof, as of the date of such termination that relate [***] to such Terminated Product, in each case solely to the extent in Novartis' or its Affiliates' or Sublicensees' possession or control;

(c) Ionis will control and be responsible for all aspects of the Prosecution and Maintenance of all Ionis Product-Specific Patents and Novartis will provide Ionis with (and will instruct its counsel to provide Ionis with) all of the material information and records in Novartis' and its counsel's possession related to the Prosecution and Maintenance of such Ionis Product-Specific Patents, in each case, with respect to the Terminated Product;

(d) If requested by Ionis, Novartis will sell to Ionis all remaining API or Finished Drug Product in Novartis' possession at a price equal to [***];

(e) Upon Ionis' reasonable request, Novartis shall support (or use Commercially Reasonable Efforts to cause to be supported by Novartis' CMO) at [***] sole cost and expense a technology transfer to Ionis (or Ionis' designated Third Party supplier) of any Novartis Technology necessary or Actually Used in the Development or Manufacture of a Terminated Product as of the effective date of termination for the manufacturing and supply of API or Finished Drug Product for such Terminated Product. In addition, Novartis will (or will use Commercially Reasonable Efforts to cause Novartis' CMO to), at [***] sole cost and expense, (i) provide reasonable support and cooperation from time to time upon Ionis' reasonable request, with Ionis's regulatory filings and interactions with Regulatory Authorities related to Novartis' or such CMO's API or Finished Drug Product manufacturing (including any required inspections), and (ii) use Commercially Reasonable Efforts to supply (or cause to be supplied by Novartis' CMO) API or Finished Drug Product to Ionis, at a price equal to [***], for a period of up to [***] from the effective date of termination to enable Ionis to identify and contract with a suitable Third Party API or Finished Drug Product manufacturer;

(f) Novartis will assign, and hereby assigns, to Ionis, for Ionis' exclusive use with respect to the Research, Development and Commercialization of the Terminated Products, all of Novartis' right, title and interest in and to regulatory filings and submissions in the possession or Control of Novartis, in each case, that are necessary and solely related to the Research, Development, Manufacture, or Commercialization of Terminated Products and will take such further action as may be reasonably requested to transfer (i) regulatory documents in Ionis' name and (ii) control of regulatory proceedings to Ionis;

(g) In the event of any failure to effect any assignment described in Section 11.5.3(f) and, with respect to any other data, results, and regulatory information covered by the Reversion License, and regulatory filings and submissions in the possession or Control of Novartis, in each case, that are necessary or Actually Used to Develop, Manufacture, or Commercialize a Terminated Product as of the effective date of termination for the Exploitation of the Terminated Product but not assigned to Ionis pursuant to Section 11.5.3(f), Novartis hereby consents and grants to Ionis and any licensee of Ionis' with rights to a Terminated Product the right to access and reference (without any further action required on the part of Novartis, whose authorization to file this consent with any Regulatory Authority is hereby granted) any such item with respect to all Terminated Products, and Novartis will promptly execute any document reasonably requested by Ionis to effect such right of access and reference; and

(h) At Ionis' reasonable request, the Parties will negotiate in good faith a transition services agreement for Novartis to perform certain mutually agreed transition services to (i) provide patients with continued access to the applicable Terminated Products, and (ii) enable Ionis (or Ionis' designee) to assume and execute the responsibilities under all Regulatory Approvals and ongoing Clinical Studies for the applicable Terminated Product, (collectively, the "***Transition Services***"), and Ionis will pay Novartis and commercially reasonable amount to perform the Transition Services.

11.5.4. **Novartis: Special Consequences of Certain Terminations**. If Novartis terminates this Agreement under Section 11.2.2(a) (Novartis' Right to Terminate), Section 11.2.3(a) (Remedies for Failure to Use Commercially Reasonable Efforts) or Section 11.2.5 (Termination for Insolvency), all of the provisions of Section 11.5.1 (Consequence of Termination of this Agreement) will apply, except that Novartis, its Affiliates, and Sublicensees will have the right to sell any remaining inventory of Terminated Product and Novartis will pay Ionis royalties in accordance with Section 7.7 (Royalty Payments) on the Net Sales of such inventory of such Terminated Products to the extent not already paid.

ARTICLE 12
CONFIDENTIALITY

12.1. Confidentiality; Exceptions. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing, the Parties agree that, during the Agreement Term and for five years thereafter, the receiving Party (the "***Receiving Party***") and its Affiliates will keep confidential and will not publish or otherwise disclose or use for any purpose other than as provided for in this Agreement any Confidential Information disclosed by the other Party or its Affiliates (the "***Disclosing Party***"). Subject to the other provisions of this Article 12 (Confidentiality), each Party shall hold as confidential such Confidential Information of the other Party and its Affiliates in the same manner and with the same protection as such Receiving Party maintains its own Confidential Information.

12.2. Prior Confidentiality Agreement Superseded. As of the Execution Date, this Agreement supersedes the Confidential Disclosure Agreement executed by Ionis and Novartis on [***] (including any and all amendments thereto). All information exchanged among Ionis and Novartis under such Confidential Disclosure Agreement are deemed Confidential Information hereunder and subject to the terms of this Article 12 (Confidentiality).

12.3. Authorized Disclosure. Except as expressly provided otherwise in this Agreement, a Receiving Party or its Affiliates may use and disclose Confidential Information of the Disclosing Party to (a) employees, agents, contractors, consultants and advisors of the Receiving Party and its Affiliates, and sublicensees and to (b) Third Parties to the extent reasonably necessary for the performance of its obligations or exercise of rights granted or reserved in this Agreement, in each case under confidentiality provisions no less restrictive than those in this Agreement. In addition, a Receiving Party or its Affiliates may disclose Confidential Information of the Disclosing Party (i) to the extent reasonably necessary to file or prosecute patent, copyright and trademark applications (subject to Section 12.4 (Press Release; Publications; Disclosure of Agreement) below), complying with applicable governmental regulations, obtaining Regulatory Approvals, conducting non-Clinical Studies or Clinical Studies, marketing a Licensed Product, or as otherwise required by Applicable Law (including the rules of the SEC and any stock exchange); *provided*, *however*, that if a Receiving Party or any of its Affiliates is required by Applicable Law to make any such disclosure of a Disclosing Party's Confidential Information it will, except where impracticable for necessary disclosures, give reasonable advance notice to the Disclosing Party of such disclosure requirement and will use its reasonable efforts to secure confidential treatment of such Confidential Information required to be disclosed; (ii) on a need-to-know basis, in communication with actual or potential lenders, potential acquirers, investors, merger partners, consultants, or professional advisors, in each case under confidentiality provisions no less restrictive than those of this Agreement; (iii) to the extent such disclosure is required to comply with existing expressly stated contractual obligations owed to such Party's or its Affiliates' licensor with respect to any intellectual property licensed to the other Party under this Agreement; or (iv) as mutually agreed to in writing by the Parties.

12.4. Press Release; Publications; Disclosure of Agreement.

12.4.1. **Announcement of Transaction**. Subject to the consent of the other Party, each Party may issue a press release announcing the signing of this Agreement after the Effective Date.

12.4.2. **Other Disclosures**.

(a) **Clinical Studies**. Novartis has the right to disclose the existence of, and the results from, any Clinical Studies conducted under this Agreement in accordance with its standard policies.

(b) **During the Research Term**. Except to the extent required to comply with Applicable Law or as otherwise permitted in accordance with this Section 12.4 (Press Release; Publications; Disclosure of Agreement), during the Research Term, neither Party nor its Affiliates will make any public announcements, press releases or other public disclosures concerning a Development Candidate or Licensed Product, this Agreement or the terms or the subject matter hereof without the prior written consent of the other Party, which consent will not be unreasonably withheld, conditioned or delayed. If, during the Research Term, a Party intends to make any public announcements, press releases or other public disclosures regarding a Licensed Product, this Agreement or the terms or the subject matter hereof, (i) such Party will submit such proposed public disclosure to the other Party for review at least [***] in advance of such proposed public disclosure, (ii) the other Party will have the right to review and recommend changes to such communication, and (iii) the publishing Party will in good faith consider any changes that are timely recommended by the other Party.

(c) **After Expiration of the Research Term**. Except to the extent required to comply with Applicable Law or as otherwise permitted in accordance with this Section 12.4 (Press Release; Publications; Disclosure of Agreement), after expiration of the Research Term, [***] will make any public announcements, press releases or other public disclosures regarding this Agreement or the terms or the subject matter hereof, or that will materially impact a Licensed Product or Development Candidate, without the prior written consent of [***], which consent will not be unreasonably withheld, conditioned or delayed.

(i) If, after expiration of the Research Term, [***] intend to make any public announcements, press releases or other public disclosures that will materially impact a Licensed Product or Development Candidate, (A) unless [***] existing confidentiality obligations to a Third Party prohibit it from doing so, [***] will submit such proposed public disclosure to [***] for review at least [***] in advance of such proposed public disclosure, (B) [***] will have the right to review and recommend changes to such communication, and (C) [***] will in good faith consider any changes that are timely recommended by [***].

(ii) If, after expiration of the Research Term, [***] intends to make any public announcements, press releases or other public disclosures regarding this Agreement or the terms or the subject matter hereof, or that are significant to a Licensed Product ([***]), (A) [***] will submit such proposed public disclosure to [***] for review at least [***] in advance of such proposed public disclosure, (B) [***] will have the right to review and recommend changes to such communication, and (C) [***] will in good faith consider any changes that are timely recommended by [***].

12.4.3. **Use of Name**. Except as set forth in Section 12.4.8 (Acknowledgment), neither Party will use the other Party's name in a press release or other publication without first obtaining the prior consent of the Party to be named.

12.4.4. **Notice of Significant Events**. Each Party will use Commercially Reasonable Efforts to immediately notify (and provide as much advance notice as possible, but at a minimum [***] advance notice to) the other Party of any material event related to a Licensed Product so the Parties may analyze the need for or desirability of publicly disclosing or reporting such event.

12.4.5. **Scientific or Clinical Presentations**.

(a) **Research Activities**. Any scientific or clinical presentation related to the Research Activities will be mutually agreed to by Novartis and Ionis before any such abstract, presentation or publication is submitted to the Third Party publisher for publication and will appropriately represent the contribution of Ionis (or its Affiliate), Novartis and any Third Party collaborators. Industry-recognized principles of both inclusion of authors and order of authors will be applied to respect appropriately the contributions of all parties to the inventions or data being presented or published. Each Party will review any such proposed publication to avoid the unauthorized disclosure of a Party's Confidential Information and to preserve the patentability of inventions arising under this Agreement. Each Party will first submit to the other Party an early draft of all such publications or presentations, whether they are to be presented orally or in written form, at least [***] prior to submission for publication including to facilitate the publication of any summaries of Clinical Studies data and results as required on the clinical trial registry of each respective Party. If at any time during such [***] period, the other Party informs such Party that its proposed publication discloses inventions made by either Party under this Agreement that have not yet been protected through the filing of a patent application, or the public disclosure of such proposed publication could be expected to have a material adverse effect on any Patent Rights or Know-How solely owned or Controlled by such other Party, then such Party will either (i) delay such proposed publication for up to [***] from the date the other Party informed such Party of its objection to the proposed publication, to permit the timely preparation and first filing of patent application(s) on the information involved or (ii) remove the identified disclosures prior to publication.

(b) **After Expiration of the Research Term**. Upon expiration of the Research Term, Novartis shall be solely responsible for any scientific or clinical presentations related to the Licensed Product that are not related to the Research Activities subject to the review procedure set forth in this Section 12.4.5(b) (After Expiration of the Research Term). Novartis will submit any such abstract, presentation or publication to Ionis whether they are to be presented orally or in written form, at least [***] prior to submission for publication. If at any time during such [***] period, Ionis informs Novartis that its proposed publication discloses inventions made by either Party under this Agreement that have not yet been protected through the filing of a patent application, or the public disclosure of such proposed publication could be expected to have a material adverse effect on any Patent Rights or Know-How solely owned or Controlled by Ionis, then such Novartis will either (i) delay such proposed publication for up to [***] from the date Ionis informed Novartis of its objection to the proposed publication, to permit the timely preparation and first filing of patent application(s) on the information involved or (ii) remove the identified disclosures prior to publication.

12.4.6. **SEC Filings**. Each Party will give the other Party a reasonable opportunity to review all material filings with the SEC describing the terms of this Agreement prior to submission of such filings, and will give due consideration to any reasonable comments by the non-filing Party relating to such filing.

12.4.7. **Subsequent Disclosure**. Notwithstanding the foregoing, to the extent information regarding this Agreement or a Licensed Product has already been publicly disclosed, either Party (or its Affiliates) may subsequently disclose the same information to the public without the consent of the other Party so long as such information remains true, correct and the most current information with respect to the subject matters set forth therein.

12.4.8. **Acknowledgment**. Novartis will [***]. Ionis may include each Licensed Product (and identify Novartis as its partner for the Licensed Product) in Ionis' drug pipelines, any press release, public presentation or publication mentioning a Licensed Product.

ARTICLE 13
MISCELLANEOUS

13.1. Dispute Resolution.

13.1.1. **General**. The Parties recognize that a dispute may arise relating to this Agreement ("***Dispute***"). Except as set forth in Section 3.3 (Decision Making), Section 7.9.5 (Third Party IP Dispute), Section 8.2.3 (Inventorship) and Section 13.1.5 (Injunctive Relief; Court Actions), any Dispute between the Parties or their respective Affiliates will be resolved in accordance with this Section 13.1 (Dispute Resolution).

13.1.2. **Continuance of Rights and Obligations during Pendency of Dispute Resolution**. If there are any Disputes in connection with this Agreement, including Disputes related to termination of this Agreement under Article 11 (Term; Termination), all rights and obligations of the Parties will continue until such time as any Dispute has been resolved in accordance with the provisions of this Section 13.1 (Dispute Resolution).

13.1.3. **Escalation**. Subject to Section 13.1.5 (Injunctive Relief; Court Actions), any claim, Dispute, or controversy as to the breach, enforcement, interpretation or validity of this Agreement will be referred to the Novartis' Global Head of Corporate and Business Development (or a designee appointed by the Global Head of Corporate and Business Development) and to the Chief Executive Officer of Ionis (or a designee appointed by the Chief Executive Officer) (the "***Executives***") for attempted resolution. If the Executives are unable to resolve such Dispute within [***] of such Dispute being referred to them, then, upon the written request of either Party to the other Party, the Dispute will be subject to arbitration in accordance with Section 13.1.4 (Arbitration), except as expressly set forth in Section 13.1.5 (Injunctive Relief; Court Actions) or Section 13.3 (Recovery of Losses).

13.1.4. **Arbitration**.

(a) If the Parties cannot resolve the Dispute through escalation pursuant to Section 13.1.3 (Escalation), and a Party desires to pursue resolution of the Dispute, any Dispute will be solely and exclusively finally settled under the Rules of Arbitration of the ICC by a panel of three arbitrators appointed in accordance with said Rules, *provided however*, that the third arbitrator, who will act as president of the arbitral tribunal, will not be appointed by the International Court of Arbitration, but by the two arbitrators which have been appointed by either of the Parties in accordance with Article 4 para 4 of said Rules.

(b) The place of arbitration will be New York, New York and the language to be used in any such Proceeding (and for all testimony, evidence and written documentation) will be English. The IBA Rules on the Taking of Evidence in International Arbitration will apply on any evidence to be taken up in the arbitration.

(c) Without limiting any other remedies that may be available under law, the arbitrators will have no authority to award damages not permitted to be recovered pursuant to Section 10.6 (Limitation of Consequential Damages). The Parties agree to select the arbitrator(s) within [***] after initiation of the arbitration. The hearing will be concluded within [***] after selection of the arbitrator(s) and the award will be rendered within [***] after the conclusion of the hearing, or of any post hearing briefing, which briefing will be completed by both Parties within [***] after the conclusion of the hearing. If the Parties cannot agree upon a schedule, then the arbitrator(s) will set the schedule following the time limits set forth above as closely as practicable.

(d) EXCEPT IN THE CASE OF COURT ACTIONS PERMITTED BY SECTION 13.1.5 (INJUNCTIVE RELIEF; COURT ACTIONS) AND FOR CLAIMS NOT SUBJECT TO ARBITRATION PURSUANT TO SECTION 13.1.4 (ARBITRATION) AS SET FORTH IN SECTION 13.1.5 (INJUNCTIVE RELIEF; COURT ACTIONS), EACH PARTY HERETO WAIVES: (1) ITS RIGHT TO TRIAL OF ANY ISSUE BY JURY, AND (2) ANY CLAIM FOR ATTORNEY FEES, COSTS AND PREJUDGMENT INTEREST.

(e) Each Party will bear its own attorneys' fees, costs, and disbursements arising out of the arbitration, and will pay an equal share of the fees and costs of the arbitrators; *provided, however*, [***].

(f) Notwithstanding any provision to the contrary, if the Dispute is regarding the existence, materiality, or failure to cure any material breach where Ionis is the alleged Breaching Party, then the arbitration will be bifurcated with respect to liability and damages, such that damages will only be determined if Novartis elects not to exercise the alternative remedy set forth in Section 11.4 (Alternative Remedy in Lieu of Termination).

13.1.5. **Injunctive Relief; Court Actions**. Notwithstanding anything to the contrary in this Agreement, each Party will be entitled to seek from any court of competent jurisdiction, in addition to any other remedy it may have at law or in equity, injunctive or other equitable relief in the event of an actual or threatened breach of this Agreement by the other Party, without the posting of any bond or other security, and such an action may be filed and maintained notwithstanding any ongoing discussions between the Parties or any ongoing arbitration Proceeding. The Parties agree that in the event of a threatened or actual material breach of this Agreement injunctive or equitable relief may be an appropriate remedy. In addition, except as set forth otherwise in Section 7.9.4 (Right to Offset) and Section 8.2.3 (Inventorship) either Party may bring an action in any court of competent jurisdiction to resolve disputes pertaining to the validity, construction, scope, enforceability, infringement or other violations of Patent Rights or other intellectual property rights, and no such claim will be subject to arbitration pursuant to Section 13.1.4 (Arbitration).

13.2. Governing Law; Jurisdiction. This Agreement and any Dispute will be governed by and construed and enforced in accordance with the laws of the State of New York, U.S.A., without reference to conflicts of laws principles. The United Nations Convention on Contract for the International Sales of Goods (1980) shall not apply to the interpretation of this Agreement.

13.3. Recovery of Losses. Neither Party will be entitled to recover any Losses relating to any matter arising under one provision of this Agreement to the extent that such Party has already recovered such Losses pursuant to other provisions of this Agreement, including recoveries under Section 10.1 (Indemnification by Novartis) or Section 10.2 (Indemnification by Ionis), and the offsets under Sections 7.9.4 (Right to Offset). Except for the offset and credits explicitly set forth in Section 4.3 (Acquisition of a Competitive Compound), Section 7.12 (Audits), Section 7.9.4 (Right to Offset), a final and binding decision of the arbitrators in accordance with Section 13.1.4 (Arbitration) or by the court of competent jurisdiction in accordance with Section 13.1.5 (Injunctive Relief; Court Actions) neither Party will have the right to set off any amount it is owed or believes it is owed against payments due or payable to the other Party under this Agreement. Notwithstanding the non-refundable or non-creditable nature of any milestone payments hereunder, but subject to the limitations set forth in Section 10.6 (Limitation of Consequential Damages), nothing in this Agreement shall limit either Party's rights to assert or obtain damages for breach of this Agreement, including damages calculated based on the payments made under this Agreement.

13.4. Assignment and Successors.

13.4.1. Neither this Agreement nor any obligation of a Party hereunder may be assigned by either Party without the consent of the other, which will not be unreasonably withheld, delayed or conditioned, except that each Party may assign this Agreement and the rights, obligations and interests of such Party, in whole or in part, without the other Party's consent, to any of its Affiliates, to any purchaser of all or substantially all of its assets or all or substantially all of its assets to which this Agreement relates or to any successor corporation resulting from any merger, consolidation, share exchange or other similar transaction. Notwithstanding the foregoing, [***]. In addition, Ionis may, subject to Section 7.8 ([***]), [***], without Novartis' consent. Except in the case where [***], any permitted assignee will assume all applicable obligations of its assignor under this Agreement. Each Party shall remain primarily liable for any acts or omissions of its permitted assigns. Subject to the terms of this Agreement, this Agreement will be binding upon and inure to the benefit of the Parties and their respective successors and permitted assigns.

13.4.2. Unless explicitly agreed otherwise in writing between the Parties, if any assignment of this Agreement or of any rights or obligations under this Agreement results in [***], then [***] ("***Transferring Party***") such that the Party ("***Non-Transferring Party***") entitled to receive a given payment under this Agreement receives [***]. Any purported assignment or transfer made in contravention of this Section 13.4 (Assignment and Successors) will be null and void. This Section 13.4 (Assignment and Successors) will apply to the assignment of Licensed Technology *mutatis mutandis*.

13.5. **Change of Control Event Involving Novartis or Ionis**. A Party subject to a Change of Control Event will provide written notice to the other Party within [***] following the closing of a Change of Control Event, and such notice will identify the Third Party acquiring company (the "***Acquirer***") and the contact information of the person at the Acquirer with whom the other Party will work to schedule meetings between the Acquirer and the other Party. Within [***] following the closing of such Change of Control Event, the Party or the Acquirer will [***]. Notwithstanding any other provision of this Agreement, in the case of a Change of Control Event [***].

13.6. **Force Majeure**. No Party will be held responsible to the other Party nor be deemed to be in default under, or in breach of any provision of, this Agreement for failure or delay in performing any obligation of this Agreement when such failure or delay is due to force majeure, and without the fault or negligence of the Party so failing or delaying. For purposes of this Agreement, force majeure means a cause beyond the reasonable control of a Party, which may include acts of God, war, terrorism, cyber-attacks, civil commotion, riot, fire, flood, earthquake, tornado, tsunami, explosion or storm, pandemic, epidemic, any action of a governmental authority or agency, national industry strike, lockout, sabotage, shortage in supply, energy shortage and failure of public utilities or common carriers. In such event the failing or delaying Party shall promptly notify the other Party of such inability and of the period for which such inability is expected to continue. The Party giving such notice will be excused from such of its obligations under this Agreement as it is thereby disabled from performing for so long as it is so disabled and shall use commercially reasonable efforts to minimize the duration of any force majeure and resume performance of its obligation as promptly as practicable. Notwithstanding the foregoing, if such force majeure event induced delay or failure of performance continues for a period of [***], after such time the Parties will negotiate in good faith any permanent or transitory modifications of the terms of this Agreement that may be necessary to arrive at an equitable solution, unless the Party giving such notice has set out a reasonable timeframe and plan to resolve the effects of such force majeure and execute such plan within such timeframe.

13.7. **Notices**. Any notice or request required or permitted to be given under or in connection with this Agreement will be deemed to have been sufficiently given if in writing and personally delivered or sent by certified mail (return receipt requested), or internationally recognized overnight express courier service (signature required), prepaid, to the Party for which such notice is intended, at the address set forth for such Party below:

If to Ionis, addressed to:

Ionis Pharmaceuticals, Inc.
2855 Gazelle Court
Carlsbad, CA 92010
Attention: Chief Business Officer

with a copy to (which copy will not constitute notice):
[***]
Attention: General Counsel

If to Novartis, addressed to:

Novartis Pharma AG
Lichtstrasse 35
4002, Basel, Switzerland
Attention: General Counsel

with a copy to: Novartis Pharma AG
Lichtstrasse 35
4002, Basel, Switzerland
Attention: Head Global Business
Development & Licensing

or to such other address for such Party as it will have specified by like notice to the other Party; *provided* that notices of a change of address will be effective only upon receipt thereof. If delivered personally or by facsimile transmission, the date of delivery will be deemed to be the date on which such notice or request was given. If sent by overnight express courier service, the date of delivery will be deemed to be the next Business Day after such notice or request was deposited with such service.

13.8. **Waiver**. Neither Party may waive or release any of its rights or interests in this Agreement except in writing. The failure of either Party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement shall not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition. No waiver by either Party of any condition or term in any one or more instances shall be construed as a continuing waiver or subsequent waiver of such condition or term or of another condition or term. No waiver shall be effective unless it has been given in writing and signed by the Party giving such waiver.

13.9. **Severability**. If any provision hereof should be held invalid, illegal or unenforceable in any jurisdiction, the Parties will negotiate in good faith a valid, legal and enforceable substitute provision that most nearly reflects the original intent of the Parties and all other provisions hereof will remain in full force and effect in such jurisdiction and will be liberally construed in order to carry out the intentions of the Parties hereto as nearly as may be possible. Such invalidity, illegality or unenforceability will not affect the validity, legality or enforceability of such provision in any other jurisdiction.

13.10. **Entire Agreement; Modifications**. This Agreement (including the attached Appendices, Schedules, and Exhibit) sets forth and constitutes the entire agreement and understanding between the Parties with respect to the subject matter hereof, and all prior agreements, understanding, promises and representations, whether written or oral, with respect thereto are superseded hereby. Each Party confirms that it is not relying on any representations or warranties of the other Party except as specifically set forth herein. No amendment, modification, release or discharge will be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

13.11. **Independent Contractors**. Nothing herein will be construed to create any relationship of employer and employee, agent and principal, partnership joint venture or legal entity of any type between the Parties. Each Party is an independent contractor. Neither Party will assume, either directly or indirectly, any liability of or for the other Party. Neither Party will have the authority to bind or obligate the other Party and neither Party will represent that it has such authority. Moreover, each Party agrees not to construe this Agreement, or any of the transactions contemplated hereby, as a partnership for any tax purposes.

13.12. **Interpretation**. Except as otherwise explicitly specified to the contrary, (a) references to a section, Exhibit, Appendix or Schedule means a Section of, or Schedule or Exhibit or Appendix to this Agreement, unless another agreement is specified, (b) the word “including” (in its various forms) means “including without limitation,” (c) the words “will” and “shall” have the same meaning, (d) references to a particular statute or regulation include all rules and regulations thereunder and any predecessor or successor statute, rules or regulation, in each case as amended or otherwise modified from time to time, (e) words in the singular or plural form include the plural and singular form, respectively, (f) references to a particular Person include such Person’s successors and assigns to the extent not prohibited by this Agreement, (g) unless otherwise specified, “$” is in reference to United States dollars, (h) the headings contained in this Agreement, in any Exhibit or Appendix or Schedule to this Agreement are for convenience only and will not in any way affect the construction of or be taken into consideration in interpreting this Agreement, (i) the word “or” will not be construed as exclusive and will have the meaning typically ascribed to the term “and/or”; (j) the words “hereof,” “herein,” and “herewith,” and words of similar import, will, unless otherwise stated, be construed to refer to this Agreement as a whole and not to any particular provision of this Agreement and (k) general words will not be given a restrictive interpretation by reason of their being preceded or followed by words indicating a particular class of acts, matters or things.

13.13. **Books and Records**. Any books and records to be maintained under this Agreement by a Party or its Affiliates or Sublicensees will be maintained in accordance with their respective Applicable Law and Accounting Standards.

13.14. **Further Actions**. Each Party will execute, acknowledge and deliver such further instruments, and do all such other acts, as may be necessary or appropriate in order to carry out the expressly stated purposes and the clear intent of this Agreement.

13.15. **Construction of Agreement**. The terms and provisions of this Agreement represent the results of negotiations between the Parties and their representatives, each of which has been represented by counsel of its own choosing, and neither of which has acted under duress or compulsion, whether legal, economic or otherwise. Accordingly, the terms and provisions of this Agreement will be interpreted and construed in accordance with their usual and customary meanings, and each of the Parties hereto hereby waives the application in connection with the interpretation and construction of this Agreement of any rule of law to the effect that ambiguous or conflicting terms or provisions contained in this Agreement will be interpreted or construed against the Party whose attorney prepared the executed draft or any earlier draft of this Agreement.

13.16. **Supremacy**. In the event of any express conflict or inconsistency between this Agreement and any Schedule, Appendix, or Exhibit hereto, the terms of this Agreement will apply. The Parties understand and agree that the Appendices identifying the Licensed Technology are not intended to be the final and complete embodiment of any terms or provisions of this Agreement, and are to be updated from time to time during the Agreement Term, as appropriate and in accordance with the provisions of this Agreement.

13.17. **Counterparts**. This Agreement (or any notice, invoice or other document to be delivered by a Party hereunder) may be signed in counterparts, each of which will be deemed an original, but all of which together will constitute one and the same instrument, notwithstanding variations in format or file designation which may result from the electronic transmission, storage and printing of copies of this Agreement from separate computers or printers, and facsimile signatures and signatures transmitted via electronic mail in PDF format will be treated as original signatures.

13.18. **Compliance with Laws**. Each Party will, and will ensure that its Affiliates will, comply with all Applicable Law in exercising its rights and fulfilling its obligations under this Agreement. No Party will, or will be required to, undertake any activity under or in connection with this Agreement which violates, or which it believes, in good faith, may violate, any Applicable Law.

13.19. **Remedies at Law**. Without limiting Section 13.3 (Recovery of Losses) and except as expressly stated in this Agreement, the rights and remedies provided in this Agreement and all other rights and remedies available to either Party at law or in equity are, to the extent permitted by law, cumulative and not exclusive of any other right or remedy now or hereafter available at law or in equity.

[*SIGNATURE PAGE FOLLOWS*]

* - * - * - *

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their representatives thereunto duly authorized as of the Execution Date.

NOVARTIS PHARMA AG

By: */s/ Guillaume Vignon*

Name: Guillaume Vignon

Title: Global Head BD&L Partnering

NOVARTIS PHARMA AG

By: */s/ Mark Victor Rogers*

Name: Mark Victor Rogers

Title: Global Head Pharma Transactions

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their representatives thereunto duly authorized as of the Execution Date.

IONIS PHARMACEUTICALS, INC.

By: */s/ Brett Monia*

Name: Brett Monia
Title: Chief Executive Officer

List of Appendices, Schedules, and Exhibits

APPENDIX 1

DEFINITIONS

For purposes of this Agreement, the following capitalized terms will have the following meanings:

"***AAA***" has the meaning set forth in SCHEDULE 11.5.3.

"***Acceptance of NDA Filing***" means the receipt of written notice from the FDA in accordance with 21 C.F.R. § 314.101(a)(2) that such NDA is officially "filed."

"***Accounting Standards***" means, with respect to Ionis, U.S. GAAP (United States Generally Accepted Accounting Principles) and means, with respect to Novartis, the IFRS (International Financial Reporting Standards), in each case, as generally and consistently applied throughout the applicable Party's organization. Each Party shall promptly notify the other in the event that it changes the Accounting Standards pursuant to which its records are maintained, it being understood that each Party may only use internationally recognized accounting standards (*e.g.*, U.S. GAAP, IFRS or equivalent).

"***Actually Used***" means, with respect to any Novartis Technology and a Terminated Product and subject to Section 11.5.3(a)(iv) (Acquisition of Alternative Technologies), that such Novartis Technology was [***]. For clarity, (1) [***] will be considered "Actually Used", and (2) [***] will be considered "Actually Used."

"***Acquired Compound***" has the meaning set forth in Section 4.3 (Acquisition of a Competitive Compound).

"***Acquirer***" has the meaning set forth in Section 13.5 (Change of Control Event Involving Novartis or Ionis).

"***Additional Ionis Research Activities***" has the meaning set forth in Section 2.4 (Research Costs).

"***Affiliate***" of an entity means any corporation, firm, partnership or other entity which directly or indirectly through one or more intermediaries controls, is controlled by or is under common control with a Party to this Agreement. An entity will be deemed to control another entity if it (a) owns, directly or indirectly, more than 50% of the outstanding voting securities (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) of such other entity, or has other comparable ownership interest with respect to any entity other than a corporation; or (b) has the power, whether pursuant to contract, ownership of securities or otherwise, to direct the management and policies of the entity.

"***Agreement***" has the meaning set forth in the Preamble of this Agreement.

"***Agreement Term***" has the meaning set forth in Section 11.1 (Agreement Term; Expiration).

"***Akcea-Novartis Collaboration Agreement***" means that certain Strategic Collaboration, Option and License Agreement between Novartis Pharma AG and Akcea Therapeutics, Inc., dated January 5, 2017, as amended on February 22, 2019.

"***Alliance Manager***" has the meaning set forth in Section 3.6 (Alliance Managers).

"***Annual***" or "***Annually***" means the period covering a Calendar Year or occurring once per Calendar Year, as the context requires.

"***Antitrust Filings***" means any filings, notices, applications or other submissions under Antitrust Law.

"***Antitrust Laws***" means any federal, state, or foreign statutes, rules, regulations, orders, or decrees that are designed to prohibit, restrict, or regulate actions having the purpose or effect of monopolization, lessening of competition or restraint of trade, including the HSR Act.

"***API***" means the bulk active pharmaceutical ingredient manufactured in accordance with cGMP (unless expressly stated otherwise) for a Licensed Product.

"***APO(a)***" means the protein product encoded by the apolipoprotein(a) gene (also known as LPA, Lipoprotein A, or Lp(a) gene) (GenBank accession # NM_005577.2; NCBI Gene ID: 4018), including any alternative splice variants, mutants, polymorphisms and fragments thereof.

"***Applicable Law***" or "***Law***" means all applicable laws, statutes, rules, regulations and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, agency or other body, domestic or foreign, including any applicable rules, regulations, guidelines, or other requirements of the Regulatory Authorities that may be in effect from time to time.

"***Audit Report***" has the meaning set forth in Section 7.12.3 (Audits).

"***Auditor***" has the meaning set forth in Section 7.12.1 (Audits).

"***Bankruptcy Code***" has the meaning set forth in Section 11.2.5(b) (Termination for Insolvency).

"***Breaching Party***" means the Party that is believed by the Non-Breaching Party to be in material breach of this Agreement.

"[***]" has the meaning set forth in SCHEDULE 11.5.3 ([***]).

"***Business Day***" means any calendar day, other than a Saturday or Sunday and December 24 to January 2, on which banking institutions in Basel, Switzerland or New York, New York are open for business.

"***Calendar Quarter***" means a period of three consecutive months ending on the last calendar day of March, June, September, or December, respectively, and will also include the period beginning on the Effective Date and ending on the last calendar day of the Calendar Quarter in which the Effective Date falls.

"***Calendar Year***" means a year beginning on January 1 (or, with respect to 2023, the Effective Date) and ending on December 31.

"***Carryover Candidate***" has the meaning set forth in Section 2.2.2 (Carryover Period).

"***Carryover Period***" has the meaning set forth in Section 2.2.2 (Carryover Period).

"***cGMP***" means current Good Manufacturing Practices as specified in the United States Code of Federal Regulations, ICH Guideline Q7A, or equivalent laws, rules, or regulations of an applicable Regulatory Authority at the time of manufacture.

"***Change of Control Event***" means any (a) direct or indirect acquisition of all or substantially all of the assets of a Party, (b) direct or indirect acquisition by a Person, or group of Persons acting in concert, of [***]% or more of the voting equity interests of a Party, (c) tender offer or exchange offer that results in any Person, or group of Persons acting in concert, beneficially owning [***]% or more of the voting equity interests of a Party, or (d) merger, consolidation, other business combination or similar transaction involving a Party, pursuant to which any Person becomes the owner of all or substantially all of the consolidated assets, net revenues or net income of a Party, taken as a whole, or which results in the holders of the voting equity interests of a Party immediately prior to such merger, consolidation, business combination or similar transaction ceasing to hold [***]% or more of the combined voting power of the surviving, purchasing or continuing entity immediately after such merger, consolidation, other business combination or similar transaction, in all cases where such transaction is entered into with any Person other than the other Party to this Agreement or its Affiliates.

"***Clinical Development Plan***" has the meaning set forth in Section 2.5 (Clinical Development Plan).

"***Clinical Study***" or "***Clinical Studies***" means a Phase 1 Trial, Phase 2 Trial, Phase 3 Trial or such other study in humans that is conducted in accordance with good clinical practices and is designed to generate data in support or maintenance of an NDA, MAA, or other similar marketing application.

"***CMO***" means a Third Party contract manufacturer Manufacturing API, clinical supplies or Finished Drug Product for any purpose under this Agreement.

"***CMO Agreement***" has the meaning set forth in Section 5.4.2 (Novartis' CMOs).

"***Combination Product***" has the meaning set forth in the definition of "Net Sales" in this Appendix 1 (Definitions).

"***Commercialize***," "***Commercialization***" or "***Commercializing***" means any and all activities directed to registering, marketing, promoting, detailing, distributing, importing, having imported, exporting, having exported, selling or offering to sell a product (including a Licensed Product) following receipt of Regulatory Approval for such product in the applicable country, including conducting pre-and post-Regulatory Approval activities, and launching and promoting the product in each country.

"***Commercially Reasonable Efforts***" means the level of effort, budget and resources normally used by the respective Party for a product owned or controlled by it, which is of similar profitability and at a similar stage in its development or product life, taking into account with respect to a product *inter alia* any issues of patent coverage, safety and efficacy, pricing, product profile, the proprietary position of the product, the competitive environment for the product and the likely timing of the product(s) entry into the market, the regulatory environment of the product and other relevant scientific, technical and commercial factors. Commercially Reasonable Efforts will be determined on a Licensed Product-by-Licensed Product and country-by-country basis. Notwithstanding any provision to the contrary in this Agreement, Novartis will not be permitted to take into consideration any Acquired Compound in determining what constitutes Commercially Reasonable Efforts.

"***Competitive Compound***" means any Oligonucleotide that is designed to bind to the RNA encoding APO(a).

"***Competitive Infringement***" has the meaning set forth in Section 8.6 (Enforcement of Patents Against Competitive Infringement).

"***Competitive Product***" has the meaning set forth in Section 4.4 (Change of Control).

"***Completion***" means (a) with respect to an IND-Enabling Toxicology Study, receipt of the final report for such IND-Enabling Toxicology Study and (b) with respect to a Clinical Study, the point in time at which database lock for such study has occurred and, if such study has a statistical analysis plan, the primary and secondary endpoints and key safety data generated (including tables, listings and figures generated based on that database lock) for such study are available.

"***Compound***" means any Oligonucleotide that is designed to bind to the RNA encoding APO(a) discovered by Ionis, Novartis, or jointly between the Parties.

"***Compound Pool***" has the meaning set forth in Section 2.2.1 (Development Candidate Data Packages).

"***Confidential Information***" means any confidential or proprietary information, data or materials, patentable or otherwise, including trade secrets, Know-How, inventions or discoveries, proprietary information, formulae, processes, techniques and other information, in any form (written, oral, photographic, electronic, magnetic, or otherwise) which is disclosed by the Disclosing Party or its Affiliates to the Receiving Party or its Affiliates in the course of performing its obligations or exercising its rights under this Agreement. "*Confidential Information*" does not include information that:

(a) was in the lawful knowledge and possession of the Receiving Party or its Affiliates prior to the time it was disclosed to the Receiving Party or its Affiliates, or was otherwise developed independently by the Receiving Party or its Affiliates, in each case, as evidenced by written records kept in the ordinary course of business, or other documentary proof of the Receiving Party or its Affiliates;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party or its Affiliates;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the Receiving Party or its Affiliates in breach of this Agreement; or

(d) was disclosed to the Receiving Party or its Affiliates, other than under an obligation of confidentiality, by a Third Party who had no obligation to the Disclosing Party or its Affiliates not to disclose such information to others.

"***Conjugate Technology***" means a group of atoms covalently bound to an Oligonucleotide designed to enhance one or more properties of the Oligonucleotide, such as targeting of antisense drugs to specific tissues and cells. Conjugate Technology includes N-acetylgalactosamine (GalNAc) ligand conjugates capable of binding to the asialoglycoprotein receptor (ASGP-R) and enhancing the targeting of antisense drugs.

"***Control***" or "***Controlled***" means possession of the legal authority or the right (whether by ownership, license or otherwise) to grant a license or sublicense hereunder without violating the terms of any agreement with any Third Party; *provided* that [***]. Notwithstanding anything to the contrary under this Agreement, with respect to any Third Party that becomes an Affiliate of a Party after the Effective Date (including a Third Party acquirer), no intellectual property of such Third Party owned or controlled by such Third Party immediately prior to the date such Third Party becoming an Affiliate of a Party hereunder will be included in the licenses granted hereunder by virtue of such Third Party becoming an Affiliate of such Party.

"***Core European Countries***" means the United Kingdom, Germany, France, Italy and Spain.

"***Cover***," "***Covered***" or "***Covering***" means, with respect to a Patent Right and a product, technology, process, method, or mode of administration that the manufacture, use, offer for sale, sale, or importation of such product or the practice of such technology, process, method, or mode of administration falls within the scope of at least one claim of such Patent Right.

"***DC Selection Date***" has the meaning set forth in Section 2.2.4 (Development Candidate Selection Process).

"***Develop***," "***Developing***" or "***Development***" means, with respect to a product (including a Licensed Product) after such product is designated as a development candidate, any and all non-clinical, clinical or regulatory activity with respect to such product to support approval by a regulatory authority to market and sell such product (including the submission of all necessary filings with applicable Regulatory Authorities to support such non-clinical and clinical activities and Regulatory Approval), including pharmacokinetic and toxicology studies required to meet the requirements for filing an IND and filing an IND with any regulatory authority.

"***Development Candidate***" means any Compound that is designated by the JSC as a development candidate in accordance with Section 2.2.4 (Development Candidate Selection Process).

"***Development Candidate Criteria***" has the meaning set forth in Section 2.1.1 (Research Plan).

"***Development Candidate Data Package***" means the data package prepared by either Party or the JRC for the JSC to review and consider designating a Licensed Compound as a Development Candidate; *provided* that such package contains [***], but in any event at least the same level of detail as the data packages the relevant Party presents to its research management committee to approve its own internal development candidates. In the case of a Development Candidate Data Package prepared by Ionis, such package may include [***].

"***Disclosing Party***" has the meaning set forth in Section 12.1 (Confidentiality; Exceptions).

"***Dispute***" has the meaning set forth in Section 13.1.1 (General).

"***DOJ***" has the meaning set forth in Section 5.11.1 (Effectiveness of the Agreement).

"***Domain Names***" means any Domain Name identical or similar with the Trademarks under any ccTLD (country code Top Level Domain) and gTLD (generic Top Level Domain) address area.

"***Draft Report***" means, with respect to an IND-Enabling Toxicology Study, an integrated, audited draft report containing the toxicology data generated from such IND-Enabling Toxicology Study.

"***Effective Date***" has the meaning set forth in Section 5.11.1 (Effectiveness of the Agreement).

"***EMA***" means the European Medicines Agency and any successor entity thereto.

"[***]" means, with respect to a Licensed Product, any "[***]" as described in [***] for such Licensed Product, or, if a standard [***] is not applicable, then [***].

"***Evaluation Period***" has the meaning set forth in Section 4.3 (Acquisition of a Competitive Compound).

"[***]" has the meaning set forth in Section [***].

"***Execution Date***" has the meaning set forth in the Preamble of this Agreement.

"***Executives***" has the meaning set forth in Section 13.1.3 (Escalation).

"***Exploit***" means, with respect to any product, to Research, Develop, have Developed, use, have used, offer for sale, have offered for sale, sell, have sold or otherwise Commercialize or have Commercialized, export, have exported, import, have imported, Manufacture, have Manufactured, or otherwise exploit such product. "***Exploitation***" and "***Exploiting***" will be construed accordingly.

"***FDA***" means the United States Food and Drug Administration and any successor entity thereto.

"***Field***" means all therapeutic, prophylactic, palliative, analgesic, and diagnostic uses in humans.

"***Finished Drug Product***" means any drug product containing API as an active ingredient, in finished form for Development or Commercialization by a Party under this Agreement.

"***First Commercial Sale***" means, on a Licensed Product-by-Licensed Product basis, the first sale of such Licensed Product by Novartis, its Affiliate or its Sublicensee to a Third Party in a country after Regulatory Approval of such Licensed Product has been obtained in such country.

"***FTC***" has the meaning set forth in Section 5.11.1 (Effectiveness of the Agreement).

"***FTE***" means the number of full-time-equivalent person-years (each consisting of a total of [***] hours) of research and development work by each Party's personnel on or directly related to the applicable activity conducted hereunder. For clarity, [***].

"***FTE Costs***" means the cost of Ionis' employees based on the time incurred at performing work under this Agreement at the then-applicable FTE Rate.

"***FTE Rate***" means $[***] per FTE per Calendar Year, which rate shall be prorated on a daily basis as necessary; *provided*, that on [***] and on January 1st of each subsequent Calendar Quarter the FTE Rate will be [***] for the Calendar Year then commencing by the percentage [***] in the Consumer Price Index for All Urban Consumers (CPI-U); US City Average calculated by the Bureau of Labor Statistics during the immediately preceding Calendar Year.

"***Generic Product***" means, with respect to a Licensed Product in a country, a pharmaceutical product (other than such Licensed Product) that (a) is sold by a Third Party other than a Sublicensee under license from Novartis in such country, (b) is authorized for use in such country in one or more of the indications for which such Licensed Product has Regulatory Approval in such country; and (c) either (i) contains the same active pharmaceutical ingredient(s) as such Licensed Product or (ii) is a product approved by way of an abbreviated regulatory mechanism by the Regulatory Authority in such country that, in each case, meets the equivalency determination by the applicable Regulatory Authority (including a determination that the product is "comparable", "interchangeable", "bioequivalent", "biosimilar" or other term of similar meaning, if applicable, with respect to such Licensed Product). A product shall not be considered to be a Generic Product if (a) Novartis or any of its Affiliates or Sublicensees was involved in or authorized the Development or Commercialization of such product, (b) Novartis or any of its Affiliates or Sublicensees has granted a license to such Third Party in respect of such product, or (c) such product is Commercialized by any Person who obtained such product in a chain of distribution that included Novartis or any of its Affiliates or Sublicensees.

"***Governmental Authority***" means any United States federal, state or local government or any foreign government, or political subdivision thereof, or any local, state, national or multinational organization or authority or any authority, agency or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, any court or tribunal (or any department, bureau or division thereof), or any arbitrator or arbitral body.

"***HSR Act***" means the United States Hart-Scott-Rodino Antitrust Improvements Act of 1976 and the rules promulgated thereunder.

"***HSR Filings***" has the meaning set forth in Section 5.11.2(a).

"***Identified Rights***" has the meaning set forth in Section 7.9.2 (New In-License Agreements).

"***IND***" means an Investigational New Drug Application (as defined in the Food, Drug and Cosmetic Act, as amended) filed with the FDA.

"***Indemnification Claim Notice***" has the meaning set forth in Section 10.3 (Notice of Claim).

"***Indemnified Party***" has the meaning set forth in Section 10.3 (Notice of Claim).

"***IND-Enabling Toxicology Study***" or "***IND-Enabling Toxicology Studies***" means the non-human primate toxicology studies of a Licensed Compound designed or otherwise required to meet the requirements for filing an IND.

"***Indirect Taxes***" means value added, goods and services, sales, use, excise, consumption and other similar indirect taxes required by law to be disclosed on the invoice.

"***Initiation***" or "***Initiate***" means, with respect to any Clinical Study, dosing of the first human subject in such Clinical Study.

"***Invoice***" means an original invoice in the form attached hereto as EXHIBIT 1 (Novartis' Form of Invoice).

"***Ionis***" has the meaning set forth in the Preamble of this Agreement.

"***Ionis Core Technology Patents***" means any Patent Rights (other than Ionis Product-Specific Patents or Ionis Manufacturing and Analytical Patents) that (a) are owned, used, developed by, or licensed to Ionis or its Affiliates, in each case to the extent Controlled by Ionis or its Affiliates on the Execution Date or at any time during the Agreement Term, (b) claim subject matter generally applicable to Oligonucleotides and (c) are necessary or reasonably useful to Research, Develop, Manufacture or Commercialize a Licensed Compound or Licensed Product, but *excluding* any Patent Rights to the extent solely related to any active pharmaceutical ingredient that is not a Licensed Compound. A list of the Ionis Core Technology Patents as of the Execution Date is set forth on APPENDIX 5 (Ionis Core Technology Patents) attached hereto.

"***Ionis Indemnitees***" has the meaning set forth in Section 10.1 (Indemnification by Novartis).

"***Ionis In-License Agreements***" has the meaning set forth in Section 7.9.1 (Existing In-License Agreements).

"***Ionis Internal Oligonucleotide Safety Database***" has the meaning set forth in Section 6.6.2 (Ionis Internal Oligonucleotide Safety Database).

"***Ionis Know-How***" means any Know-How, excluding Ionis' interest in any Jointly-Owned Program Know-How, that is (a) owned, used, developed by, or licensed to Ionis or its Affiliates, in each case to the extent Controlled by Ionis or its Affiliates on the Execution Date or at any time during the Agreement Term and (b) necessary or reasonably useful to Research, Develop, Manufacture or Commercialize a Licensed Compound or Licensed Product, but *excluding* any Know-How to the extent solely related to any active pharmaceutical ingredient that is not a Licensed Compound. Ionis Know-How does not include the Ionis Manufacturing and Analytical Know-How.

"***Ionis Manufacturing and Analytical Know-How***" means Know-How, excluding Ionis' interest in any Jointly-Owned Program Know-How, that (a) relates to the synthesis or analysis of a Licensed Compound or Licensed Product regardless of sequence or chemical modification, (b) is owned, used, developed by, or licensed to Ionis or its Affiliates, in each case to the extent Controlled by Ionis or its Affiliates on the Execution Date or at any time during the Agreement Term and (c) is necessary or reasonably useful to Research, Develop, Manufacture or Commercialize a Licensed Compound or Licensed Product, but *excluding* any Know-How to the extent solely related to any active pharmaceutical ingredient that is not a Licensed Compound. Ionis Manufacturing and Analytical Know-How do not include the Ionis Know-How.

"***Ionis Manufacturing and Analytical Patents***" means Patent Rights, excluding Ionis' interest in any Jointly-Owned Program Patents, that (a) claim Manufacturing Technology owned, used, developed by, or licensed to Ionis or its Affiliates, in each case to the extent Controlled by Ionis or its Affiliates on the Execution Date or at any time during the Agreement Term and (b) are necessary or reasonably useful to Research, Develop, Manufacture or Commercialize a Licensed Compound or Licensed Product, but *excluding* any Patent Rights to the extent solely related to any active pharmaceutical ingredient that is not a Licensed Compound. A list of Ionis Manufacturing and Analytical Patents as of the Execution Date is set forth on Appendix 6 (Ionis Manufacturing and Analytical Patents) attached hereto.

"***Ionis Product-Specific Patents***" means all Product-Specific Patents that are (a) Controlled by Ionis or its Affiliates on the Execution Date or at any time during the Agreement Term and (b) necessary or reasonably useful to Research, Develop, Manufacture or Commercialize a Licensed Compound or Licensed Product, but *excluding* any Patent Rights to the extent solely related to any active pharmaceutical ingredient that is not a Licensed Compound. A list of Ionis Product-Specific Patents as of the Execution Date is set forth on Appendix 7 (Ionis Product-Specific Patents) attached hereto.

"***Ionis Program Know-How***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Ionis Program Patents***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Ionis Program Technology***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Ionis Research Activities Technology***" means any Know-How or Patent Rights that are (a) Controlled by Ionis or its Affiliates as of the Execution Date or any time during the Agreement Term and (b) necessary or reasonably useful for Novartis to perform any Research Activities or to conduct Research during the Carryover Period or the period after [***] until [***] for the first Licensed Product.

"***Joint Patent Committee***" or "***JPC***" has the meaning set forth in Section 8.1.1 (Joint Patent Committee).

"***Jointly-Owned Program Know-How***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Jointly-Owned Program Patents***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Jointly-Owned Program Technology***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Joint Research Committee***" or "***JRC***" has the meaning set forth in Section 3.2.1 (Establishment).

"***JSC***" has the meaning set forth in Section 3.1.1 (Establishment).

"***Know-How***" means inventions, technical information, know-how and materials, including technology, data, compositions, formulas, biological materials, assays, reagents, constructs, compounds, discoveries, procedures, processes, practices, protocols, methods, techniques, results of experimentation or testing, knowledge, trade secrets, skill and experience, in each case whether or not patentable or copyrightable, and in each case that are unpatented.

"***Knowledge***" means the actual knowledge of a Party's or any of its Affiliate's [***] as of the Effective Date; *provided* that, with respect to information regarding the status of Patent Rights or other intellectual property rights, "*Knowledge*" means the actual knowledge of a Party's or any of its Affiliate's [***] as of the Effective Date [***].

"***Licensed Compound***" has the meaning set forth in Section 2.2.1 (Development Candidate Data Packages).

"***Licensed Know-How***" means (a) Ionis Manufacturing and Analytical Know-How, (b) Ionis Program Know-How, (c) Ionis' and its Affiliate's interest in any Jointly-Owned Program Know-How, and (d) Ionis Know-How. For clarity, Licensed Know-How does not include any Know-How covering formulation technology or delivery devices (other than Conjugate Technology).

"***Licensed Patents***" means (a) the Ionis Product-Specific Patents, (b) the Ionis Core Technology Patents, (c) the Ionis Manufacturing and Analytical Patents, (d) subject to Section 8.4 (Patent Costs), Ionis' and its Affiliate's interest in any Jointly-Owned Program Patents, and (e) the Ionis Program Patents. For clarity, Licensed Patents do not include any Patent Rights claiming formulation technology or delivery devices (other than Conjugate Technology).

"***Licensed Product***" means any product containing a Development Candidate as an active pharmaceutical ingredient. For clarity, all products with the same active pharmaceutical ingredient(s) will be deemed a single "Licensed Product" hereunder.

"***Licensed Product License***" has the meaning set forth in Section 5.1.2 (Licensed Product License).

"***Licensed Technology***" means any and all Licensed Patents and Licensed Know-How.

"***Losses***" has the meaning set forth in Section 10.1 (Indemnification by Novartis).

"***MAA***" means a marketing authorization application filed with the EMA after Completion of Clinical Studies to obtain approval for a Licensed Product under the centralized European filing procedure or, if the centralized EMA filing procedure is not used, filed using the applicable procedures in any European Union country or other country in Europe.

"***MAA Approval***" means, with respect to a Licensed Product in Europe, approval of the MAA from the applicable Regulatory Authority in at least [***] Core European Countries sufficient for the Manufacture, distribution, use, marketing and sale of such Licensed Product and pricing and reimbursement approval in such [***] Core European Countries in accordance with Applicable Laws has been obtained, *provided* that with respect to the Core European Countries where marketing approval and pricing and reimbursement approval are not granted simultaneously (e.g., Germany), separate pricing and reimbursement approval shall not be required if and to the extent Novartis, after the grant of the relevant marketing authorization, starts selling the Licensed Product in such Core European Countries and such sales generate Net Sales.

"***Major Market***" means any of the following countries: the United States, the United Kingdom, Germany, France, Italy and Spain.

"***Major Regulatory Communications***" means any official, substantive response received from a Regulatory Authority related to a Major Regulatory Submission (e.g., meeting minutes).

"***Major Regulatory Submissions***" means, with respect to a Licensed Product, the (a) [***], (b) [***], (c) [***], (d) [***], (e) [***], (f) [***], and (g) [***].

"***Manufacture***" or "***Manufactured***" or "***Manufacturing***" means any activity involved in or relating to the manufacturing, quality control testing (including in-process, release and stability testing), releasing or packaging, for non-clinical and clinical purposes, of API or a Licensed Product in finished form.

"***Manufacturing Technology***" means (a) methods and materials used in the synthesis or analysis of an Oligonucleotide regardless of sequence or chemical modification, (b) methods of manufacturing components of an Oligonucleotide, and (c) methods and materials used in Manufacturing a Licensed Product.

"***Manufacturing Technology Transfer Plan***" has the meaning set forth in Section 5.9.2 (Ionis Manufacturing and Analytical Know-How).

"***Material Research Costs***" means, with respect to any FTE Costs and Out-of-Pocket Costs incurred by Ionis in conducting Additional Ionis Research Activities, any FTE Costs and Out-of-Pocket Costs that are in excess of $[***].

"[***]" has the meaning set forth in Section 7.8 ([***]).

"***NDA***" means a New Drug Application filed with the FDA after Completion of Clinical Studies to obtain Regulatory Approval for a Licensed Product in the United States.

"***NDA Approval***" means, with respect to a Licensed Product in the United States, FDA approval of an NDA sufficient for the Manufacture, distribution, use, marketing and sale of such Licensed Product.

"***Necessary Platform IP***" has the meaning set forth in Section 7.9.3(a) (New Necessary Platform IP).

"***Net Sales***" means the net sales recorded by Novartis or any of its Affiliates or their Sublicensees (excluding, for clarity, any distributors or wholesalers) for any Licensed Product sold to Third Parties other than Sublicensees as determined in accordance with Novartis' Accounting Standards as consistently applied, less a deduction of [***] percent ([***]%) for direct expenses related to the sales of the Licensed Product, distribution and warehousing expenses and uncollectible amounts on previously sold products. The deductions booked on an accrual basis by Novartis and its Affiliates under its Accounting Standards to calculate the recorded net sales from gross sales include the following:

(i) normal trade and cash discounts;

(ii) amounts repaid or credited by reasons of defects, rejections, recalls or returns;

(iii) rebates and chargebacks to customers and other Third Parties (including Medicare, Medicaid, Managed Healthcare and similar types of rebates);

(iv) amounts provided or credited to customers through coupons and other discount programs;

(v) delayed ship order credits, discounts or payments related to the impact of price increases between purchase and shipping dates or retroactive price reductions;

(vi) fee for service payments to customers for any non-separable services (including compensation for maintaining agreed inventory levels and providing information); and

(vii) other reductions or specifically identifiable amounts deducted for reasons similar to those listed above in accordance with Novartis' Accounting Standards.

With respect to the calculation of Net Sales:

(a) Net Sales only include the value charged or invoiced on the first arm's length sale to a Third Party. Sales between or among Novartis and its Affiliates and Sublicensees shall be disregarded for purposes of calculating Net Sales;

(b) If a Licensed Product is delivered to the Third Party before being invoiced (or is not invoiced), Net Sales will be calculated at the time all the revenue recognition criteria under Novartis' Accounting Standards are met;

(c) In the event that the Licensed Product is in finished dosage form containing the Licensed Compound in combination with one (1) or more other active ingredients (such active ingredients, "***Other Components***," and such Licensed Product, a "***Combination Product***"), the Net Sales will be calculated by multiplying the Net Sales of the Combination Product by the fraction, A/(A+B) where A is the weighted (by sales volume) average sale price in the relevant country of the Licensed Product containing the Licensed Compound as the sole active ingredient in finished form, and B is the weighted average sale price (by sales volume) in that country of the product(s) containing the Other Components as the sole active ingredient(s) in finished form. Regarding prices comprised in the weighted average price when sold separately referred to above, if these are available for different dosages from the dosages of the Licensed Compound and the Other Components, then Novartis shall be entitled to make a proportional adjustment to such prices in calculating the royalty-bearing Net Sales of the Combination Product. If the weighted average sale price cannot be determined for the Licensed Product or other product(s) containing the single Licensed Compound or Other Components, the calculation of Net Sales for Combination Products will be agreed by the Parties based on the relative value contributed by each component (each Party's agreement not to be unreasonably withheld or delayed).

"***Non-Breaching Party***" means the Party that believes the Breaching Party is in material breach of this Agreement.

"***Non-Transferring Party***" has the meaning set forth in Section 13.4.2 (Assignment and Successors).

"***Novartis***" has the meaning set forth in the Preamble of this Agreement.

"***Novartis Background Know-How***" means any Know-How that (a) is Controlled by Novartis or its Affiliates as of the Execution Date or any time during the Agreement Term, (b) is not Program Know-How and (c) is necessary or actually used to Develop, Research, Manufacture or Commercialize a Licensed Product.

"***Novartis Background Patents***" means Patent Rights that (a) Controlled by Novartis or its Affiliates as of the Execution Date or any time during the Agreement Term, (b) are not Program Patents and (c) are necessary or actually used to Develop, Research, Manufacture or Commercialize a Licensed Product.

"***Novartis Background Technology***" means Novartis Background Patents and Novartis Background Know-How.

"***Novartis Compound***" means a Licensed Compound that was discovered by Novartis prior to the Effective Date or outside of activities conducted pursuant to this Agreement.

"***Novartis Indemnitees***" has the meaning set forth in Section 10.2 (Indemnification by Ionis).

"***Novartis Know-How***" means any Know-How that is Controlled by Novartis or its Affiliates on the Execution Date or at any time during the Agreement Term.

"***Novartis Patents***" means any Patent Rights included in the Novartis Technology.

"***Novartis Product-Specific Patents***" means all Product-Specific Patents that are (a) owned, used, developed by, or licensed to Novartis or its Affiliates, in each case to the extent Controlled by Novartis or its Affiliates on the Execution Date or at any time during the Agreement Term and (b) necessary or actually used to Develop, Research, Manufacture or Commercialize a Licensed Product.

"***Novartis Program Know-How***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Novartis Program Patents***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Novartis Program Technology***" has the meaning set forth in Section 8.2.2(a) (Allocation of Ownership).

"***Novartis Proposed Development Candidate***" has the meaning set forth in Section 2.2.3 (Novartis Proposed Development Candidate).

"***Novartis-Prosecuted Patents***" has the meaning set forth in Section 8.3.2(b) (Other Matters Pertaining to Prosecution and Maintenance of Patents).

"***Novartis Research Activities Technology***" means any Know-How or Patent Rights that are (a) Controlled by Novartis or its Affiliates as of the Execution Date or any time during the Agreement Term and (b) necessary or reasonably useful for Ionis to perform any activities allocated to Ionis under the Research Plan or to conduct Research during the Carryover Period.

"***Novartis Royalty Bearing Patent***" means, with respect to a Licensed Product, any Novartis Patent that specifically Covers the composition of matter or method of use of such Licensed Product or the Licensed Compound included in such Licensed Product.

"***Novartis Technology***" means Novartis' interest in Novartis Program Technology, Novartis Product-Specific Patents, Novartis Know-How, Novartis Background Technology, and any Trademarks described in Section 5.8 (Trademark and Domain Names), that, in each case, is owned, used, developed by, or licensed to Novartis or its Affiliates (other than from Ionis pursuant to this Agreement) that are necessary or actually used to Develop, Research, Manufacture or Commercialize a Licensed Product.

"***Oligonucleotide***" means a synthetic compound that comprises or consists of at least one strand of at least five linked nucleosides (including any analog, variant, mimic, or mimetic thereof). For clarity, the nucleosides and internucleoside linkages of Oligonucleotides may be unmodified or modified. Oligonucleotides may include additional moieties, such as one or more covalently attached groups. Oligonucleotides may be [***].

"***Orange Book Patents***" means, on a country-by-country basis, the Licensed Patents that are listed with, or are required to be listed with, applicable Regulatory Authorities Covering any Licensed Product being Developed or Researched by Novartis, its Affiliates or Sublicensees hereunder that Novartis, its Affiliate or Sublicensee intends to, or has begun to, Commercialize, and that have become the subject of an NDA, MAA or other marketing application submitted to any applicable Regulatory Authority, such listings to include, without limitation, all so-called "*Orange Book*" listings required under the Hatch-Waxman Act and all so-called "*Patent Register*" listings as required in Canada. Orange Book Patents will include any and all foreign equivalent and counterpart Patent Rights to the Patent Rights described above.

For the avoidance of doubt, on a country-by-country basis, where there is:

(a) a mandatory patent listing process in such country, only Licensed Patents that are listed in such country's patent listing will be considered "*Orange Book Patents*" (and therefore royalty-bearing) in such country, irrespective of whether the foreign equivalent Patent Rights of such Licensed Patents are listed in another country;

(b) a voluntary patent listing process in such country, both (x) Licensed Patents that are listed in such country's patent listing, and (y) Licensed Patents that are not listed in such country's patent listing but are the foreign equivalent Patent Rights of the Licensed Patents listed in the mandatory patent listing of another country, in each case will be considered "*Orange Book Patents*" (and therefore royalty-bearing) in such country; and

(c) no patent listing process in such country, Licensed Patents that are the foreign equivalent of the Licensed Patents listed in the mandatory patent listing of another country, in each case will be considered "*Orange Book Patents*" (and therefore royalty-bearing) in such country, irrespective of whether the foreign equivalent Patent Rights of such Licensed Patents are listed in another country.

For example, if country "A" has a mandatory patent listing process that only requires that Licensed Patents "X" "Y" and "Z" be listed, and country "B" has a mandatory patent listing process that only requires that Licensed Patents "Y" and "Z" be listed, then Licensed Patents "X" "Y" and "Z" will be royalty-bearing Orange Book Patents in country "A", and only Licensed Patents "Y" and "Z" will be royalty-bearing Orange Book Patents in country "B".

For another example, if country "A" has a voluntary patent listing process that permits but does not require that Licensed Patents "X" "Y" and "Z" be listed and Novartis only lists in such patent listing Licensed Patents "X" and "Y", and country "B" has a mandatory patent listing process that requires that Licensed Patents "X" "Y" and "Z" be listed, then the applicable foreign equivalent of Licensed Patents "X" "Y" and "Z" will be royalty-bearing Orange Book Patents in country "A" and in country "B".

"[***]" has the meaning set forth in Section 5.3.2 (Sublicensing Requirements).

"***Other Components***" has the meaning set forth in the definition of "Net Sales" in this APPENDIX 1 (Definitions).

"***Out-of-Pocket Costs***" means with respect to any activity (including Development), [***].

"***Party***" or "***Parties***" has the meaning set forth in the Preamble of this Agreement.

"***Party Vote***" has the meaning set forth in Section 3.3.1 (Committee Decisions).

"***Patent Costs***" means the reasonable fees and expenses paid to outside legal counsel, and filing, maintenance and other reasonable Out-of-Pocket Costs, incurred in connection with the Prosecution and Maintenance of Patent Rights.

"***Patent Rights***" means (a) patents, patent applications and similar government-issued rights protecting inventions in any country or jurisdiction however denominated, (b) all priority applications, divisionals, continuations, substitutions, continuations-in-part of and similar applications claiming priority to any of the foregoing, and (c) all patents and similar government-issued rights protecting inventions issuing on any of the foregoing applications, together with all registrations, reissues, renewals, re-examinations, confirmations, supplementary protection certificates, and extensions of any of (a), (b) or (c).

"***Permitted Licenses***" means (a) licenses granted by Ionis or its Affiliates after the Effective Date to any Third Party under the Ionis Core Technology Patents, the Ionis Manufacturing and Analytical Patents, or the Ionis Manufacturing and Analytical Know-How (but not under the Ionis Product-Specific Patents) to (x) use Oligonucleotides (or supply Oligonucleotides to end users) solely to conduct research, or (y) enable such Third Party to manufacture or formulate Oligonucleotides, where (i) such Third Party is primarily engaged in providing contract manufacturing or services and is not primarily engaged in drug discovery, development or commercialization of therapeutics; and (ii) Ionis and its Affiliates do not assist such Third Party to identify, discover or make an Oligonucleotide designed to bind to the RNA encoding APO(a); and (b) material transfer, collaboration, or sponsored research agreements with academic collaborators or non-profit institutions solely to conduct non-commercial research.

"***Person***" means any corporation, limited or general partnership, limited liability company, joint venture, trust, unincorporated association, governmental body, authority, bureau or agency, any other entity or body, or an individual.

"***Phase 1 Trial***" means, with respect to a Licensed Product, a human clinical trial that is intended to initially evaluate the safety, metabolism and pharmacokinetics of such Licensed Product that would otherwise satisfy the requirements of 21 C.F.R. § 312.21(a) or an equivalent clinical trial in a country other than the United States.

"***Phase 2 Trial***" means, with respect to a Licensed Product, a human clinical trial for which the primary endpoints include a determination of safety, dose ranges or an indication of efficacy of such Licensed Product in patients being studied as described in 21 C.F.R. § 312.21(b), or an equivalent clinical trial in a country other than the United States.

"***Phase 2a Trial***" means, with respect to a Licensed Product, the first Phase 2 Trial for such Licensed Product. A Phase 2a Trial does not need to generate sufficient data to commence a Phase 3 Trial.

"***Phase 2b Trial***" means, with respect to a Licensed Product, the first to occur of: (a) the second Phase 2 Trial for such Licensed Product or (b) any Phase 2 Trial the principal purpose of which is a determination of efficacy and safety, in the target population, at the intended clinical dose or doses or range of doses, on a sufficient number of subjects and for a sufficient period of time to confirm the optimal manner of use of the Licensed Product (dose and dose regimen) prior to the Initiation of a Phase 3 Trial.

"***Phase 3 Trial***" means, with respect to a Licensed Product, a human clinical trial (regardless of whether actually designated as "Phase 3") that is prospectively designed, along with other Phase 3 Trials, to demonstrate statistically whether such Licensed Product is safe and effective for use in humans in the indication being investigated as described in 21 C.F.R. § 312.21(c), or an equivalent clinical trial in a country other than the United States.

"***Prior Agreements***" means the agreements listed on Appendix 8 (Prior Agreements) attached hereto as they are in effect as of the Execution Date without giving effect to any amendments or modifications thereafter.

"***Proceeding***" means an action, suit or proceeding.

"***Product-Specific Patents***" means Patent Rights Controlled by a Party or any of its Affiliates on or after the Execution Date (including a Party's interest in Jointly-Owned Program Patents) claiming: (a) the specific composition of matter of a Licensed Product or the Licensed Compound contained in such Licensed Product, or (b) methods of using such a Licensed Product or Licensed Compound contained in such Licensed Product as a prophylactic or therapeutic.

"***Program Know-How***" has the meaning set forth in Section 8.2.2(c) (Program Technology).

"***Program Patents***" has the meaning set forth in Section 8.2.2(c) (Program Technology).

"***Program Technology***" has the meaning set forth in Section 8.2.2(c) (Program Technology).

"[***]" has the meaning set forth in Section 11.5.3(a)(iv) (Acquisition of Alternative Technologies).

"***Proposed Development Candidate***" has the meaning set forth in Section 2.2.1 (Development Candidate Data Packages).

"***Prosecution and Maintenance***" or "***Prosecuting and Maintaining***" means, with regard to a Patent Right, the preparing, filing, prosecuting, maintaining and managing of such Patent Right, including strategies in relation to the Unified Patent Court and Unitary Patent in Europe, such as but not limited to the filing or withdrawing of an opt-out of a European Patent and validating as a Unitary Patent or a classical European Patent, as well as handling re-examinations, reissues, and requests for patent term extensions with respect to such Patent Right, together with the conduct of interferences, the defense of oppositions and other similar Proceedings with respect to the particular Patent Right. For clarification, "*Prosecution and Maintenance*" or "*Prosecute and Maintain*" will not include any other enforcement actions taken with respect to a Patent Right.

"***Receiving Party***" has the meaning set forth in Section 12.1 (Confidentiality; Exceptions).

"***Regulatory Approval***" means (a) an NDA Approval, (b) an MAA Approval, or (c) such other approval by a Regulatory Authority in any other jurisdiction sufficient for the Manufacture, distribution, use, marketing and sale of a Licensed Product, which for the avoidance of doubt shall include pricing and reimbursement approval from a Regulatory Authority when applicable.

"***Regulatory Authority***" means any Governmental Authority, including the FDA, EMA or PMDA (*i.e.*, the Japanese Ministry of Health and Welfare, or any successor agency thereto), that has responsibility for granting any licenses or approvals or granting pricing or reimbursement approvals necessary for the marketing and sale of a Licensed Product in any country.

"***Regulatory Exclusivity Period***" means, with respect to any Licensed Product in any country or jurisdiction in the Territory, the period of time during which: (a) a Party or its Affiliate or Sublicensee has been granted the exclusive legal right by a Regulatory Authority, other than through a Patent Right, including orphan drug exclusivity, pediatric exclusivity, rights conferred in the U.S. under the FD&C Act, rights in the EU under Directive 2001/83/EC, or rights similar thereto in other countries or regulatory jurisdictions in the Territory, or is otherwise entitled to the exclusive legal right by operation of Applicable Law in such country to market and sell such Licensed Product, and such right precludes the receipt of Regulatory Approval of any Third Party product that is deemed to be the same or a similar drug, in each case, under applicable orphan drug regulations; or (b) the data and information submitted by a Party or its Affiliate or Sublicensee to the relevant Regulatory Authority in such country or jurisdiction for purposes of obtaining Regulatory Approval of such Licensed Product may not be disclosed, referenced, or relied upon in any way by any Third Party or such Regulatory Authority to support the Regulatory Approval or marketing of any product by any Third Party in such country or jurisdiction, or if such data and information is disclosed, referenced, or relied upon to support a Regulatory Approval granted to any Third Party in such country or jurisdiction, then the product may not be placed on the market for any indication.

"***Research***" means conducting research activities with or in order to identify Compounds and to evaluate any such Compound for potential designation as a Development Candidate, including nonclinical research, gene function, gene expression and target validation research, lead optimization, and which may include small pilot toxicology studies. When used as a verb, "***Researching***" means to engage in Research.

"***Research Activities***" has the meaning set forth in Section 2.1.1 (Research Plan).

"***Research Plan***" has the meaning set forth in Section 2.1.1 (Research Plan).

"***Research Report***" has the meaning set forth in Section 2.10.2 (Research Reports).

"***Research Term***" has the meaning set forth in Section 2.3 (Research Term).

"***Reversion License***" has the meaning set forth in Section 11.5.3(a)(i)(3) (License Grant).

"***Reversion License Dispute***" has the meaning set forth in Section 11.5.3(a)(ii) (Reversion License Economics).

"***Royalty Report***" has the meaning set forth in Section 7.11.1 (Commencement).

"***Royalty Term***" has the meaning set forth in Section 7.7.2(a) (Royalty Term).

"***Shared Ionis Identified Rights***" has the meaning set forth in Section 7.9.3 (Ionis In-License Agreements).

"***Shared Novartis Identified Rights***" has the meaning set forth in Section 7.9.4 (Right to Offset).

"[***]" means [***].

"[***]" means, with respect to [***].

"***Sublicensee***" means a Third Party to whom a Party or its Affiliates or Sublicensees has granted a sublicense or license under any Licensed Technology or Novartis Technology, as the case may be, licensed to such Party in accordance with the terms of this Agreement.

"***Technology Transfer Plan***" has the meaning set forth in Section 5.9.1 (Licensed Know-How – Generally).

"***Terminated Products***" means:

(a) With respect to termination of this Agreement in its entirety prior to designation of a Development Candidate, or this Agreement expires in accordance with Section 11.1.3, (i) any Licensed Compounds that are not Novartis Compounds and (ii) any Novartis Compounds that satisfy the Development Candidate Criteria as of the date of such termination;

(b) with respect to termination of this Agreement in part with respect to a Licensed Product, (i) such Licensed Product and (ii) such Licensed Product's Backup Compounds, if any; and

(c) with respect to termination of this Agreement in its entirety, (i) any Licensed Product that is being Developed or Commercialized by Novartis, its Affiliates or Sublicensees as of the effective date of termination of this Agreement and (ii) such Licensed Product's Backup Compounds, if any.

For purposes of the definition of "Terminated Products," "***Backup Compounds***" means, with respect to a Licensed Product, any Licensed Compounds that (i) satisfy the Development Candidate Criteria and (ii) were presented by Ionis to the JRC as potential Development Candidates at the same time as the Development Candidate contained in such Licensed Product was so presented.

"***Territory***" means worldwide.

"***Third Party***" means a Person other than the Parties or their respective Affiliates.

"***Third Party Claims***" has the meaning set forth in Section 10.1 (Indemnification by Novartis).

"***Trademark***" means any trademark owned and controlled by Novartis and used by Novartis in connection with the marketing of a Licensed Product.

"***Transferring Party***" has the meaning set forth in Section 13.4.2 (Assignment and Successors).

"***Transition Services***" has the meaning set forth in Section 11.5.3(h) (Ionis: Special Consequences for Certain Termination).

"***United States***" or "***U.S.***" means the 50 states of the United States of America and all of its territories and possessions and the District of Columbia.

"***Upfront Fee***" has the meaning set forth in Section 7.1 (Upfront Fee).

"***Valid Claim***" means a claim (a) of any issued, unexpired United States or foreign Patent Right, which will not, in the country of issuance, have been donated to the public, disclaimed, nor held invalid or unenforceable by a court of competent jurisdiction in an unappealed or unappealable decision or (b) of any United States or foreign patent application within a Patent Right, which will not, in the country in question, have been cancelled, withdrawn, abandoned nor been pending for more than seven years from the date of filing of the earliest patent application to which such patent application claims priority in the country of question, not including in calculating such seven-year period of time in which such application is in interference or opposition or similar proceedings or time in which a decision of an examiner is being appealed. For clarity, on a country-by-country basis, a patent application pending for more than seven years will not be considered to have any Valid Claim for purposes of this Agreement unless and until a patent meeting the criteria set forth in clause (a) above with respect to such application issues.

"***Warranty Patents***" means (a) with respect to any representation or warranty made as of the Execution Date, any Patent Rights that are (i) Controlled by Ionis or its Affiliates as of the Execution Date and (ii) necessary or reasonably useful to perform the Research Activities, and (b) with respect to any representation or warranty made [***], the Licensed Patents that are necessary or reasonably useful to Exploit the applicable Development Candidate or Licensed Products that contain such Development Candidate.

"***Warranty Technology***" means (a) with respect to any representation or warranty made as of the Execution Date, any Know-How or Patent Rights that are (i) Controlled by Ionis or its Affiliates as of the Execution Date and (ii) necessary or reasonably useful to perform the Research Activities, and (b) with respect to any representation or warranty made [***], the Licensed Technology that is necessary or reasonably useful to Exploit the applicable Development Candidate or Licensed Products that contain such Development Candidate. For clarity, Warranty Technology includes Warranty Patents.

APPENDIX 2

Ionis In-License Agreements

1. [***].

   [***]

2. [***].

APPENDIX 3

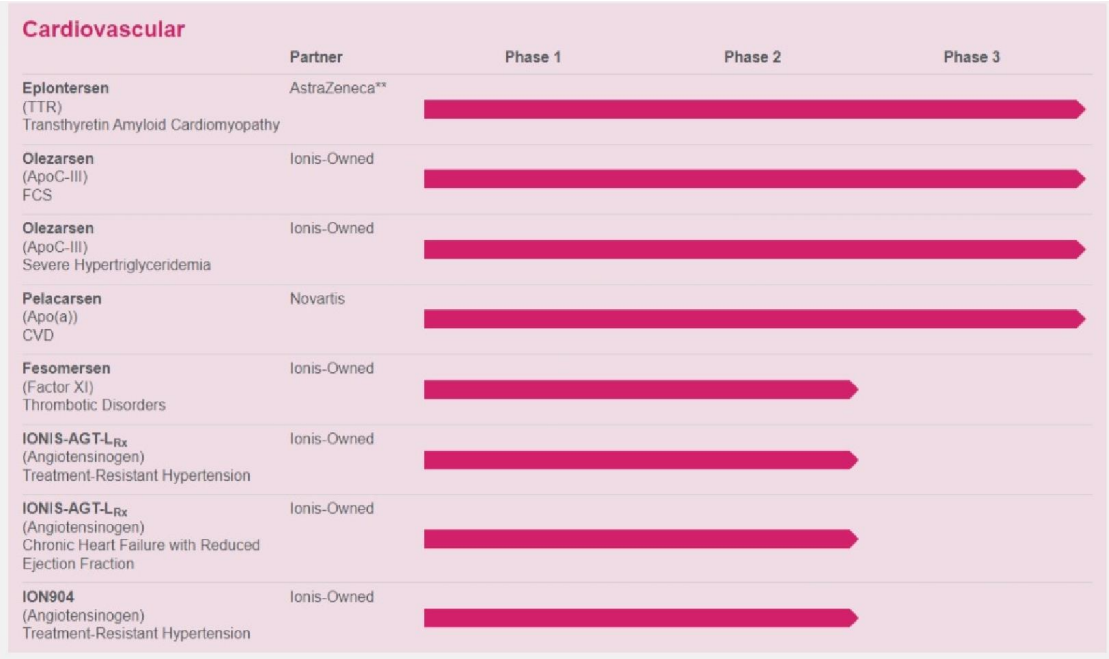
License Conditions; Limitations

[***]

1. [***]
2. [***]
3. [***]
4. [***]
5. [***]
6. [***]
7. [***]
8. [***]
9. [***]
10. [***]

APPENDIX 4

Ionis Development Pipeline


Cardiovascular
Partner
Phase 1
Phase 2
Phase 3
Eplontersen
(TTR)
Transthyretin Amyloid Cardiomyopathy
AstraZeneca**
Olezarsen
(ApoC-III)
FCS
Ionis-Owned
Olezarsen
(ApoC-III)
Severe Hypertriglyceridemia
Ionis-Owned
Pelacarsen
(Apo(a))
CVD
Novartis
Fesomersen
(Factor XI)
Thrombotic Disorders
Ionis-Owned
IONIS-AGT-LRx
(Angiotensinogen)
Treatment-Resistant Hypertension
Ionis-Owned
IONIS-AGT-LRx
(Angiotensinogen)
Chronic Heart Failure with Reduced Ejection Fraction
Ionis-Owned
ION904
(Angiotensinogen)
Treatment-Resistant Hypertension
Ionis-Owned


Specialty Rare
Partner
Phase 1
Phase 2
Phase 3
Donidalorsen
(PKK)
Hereditary Angioedema
Ionis-Owned
Sapablursen
(TMPRSS6)
Polycythemia Vera
Ionis-Owned
Other Medicines
Partner
Phase 1
Phase 2
Phase 3
Bepirovirsen
(Hepatitis B Virus)
Hepatitis B Virus Infection
GSK
IONIS-FB-LRx
(Complement Factor B)
IgA Nephropathy
Roche
IONIS-FB-LRx
(Complement Factor B)
Geographic Atrophy/AMD
Roche
Cimdelirsen
(GHr)
Acromegaly
Ionis-Owned
ION224
(DGAT2)
Non-Alcoholic Steatohepatitis
Ionis-Owned
ION839
(PNPLA3)
Non-Alcoholic Steatohepatitis
AstraZeneca
ION455
(Undisclosed)
Non-Alcoholic Steatohepatitis
AstraZeneca
ION532
(APOL1)
Chronic Kidney Disease
AstraZeneca

Appendix 5

Ionis Core Technology Patents*

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
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* pending identification or evaluation of Licensed Compounds

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
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Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
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Appendix 6

Ionis Manufacturing and Analytical Patents*

Ionis Docket Number	Country	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]	[***]	[***]
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* pending identification or evaluation of Licensed Compounds

APPENDIX 7

Ionis Product-Specific Patents*

None.

* pending identification or evaluation of Licensed Compounds

APPENDIX 8

Prior Agreements

1. [***]

2. [***]

3. [***]

4. [***]

5. [***]

6. [***]

7. [***]

8. [***]

9. [***]

10. [***]

SCHEDULE 2.1.1

Research Plan

[***]

SCHEDULE 5.4.2(a)

[***]

[***]

SCHEDULE 9.2

Ionis Disclosure Schedule

[***]

SCHEDULE 11.5.3

[***]

[***]

Exhibit 1

EXHIBIT 1

Novartis' Form of Invoice

Exhibit 1

Sender's Logo

INVOICE

Name
Street
Town, Country
Phone and Fax Nr.

INVOICE Date: xx.xx.xxxx
INVOICE No.: xxxx

Bill To:
NOVARTIS PHARMA AG
Zentraler Faktureneingang
Attn: Barbara Schultheiss
PO Box
CH-4002 Basel
Switzerland

Purchase Order: xxxx
[Reference to Novartis Purchase Order]

DESCRIPTION	**AMOUNT (xxx)**
[Please specify the service or event for which the invoice is due] *[Please reference the agreement and paragraph thereof describing the payment obligation]* *[Please specify the service period, e.g. Q1 20xx]*	*[specify the currency]* 000'000.00
VAT (if applicable)	000'000.00

Please remit by wire transfer within 60 days to:
[payment term as per agreement]
Receiving Bank – (name, address and country).
Swift Code -
Bank account number -
IBAN (mandatory for Europe)
ABA Number -

Have an electronic copy of this invoice please sent to:

- [***]
- [***]
- [***]

TOTAL 000'000,00

If you have any questions concerning this invoice, contact …… or e-mail to ……
[reference to invoice senders subject matter expert]

Novartis Pharma AG: VAT –Reg. No. CHE-116.268.023 MWST

Exhibit 1

Exhibit 10.2

Certain portions of this exhibit, marked by [***], have been excluded because they are both not material and are the type that the registrant treats as private or confidential.

AMENDED AND RESTATED LEASE AGREEMENT

DATED AS OF AUGUST 21, 2023

Between

LOTS 21 & 22 OWNER (DE) LLC
a Delaware limited liability company

AS LANDLORD

and

IONIS PHARMACEUTICALS, INC.,

a Delaware corporation

AS TENANT

BASIC LEASE INFORMATION

For convenience of the parties, certain basic provisions of this Lease are set forth herein, and are, together with any Exhibits and Schedules, expressly incorporated into the Lease. The provisions set forth herein are subject to the remaining terms and conditions of this Lease and are to be interpreted in light of such remaining terms and conditions.

TERMS OF LEASE	**DESCRIPTION**
"**Commencement Date**":	The date that is the earlier of: (i) ten (10) months after the Delivery Date, as defined in the Work Letter, or (ii) the date Tenant begins operating in the Premises for business purposes.
"**Premises**":	That certain Land described on Exhibit A attached hereto and the Building and other improvements to be constructed thereon, located on Lots 21 & 22, Whiptail Loop W in Carlsbad, 92010 California consisting of approximately 164,757 gross square feet, and the appurtenances thereto, as defined and further described in the Work Letter. The square footage of the Premises set forth above is deemed conclusive and shall not be subject to remeasurement
"Companion Lease":	That certain lease to be executed between Landlord or its affiliate and Tenant pursuant to the PSA for certain real property located at 2850, 2855 & 2859 Gazelle Court, Carlsbad, 92010 California (the "**Companion Premises**") and the buildings consisting of approximately 246,699 square feet and other improvements located thereon and appurtenances thereto, as described therein.
"**Term**": (Article 1)	The period commencing on the Commencement Date and ending on the Expiration Date.
"Expiration Date"	The date that is one hundred eighty (180) months after the Commencement Date, together with any Extension Period as to which an Extension Option is exercised under Section 1.4.
"**Escalation**": (Article 2)	The percentage of increase, if any, shown by the Consumer Price Index for All Urban Consumers U.S. City Average, All Items (base years 1982-1984 = 100) ("**Index**"), published by the United States Department of Labor, Bureau of Labor Statistics, for the month immediately preceding the Adjustment Date as compared with the Index for the month immediately preceding the Commencement Date (with respect to the first Adjustment Date), or the month immediately preceding the prior Adjustment Date (for all subsequent Adjustment Dates), but the percentage of increase shall not be less than 2.5% nor greater than 5.5%.

TERMS OF LEASE	DESCRIPTION
"**Option to Renew**": (Article 1)	Tenant shall have two (2), five year (5) options at ninety-five percent (95%) of Fair Market Rent.
"**Base Rent**": (Article 2)	For the period beginning on the Commencement Date until the first Adjustment Date, a fixed annual amount (payable in monthly installments) determined by multiplying six and thirty-five hundredths percent (6.35%) by the Construction Costs, as defined in the Work Letter, and thereafter the amount calculated pursuant to Section 2.1.3. A hypothetical example of the calculation of Base Rent is shown on Schedule 1, which shall be for illustrative purposes only and shall not be deemed a representation of the actual amounts or categories to be used in the calculation of Base Rent.
"**Net Lease**": (Article 2)	Landlord and Tenant acknowledge and agree that this is an "absolute net lease" and that Landlord shall receive the Base Rent during the Term, free from all charges, assessments, impositions, expenses and deductions of any and every kind or nature whatsoever relating to the Premises. Landlord shall have no obligations relating to the repair, maintenance or operation of the Premises, or any part thereof. Tenant shall be solely responsible for same.
"**Purchase Option**": (Article 11)	Tenant shall have a right of first offer to purchase the entire Premises.
"**Security Deposit/Letter of Credit**": (Article 2)	Tenant shall provide a Letter of Credit equal to the sum of (a) ten (10) months of the initial Base Rent, *plus* (b) $6,458,200, subject to adjustment as provided in Section 2.5.1. The amount referenced in clause (b) above is referred to as the "**Day 2 Improvements Security**".
"**Permitted Use**": (Article 3)	Premises may be used solely for biotechnology and other life sciences uses, including research and development, laboratory, manufacturing, assembly, storage, warehousing, office and administrative uses, all of which must be ancillary to biotechnology and other life sciences uses and, in each such case, to the extent Tenant remains in compliance with current zoning for the Premises and all Applicable Laws.

TERMS OF LEASE	DESCRIPTION
"Work Letter": (Exhibit B)	The "Work Letter" attached hereto as Exhibit B.
"**Address of Tenant**": (Article 10)	Ionis Pharmaceuticals, Inc. 2855 Gazelle Ct. Attention: General Counsel Email: [***] With a copy to: Cooley LLP 11951 Freedom Drive Suite 1400 Reston, VA 20190 Attn: Michelle Garcia Schulman, Esq. Email: [***]

TERMS OF LEASE	DESCRIPTION
"**Address of Landlord**": (Article 10)	c/o Oxford Property Group 125 Summer Street, 12th Floor Boston, MA 02110 United States Attn: Kristin Binck, Esq., Vice President, Legal Email: [***] With a copy to: c/o Oxford Property Group 101 Second St, Suite 300 San Francisco, CA 94105 Attn: Abby Mondani and DLA Piper LLP (US) 33 Arch Street, 26th floor Boston, MA 02110 United States Attn: John L. Sullivan, Esq. Email: [***] and all legal notices shall also be sent to: [***]

TABLE OF CONTENTS

Schedule 1	Example Showing Calculation of Base Rent
Exhibit A	Legal Description of the Premises
Exhibit B	Work Letter
Exhibit C	Form of Tenant Estoppel Certificate
Exhibit D	Form of Memorandum of Lease
Exhibit E	Form of SNDA
Exhibit F	Form of Non-Disclosure and Confidentiality Agreement
Exhibit G	Landlord Signage
Exhibit H	Commencement and Termination Date Agreement
Exhibit I	Tenant Construction Manual
Exhibit J	Tenant Standard Operating Procedures

AMENDED AND RESTATED LEASE AGREEMENT

This Amended and Restated Lease Agreement (this "**Lease**"), dated as of August 21, 2023 (the "**Effective Date**"), is made between Lots 21 & 22 Owner (DE) LLC, a Delaware limited liability company ("**Landlord**"), and Ionis Pharmaceuticals, Inc., a Delaware corporation ("**Tenant**"). Landlord and Tenant are parties to a Lease Agreement dated August 21, 2023 (the "**Original Lease**"), which Original Lease is being amended and restated in its entirety on this September 25, 2023 (the "**A&R Effective Date**"), to reflect certain modifications to the scope of Landlord's Construction Work and Tenant Improvements (each as defined herein). As of the A&R Effective Date, the Original Lease shall be of no further force and effect and shall be superseded in its entirety by this Lease.

ARTICLE 1
LEASE OF PREMISES; TERM

1.1 Lease. Landlord hereby leases to Tenant, and Tenant hereby leases from Landlord, the Premises for the Term. All of the terms and covenants of this Lease shall be effective as of the Effective Date. After the Commencement Date, Tenant and Landlord shall execute, acknowledge and deliver a written agreement in the form attached hereto as Exhibit H memorializing the Commencement Date, the Expiration Date, the original Term, and the commencement and termination dates of the Extension Terms if such are exercised.

1.2 As Is; No Representations. Tenant's lease of the Premises is on an "AS IS WHERE IS" basis, and Landlord shall have no obligation to prepare the Premises for Tenant's occupancy or to pay for or construct any improvements to the Premises, except for performance of the Landlord's Construction Work as defined in the Work Letter (including with respect to any Warranty Issue [as defined in the Work Letter] arising after completion of Landlord's Construction Work, to the extent required by the Work Letter) and with respect to payment of the TI Allowance as defined in the Work Letter and as otherwise expressly set forth in this Lease. Landlord has not made any representation or warranty to Tenant regarding (a) the condition or suitability of the Premises for the conduct of Tenant's business (including, without limitation, any utilities serving the Premises, any structural components of the improvements or the condition of any Building system, except as otherwise expressly set forth in the Work Letter), (b) the restrictions that may affect the conduct of Tenant's business in, or Tenant's use of, the Premises, or any other rights or benefits under this Lease, (c) the suitability of the Premises for Tenant's intended Permitted Use, or (d) compliance with Environmental Laws at the Premises or any environmental conditions at, or Hazardous Materials on, under, above, emanating to or from, or having emanated to or from, the Premises. TENANT EXPRESSLY WAIVES ANY WARRANTY OF CONDITION OR OF HABITABILITY OR SUITABILITY FOR OCCUPANCY, USE, HABITATION, FITNESS FOR A PARTICULAR PURPOSE OR MERCHANTABILITY, EXPRESS OR IMPLIED, RELATING TO THE PREMISES. Except in connection with the performance of Landlord's Construction Work, as provided in the Work Letter, Tenant assumes full responsibility for all costs and expenses required to cause the Premises to comply with all Applicable Laws. "**Applicable Laws**" means all applicable present and future federal, state, municipal and local laws, codes, ordinances, rules and regulations of governmental authorities, committees, associations, or other regulatory committees, agencies or governing bodies having jurisdiction over the Premises or any portion thereof, Landlord or Tenant, including both statutory and common law and Environmental Laws. "**Environmental Laws**" means any applicable present and future federal, state and local laws, statutes, ordinances, rules, and regulations, as well as common law, relating to protection of human health, natural resources or the environment or governing the use, transport, or disposal of biological, bio-hazardous wastes, or radiological elements. The term "Environmental Laws" includes, but is not limited to, the Comprehensive Environmental Response, Compensation and Liability Act of 1980, as amended ("**CERCLA**"), 42 U.S.C. §9601 et seq.; the Toxic Substance Control Act, 15 U.S.C. §2601 et seq.; the Hazardous Materials Transportation Act, 49 U.S.C. §5101 et seq.; the Resource Conservation and Recovery Act, 42 U.S.C. §6901, et seq.; the Clean Water Act, 33 U.S.C. §1251 et seq.; the Safe Drinking Water Act, 42 U.S.C. §300f et seq.; the Clean Air Act, 42 U.S.C. §7401 et seq.; Federal Water Pollution Control Act, 33 U.S.C. §§ 1251 et seq.; Clean Air Act, 42 U.S.C. §§ 7401 et seq.; Emergency Planning and Community Right-To-Know Act, 42 U.S.C. §§ 11001 et seq.; Occupational Safety and Health Act, 29 U.S.C. §§ 65 et seq.; California Labor Code §63.82, California Health and Safety Code §25249.5, et seq., and all other applicable federal, state and local laws, regulations, ordinances, rules, and orders that are equivalent or similar to the laws recited above, or otherwise relate to human health, natural resources or the environment, in each case together with their implementing regulations, guidelines, rules, or orders, and all state, regional, county, municipal, and other local laws, regulations, ordinances, rules, and orders that are equivalent or similar to the federal and state laws recited above.

1.3 Holdover. If Tenant retains possession of any portion of the Premises after the Termination Date (as hereinafter defined) without Landlord's written consent, then Landlord shall be entitled to exercise all remedies that may be available under this Lease or at law or in equity, and Tenant shall (a) be a tenant at sufferance only, (b) be liable to perform all of the obligations of Tenant set forth in this Lease, and (c) (i) for the first ninety (90) days following the Termination Date, pay Base Rent at a rate of one hundred twenty-five percent (125%) of the monthly Base Rent in effect immediately prior to the Termination Date, and (ii) for each month thereafter, pay Base Rent at a rate of one hundred fifty percent (150%) of the monthly Base Rent in effect immediately prior to the Termination Date, prorated on a daily basis. If Tenant retains possession of any portion of the Premises for more than thirty (30) days following the Termination Date without Landlord's written consent, Tenant shall also pay to Landlord all damages, direct, consequential, or indirect, sustained by Landlord by reason of any such holding over. Otherwise, such holding over shall be on the terms and conditions set forth in this Lease as far as applicable. "**Termination Date**" means the date on which this Lease terminates for any reason, including the Expiration Date. The provisions of this Section 1.3 shall not operate as a waiver by Landlord of any right of re-entry provided in this Lease.

1.4 Extension Option.

1.4.1 Exercise of Extension Option. Tenant shall have two (2) successive options (each, an "**Extension Option**") to extend the Term of this Lease for a period of five (5) years each (each, an "**Extension Period**"), on the same terms and conditions in effect under this Lease immediately prior to the Extension Period, except that Base Rent shall be determined as set forth below and Tenant shall have no further right to extend the Term of this Lease after the end of the second (2nd) Extension Period; provided, however, it shall be a condition of Tenant's exercise of the Extension Option that Tenant also exercise the corresponding "Extension Option" as defined in the Companion Lease. If Tenant exercises an Extension Option, such extension shall apply to the entire Premises. Tenant may exercise an Extension Option only by giving Landlord irrevocable and unconditional written notice thereof (the "**Extension Notice**") on or before the date which is twelve (12) months prior to the commencement date of each applicable Extension Period and such Extension Period shall commence on the day immediately succeeding the expiration date of the preceding Term or the preceding Extension Period, as the case may be, and shall end at midnight Eastern Time on the last day of the applicable Extension Period. Such exercise shall, at Landlord's election, be null and void if any Event of Default shall have occurred and is continuing at the date of such notice. Upon delivery of the Extension Notice, Tenant shall be irrevocably bound to lease the Premises for the Extension Period. If Tenant shall fail to timely exercise the Extension Option in accordance with the provisions of this Section 1.4, then the Extension Option shall terminate, and shall be null and void and of no further force and effect. If this Lease or Tenant's right to possession of the Premises shall terminate in any manner whatsoever before Tenant shall exercise the Extension Option, then immediately upon such termination the Extension Option shall simultaneously terminate and become null and void. Time is of the essence with regard to this Section 1.4.

1.4.2 Base Rent Determination. The Base Rent starting on the Commencement Date of each Extension Period and continuing for sixty (60) months thereafter will be ninety-five percent (95%) of the then-prevailing market rate for new leases for comparable life sciences office and lab space to the Premises in comparable buildings to the Building in the Market Area (defined below) that a willing, comparable, non-equity tenant (excluding sublease and assignment transactions) would pay, and a willing, comparable landlord would accept, at arm's length, for a similar life sciences laboratory and research space in a first-class or "Class A" property ("Fair Market Rent"); provided, however, in no event shall the Fair Market Rent rate per month for the first year of each Extension Period be less than 103% of the Base Rent rate for the last month of the immediately preceding portion of the Term. Thereafter, escalations in the Base Rent shall be established using standard market escalations in the determination of Fair Market Rent, but in no event shall escalations in Base Rent be increased by less than three percent (3%) on each annual anniversary of the Commencement Date of the Extension Term. Fair Market Rent will reflect all monetary and non-monetary considerations and other relevant factors taken into account for comparable transactions, including, without limitation, the location of the Premises, age, quality and layout of the existing improvements in the Premises, brokerage commissions, improvements paid for by tenant improvement allowances, moving allowances, and all other relevant tenant concessions. Fair Market Rent will be adjusted to take into account the size of the Premises, the length of the Extension Period, and the credit of Tenant. The term "**Market Area**" means the real estate market area that includes Carlsbad, Sorrento Valley, Sorrento Mesa, University Town Center, and Delmar Heights.

1.4.3 Fair Market Rent. Landlord will notify Tenant of its determination of the Fair Market Rent (consistent with the methodology reflected above) for the applicable Extension Period no later than ninety (90) days prior to the commencement date of the applicable Extension Period. If Tenant delivers written notice to Landlord within ten (10) business days after its receipt of Landlord's determination of Fair Market Rent whereby Tenant disagrees with Landlord's determination of the Fair Market Rent, Tenant shall include in its notice Tenant's determination of the Fair Market Rent, and Landlord and Tenant will diligently and in good-faith confer for a period of thirty (30) days thereafter (the "**Negotiation Period**") in an attempt to agree on the Fair Market Rent. If Landlord and Tenant are unable to agree on the Fair Market Rent during the Negotiation Period, then, within five (5) business days after the expiration of such period, Landlord and Tenant shall jointly appoint an independent arbitrator (the "**Arbitrator**") who shall not have previously been employed by or otherwise worked with either Landlord or Tenant with experience in real estate activities, including at least ten (10) years' experience serving as a broker, appraiser and/or attorney in leasing transactions involving commercial life sciences laboratory and research space of comparable size and Class A quality to the Premises (collectively, the "Qualifications"), which Arbitrator shall, within twenty (20) days following the Arbitrator's appointment, determine and report in writing to Landlord and Tenant the by selecting either Landlord's or Tenant's determination of the Fair Market Rent for the Extension Period, according to whichever of the applicable determinations is closer to the Fair Market Rent, as determined by the Arbitrator. If Landlord and Tenant cannot agree on the Arbitrator in accordance with the foregoing, Landlord or Tenant may apply to the American Arbitration Association to appoint the Arbitrator in accordance with the aforementioned criteria. The Arbitrator shall have no discretion other than to select Landlord's or Tenant's determination of the Fair Market Rent as aforesaid. The costs of the Arbitrator shall be shared equally by Landlord and Tenant, and each of Landlord and Tenant shall reasonably cooperate with the Arbitrator in providing documentation and any other reasonable evidence regarding how Landlord or Tenant, as applicable, arrived at its determination of the Fair Market Rent. If the Renewal Period commences prior to the final determination of the Fair Market Rent, Tenant shall pay to Landlord the monthly rate in effect immediately prior to the commencement of the applicable Renewal Period, subject to adjustment upon resolution of such dispute.

1.4.4 General. Notwithstanding any provision of this Section to the contrary, the Extension Option shall be void, at Landlord's election, if (i) Tenant is in default hereunder, after any applicable notice and cure periods have expired, at the time Tenant elects to extend the Term or at the time the Term would expire but for such extension, or (ii) any Transfer has occurred under Article 5 of the Lease (other than a Permitted Transfer, or a sublease(s) comprising less than twenty-five percent (25%) of the Premises).

ARTICLE 2
RENT

2.1 Base Rent and Additional Rent.

2.1.1 Tenant shall pay to Landlord, without notice or demand and without deduction or set-off of any amount for any reason whatsoever, the annual Base Rent in equal monthly payments, in advance, beginning on the Commencement Date, and thereafter on or before the first day of each full calendar month during the Term. Base Rent as well as any other amounts payable by Tenant to Landlord under the terms of this Lease shall be paid by wire or electronic transfer of funds pursuant to directions provided to Tenant by Landlord. In addition to Base Rent, Tenant shall pay to Landlord a property management fee ("**Management Fee**") of one percent 1%) of the gross annual revenue form the Premises, which amount shall be paid in equal monthly payments on the same date and in the same manner as Base Rent.

2.1.2 No later than one hundred eighty (180) days after the Delivery Date, Landlord will provide written notice (the "**Estimated Calculation Notice**") of Landlord's calculation of the initial amount of Base Rent using a preliminary estimate of the Construction Costs, to the extent they are known at the time of the Estimated Calculation Notice. Until the Landlord provides the Final Calculation Notice (as defined below), commencing on the Commencement Date, Tenant shall pay the estimated annual Base Rent amount set forth in the Estimated Calculation Notice in equal monthly installments for the applicable month(s). On or before the date that is one hundred eighty (180) days after the date that the Tenant Improvements with respect to the Day 2 Space (as defined in the Work Letter) and the TI by Landlord are substantially completed Landlord will provide written notice (the "**Final Calculation Notice**") of Landlord's calculation of the initial amount of Base Rent using the final amount of Construction Costs. Tenant will pay any underpayment of Base Rent, and Landlord will credit to Tenant's account any overpayment of Base Rent, based upon the difference between the estimated Base Rent actually paid by Tenant and the amount of Base Rent set forth in the Final Calculation Notice. If the Commencement Date is not the first day of a calendar month, Tenant shall pay to Landlord on the Commencement Date the prorated Base Rent for period from the Commencement Date until the end of the calendar month in which the Commencement Date occurs. Base Rent due for any partial calendar month at the end of the Term shall also be prorated and paid on the first day of such calendar month. Tenant shall pay to Landlord all items of Rent (as defined below), without deduction or offset and without notice or demand (except as specifically provided in this Lease in respect of Additional Rent (as defined below)), and Tenant shall deliver such payments to the payment address set forth in the Basic Lease Information, or to such other person, at such other place, or in such other manner as Landlord may designate by giving to Tenant Notice (as defined below) thereof. "**Additional Rent**" means all other amounts payable by Tenant to Landlord in accordance with this Lease, other than Base Rent. "**Rent**" means all amounts payable by Tenant to Landlord in accordance with this Lease, including, but not limited to Base Rent and Additional Rent.

2.1.3 Landlord shall, on or within thirty (30) days prior to each Adjustment Date, calculate the Escalation after the United States Department of Labor publishes the Index on which the amount of the increase will be based. Landlord's determination of the Escalation shall be binding absent manifest error. Landlord shall give written notice of the Escalation, multiplied by the number of installments of rent due under this Lease since the Adjustment Date. Tenant shall pay this amount, together with the monthly rent next becoming due under this Lease, and shall thereafter pay the monthly rent due under this Lease at this increased rate, which shall constitute Base Rent. Landlord's failure to make the required calculations promptly shall not be considered a waiver of Landlord's rights to adjust the monthly Base Rent due, nor shall it affect Tenant's obligations to pay the increased Base Rent, subject to this Section 2.1.3. If Landlord does not deliver its calculation of the Escalation within twelve (12) months after the applicable Adjustment Date, Tenant may provide Landlord with a written request for the calculation of the Escalation, and, if Landlord fails to provide the calculation of Escalation (which request shall include, in bold and prominent print on the first page, a notation that "**FAILURE TO RESOND TO THIS REQUEST WITHIN 30 DAYS MAY RESULT IN THE LOSS OF RIGHTS PURSUANT TO SECTION 2.1.3 OF THE LEASE**") within thirty (30) days after Tenant's written request, Tenant shall not be required to so pay the increased Base Rent in arrearage for the applicable period based on an Escalation; provided, however, the foregoing waiver of Tenant's obligation to pay arrearage amounts for the applicable period shall not affect Landlord's calculation of any future Escalations. If the Index is changed so that the base year differs from that in effect on the Commencement Date, the Index shall be converted in accordance with the conversion factor published by the United States Department of Labor, Bureau of Labor Statistics. If the Index is discontinued or revised during the Term, the government index or computation with which it is replaced shall be used to obtain substantially the same result as if the Index had not been discontinued or revised. The "**Adjustment Date**" means the first anniversary of the Commencement Date and on each successive anniversary thereafter during the Term, including any exercised Extension Period.

2.2 Expenses; Taxes; Insurance Expenses.

2.2.1 Expenses. Except as provided in the Work Letter regarding any Warranty Issue, Tenant shall perform all obligations with respect to the maintenance, operation, repair and replacement of the Premises and shall pay directly for all costs and expenses incurred in connection therewith, including, but not limited to: all insurance, maintenance, repair and replacement of any improvements (including, without limitation, the Building, the structural and nonstructural components of the Building, the Building systems, equipment (owned and maintained), the foundation, roof, walls, heating, ventilation, air conditioning, plumbing, electrical, mechanical, utility (owned and maintained) and safety systems, paving and parking areas, roads and driveways); maintenance of exterior areas such as gardening and landscaping, snow removal and signage; maintenance and repair of roof membrane, flashings, gutters, downspouts, roof drains, skylights and waterproofing; painting; lighting; cleaning; refuse removal; security; utilities for, or the maintenance of, outside areas; Premises personnel costs; rentals or lease payments paid by Tenant for rented or leased personal property used in the operation or maintenance of the Premises; and fees for required licenses and permits, including in order to operate for the Permitted Use.

2.2.2 Taxes. Subject to Tenant's right to contest Taxes as set forth below, Tenant will pay directly all Taxes allocable to the Term in a timely manner and prior to when the same shall become due and payable. Landlord and Tenant shall cooperate to place all Taxes in the name of Tenant, however, if and to the extent any Taxes are billed to Landlord, then Tenant shall pay the same upon receipt of such bill from Landlord and provide Landlord with evidence of such payment promptly thereafter. In any event, Tenant shall pay all Taxes prior to the date due. "**Taxes**" means all real property taxes and other assessments on the Premises, including, but not limited to, real estate taxes, personal property taxes, transfer taxes, documentary stamps or taxes, fees, assessments and other charges of any kind or nature, whether general, special, ordinary, or extraordinary (without regard to any different fiscal year used by such governmental authority) that are levied in respect of this Lease or the Premises (or Landlord's interest therein), or in respect of any improvement, fixture, equipment, or other property of Landlord, real or personal, located at the Premises, and used in connection with operation of the Premises. Tenant and Landlord acknowledge that Proposition 13 was adopted by the voters of the State of California in the June 1978 election ("**Proposition 13**") and that assessments, taxes, fees, levies and charges may be imposed by governmental agencies for such services as fire protection, street, sidewalk and road maintenance, refuse removal and for other governmental services formerly provided without charge to property owners or occupants, and, in further recognition of the decrease in the level and quality of governmental services and amenities as a result of Proposition 13, Taxes shall also include any governmental or private assessments or contribution towards a governmental or private cost-sharing agreement charged to the Premises for the purpose of augmenting or improving the quality of services and amenities normally provided by governmental agencies. Taxes shall not include (i) Landlord's corporate franchise taxes, estate taxes, inheritance taxes or net income taxes, or (ii) transfer taxes or other taxes incurred in connection with Landlord's sale of the Premises or any interest therein, other than taxes resulting from Proposition 13 reassessment. Tenant shall furnish to Landlord, within thirty (30) days after the last day when any Tax must be paid by Tenant as provided in this Section 2.2.2, official receipt of the appropriate taxing authority or other proof satisfactory to Landlord, evidencing the payment thereof. Tenant shall have the right, at Tenant's sole cost and upon reasonable prior notice to Landlord, to initiate and prosecute any proceeding for the purpose of contesting the assessed valuation of the Premises or any personal property for tax purposes in good faith; provided, that this right to contest shall not be deemed or construed to relieve, modify or extend Tenant's obligation to pay any Taxes allocable to the Term in a timely manner and prior to when the same shall become due and payable and that prior to any such contest, Tenant (a) pays the Tax under protest, (b) obtains and maintains a stay of all proceedings for enforcement and collection by posting a bond or other security required by law, or (c) if Tenant lawfully withholds payments of any contested amounts of Taxes during the contest, Tenant has or establishes unrestricted cash reserves to be held by Landlord in an amount equal to 125% of (x) the amount of Tenant's obligations being contested plus (y) any additional interest, charge or penalty arising from such contest; provided, however, that Landlord shall (1) promptly release such reserve upon resolution of such contest, and/or (2) use such reserve to pay Taxes directly to the applicable taxing authority following resolution of such contest. Tenant shall provide Landlord with all notices received or sent to the taxing authorities, as well as regular updates relating to any such contest and afford Landlord an opportunity to participate in all such proceedings. Tenant shall indemnify and defend Landlord and save Landlord harmless from all losses, judgments, costs (including without limitation, attorneys' fees), liabilities and expenses incurred in connection with such proceedings and shall, promptly after the final determination of such contest, fully pay and discharge the amounts which shall be levied, assessed, charged or imposed or be determined to be payable therein or in connection therewith, together with all penalties, fines, costs and expenses thereof or in connection therewith). Landlord shall have the right to (a) contest or dispute any Taxes (or file an appeal related thereto), without Tenant's prior written consent, at Landlord's sole cost and expense, or (b) request that Tenant contest or dispute such Taxes (or file an appeal related thereto), in which event, Tenant, in Tenant's sole discretion, may agree to contest or dispute such Taxes, at Tenant's sole cost and expense. If an Event of Default occurs or if otherwise required by any Mortgagee or lender of Landlord, Landlord, at its option, may require Tenant to make monthly estimated payments to Landlord on account of Taxes. The monthly payments shall be one twelfth (1/12th) of the amount of Taxes due for the applicable year as reasonably estimated by Landlord and shall be payable as Additional Rent on or before the first day of each month during the Term, in advance; provided, that, Landlord shall have the right to revise such estimates from time to time. So long as no Event of Default is then continuing, any amounts received by Landlord pursuant to the immediately preceding sentence shall be disbursed to Tenant by Landlord for payment to the applicable taxing authority (or paid to the applicable taxing authority directly by Landlord) when directed by Tenant, accompanied by evidence of the amount due. Upon Tenant's request, Landlord shall provide Tenant with evidence of any such payments of Taxes made directly by Landlord.

2.2.3 Landlord's Insurance. Tenant shall reimburse or, at Landlord's request, pay directly, all premiums, deductibles, and other costs incurred by Landlord in connection with obtaining and maintaining the insurance coverage described in Section 6.2.1 below (collectively, the "**Insurance Expenses**"). Tenant shall pay the Insurance Expenses no later than fifteen (15) days after demand. If an Event of Default occurs or if otherwise required by any Mortgagee or lender of Landlord, Landlord, at its option, may require Tenant to make monthly estimated payments to Landlord on account of Insurance Expenses. The monthly payments shall be one twelfth (1/12th) of the amount of Insurance Expenses due for the applicable year as reasonably estimated by Landlord and shall be payable as Additional Rent on or before the first day of each month during the Term, in advance; provided, that, Landlord shall have the right to revise such estimates from time to time. If Landlord requires monthly payments of the Insurance Expenses, Landlord will use reasonable efforts to provide a statement reconciling such payments within ninety (90) days after the end of each calendar year, and any underpayments shall paid by Tenant within fifteen (15) days after Tenant's receipt of the statement, and any overpayments shall be credited to the next payment of Rent that becomes due under the Lease.

2.3 Net Lease.

2.3.1 Absolute Triple Net Lease. It is intended by the parties that this Lease be an absolute "triple net lease," imposing upon Tenant the obligation to pay all charges of every kind and nature in connection with the use, operation, management, maintenance, repair, and occupancy of the Premises, whether or not recited herein and whether foreseeable or unforeseeable, including, but not limited to, utilities, fees, costs, real estate taxes, sales and use taxes, all operation, management, maintenance and repair costs associated with the Premises and the improvements located thereon and costs of compliance with Environmental Laws, except as expressly provided in this Lease. Tenant shall pay to Landlord, net throughout the Term, the Rent due hereunder free of any offset, abatement, or other deduction whatsoever, without notice or demand. Except to the extent due to the gross negligence or willful misconduct of, or breach of contract by, Landlord or any of Landlord's assignees, agents, servants, employees, invitees and contractors (or any of Landlord's assignees respective agents, servants, employees, invitees and contractors) (collectively, "**Landlord Parties**"; any of them, a "**Landlord Party**"), Tenant assumes the sole responsibility for the condition, use, operation, maintenance, management and compliance with Environmental Laws of the Premises, and Landlord shall have no responsibility in respect thereof and shall have no liability for damage to Tenant's personalty on any account or for any reason whatsoever. Notwithstanding the foregoing or anything to the contrary in this Lease, Tenant shall not be required to pay, or reimburse Landlord for: (i) depreciation charges, penalties, premiums, interest and principal payments on mortgages and other debt costs, ground rental payments and real estate brokerage and leasing commissions incurred by Landlord; (ii) costs incurred for Landlord's general overhead and any property or asset management fee other than as expressly set forth in this Lease; (iii) costs of selling or financing any of Landlord's interest in the Premises; (iv) costs incurred by Landlord which are reimbursed by property insurance proceeds actually received by Landlord where such proceeds result from a claim subject to the provisions of Section 6.2.3. below; and (v) reserves in excess of commercially reasonable amounts for comparable properties (and such reserves shall only be payable by Tenant if required by Landlord's lender or in accordance with commercially reasonable business practices for comparable properties).

2.3.2 Payments to Third Parties. Subject to Section 2.2.3(c) below, Landlord and Tenant recognize that there may be recurring payments to third parties, including governmental entities, for various items including inspections of storm water retention areas, inspections of pump stations, fees for storm water runoff, and assessments for maintenance and repairs under a Title Instrument (as defined below). Tenant is solely responsible for paying any fees or expenses imposed by governmental regulations or third parties, including those that may be required to obtain, modify and maintain compliance with any permits, licenses and approvals required by Applicable Laws, including for the use of and operation at the Premises by Tenant for the Permitted Use, or allocated to the Premises under any such Title Instrument. Tenant acknowledges that matters of the type contemplated by this Section may not be known to Landlord until after this Lease has been signed by Landlord and Tenant.

2.3.3 Title Instruments. In addition to the foregoing, during the term of this Lease, Tenant shall timely perform all obligations of the owner of the Premises under, and pay all expenses which the owner of the Premises may be required to pay in accordance with any declarations, covenants, conditions and restrictions or reciprocal easement agreements or any other documents or instruments that are of record now and affect the Premises (or of record in the future if created or filed by or with the consent of Tenant), including, without limitation, any documents or instruments recorded in connection with any Future Development (referred to collectively herein as the "**Title Instruments**"); provided, however, Tenant need not pay any debt service on loans that encumber the fee estate and that do not encumber Tenant's leasehold estate and Tenant need not pay any rent on any lease that is senior in priority to this Lease. Tenant promptly shall comply with all of the terms and provisions of all Title Instruments, including all insurance requirements, regardless of whether any such requirements exceed the requirements otherwise set forth in this Lease. Notwithstanding the foregoing, except as provided in Section 10.5, Landlord shall not enter into new Title Instruments or modify existing Title Instruments during the Term without Tenant's prior written consent, which may be withheld in Tenant's reasonable discretion; provided, however, that Tenant's prior written consent shall not be required with respect to (i) any financing obtained by Landlord secured by Landlord's interest in the Premises, (ii) Title Instruments necessary to effectuate transfers to third-party purchasers of the Premises, or (iii) any new Title Instruments or the modification of existing Title Instruments that do not (x) materially and adversely affect Tenant's use or occupancy of the Premises or (y) impose any fees or costs that would be payable by Tenant unless Landlord agrees to pay such fees.

2.4 Interest and Late Charge. If Tenant fails to pay Rent as and when due and such failure continues for three (3) business days following written notice from Landlord, then, together with each payment of Rent that Tenant pays to Landlord after such payment is due, Tenant shall pay to Landlord the Late Charge (as defined below) and interest calculated on the amount of such payment over the period commencing on the day immediately following the day on which such payment was due and ending on the day on which Tenant pays to Landlord such payment at the rate of the lesser of six percent (6%) over the "Prime Rate" announced from time to time by Bank of America or its successor or the maximum lawful rate of interest. Notwithstanding the foregoing, Landlord shall not be required to provide prior notice of Tenant's failure to pay Base Rent or any recurring obligation to pay Rent more than once during any twelve (12) month period, after which Tenant's failure to pay such amount shall be subject to the Late Charge and default interest provided above if Tenant fails to pay the amount when due and such failure continues for three (3) business days after the due date. "**Late Charge**" means, in respect of any such payment, five percent (5%) of such payment. In addition, Tenant shall pay to Landlord a reasonable fee for any checks returned by Tenant's bank for any reason.

2.5 Security Deposit/Letter of Credit.

2.5.1 Within three (3) Business Days of Tenant's execution of this Lease, and in lieu of a cash security deposit, Tenant shall provide a letter of credit (the "**Letter of Credit**") in the amount set forth as the "Security Deposit/Letter of Credit" in the Basic Lease Information. Any cash security deposit drawn from the Letter of Credit may be mingled with other funds of Landlord and no fiduciary relationship shall be created with respect to such deposit, nor shall Landlord be liable to pay Tenant interest thereon. The initial amount of the Letter of Credit shall be determined using Landlord's reasonable estimate of the Base Rent at the time of the execution of the Lease, and within thirty (30) days after delivery of the Final Calculation Notice the Letter of Credit shall be modified or reissued in the required amount as determined using the Base Rent set forth in the Final Calculation Notice. Provided that Tenant has not assigned its interest in this Lease (other than with respect to a Permitted Transfer) and there is no uncured Event of Default, on each of (i) the second (2nd) anniversary of the Commencement Date, and (ii) the fourth (4th) anniversary of the Commencement Date, and (iii) the date when Tenant has either commenced the Tenant Improvements for the Day 2 Space in accordance with the Work Letter or the parties have otherwise entered into a mutually agreeable modification to this Lease that eliminates Tenant's phasing of the Tenant Improvements such that the entire Premises is fit-out in one phase, Tenant may notify Landlord in writing (the "**Reduction Request**") and request the reduction of the Letter of Credit. The amount of reduction of the Letter of Credit shall be (A) equal to two (2) months of the initial Base Rent for each of the conditions described in clauses (i) and (ii) in the foregoing sentence, and (B) an amount equal to the Day 2 Improvements Security for the condition described in clause (iii) of the foregoing sentence (in each case, the "**Reduction Amount**"). Provided that the applicable conditions above have been satisfied at the time Landlord receives a Reduction Request, Landlord shall instruct the Bank, within sixty (60) days after Landlord's receipt of the Reduction Request, that the Letter of Credit may be reduced by the applicable Reduction Amount. In no event shall the Letter of Credit be reduced to an amount less than six (6) months of the initial Base Rent.

2.5.2 The Letter of Credit (i) shall be irrevocable and shall be issued by a commercial bank that has a financial condition reasonably acceptable to Landlord and that is otherwise an Eligible Bank (as defined below) and has an office in San Francisco, California that accepts requests for draws on the Letter of Credit; provided, Silicon Valley Bank shall be deemed an approved issuer of the Letter of Credit so long as Silicon Valley Bank remains an Eligible Bank, (ii) shall require only the presentation to the issuer (which may be in a location other than San Francisco if permitted on the basis of a fax or electronic submittal only) a certificate of the holder of the Letter of Credit stating that Landlord is entitled to draw on the Letter of Credit pursuant to the terms of the Lease, (iii) shall be payable to Landlord or its successors in interest as the Landlord and shall be freely transferable without cost to any such successor or any lender holding a collateral assignment of Landlord's interest in the Lease, (iv) shall be for an initial term of not less than one year and contain a provision that such term shall be automatically renewed for successive one-year periods unless the issuer shall, at least forty five (45) days prior to the scheduled expiration date, give Landlord notice of such nonrenewal, (v) shall be transferrable by Landlord without any cost to Landlord or the transferee (or, if there is a transfer fee, Tenant shall pay such fee and such transfer shall not be conditioned upon payment of such fee), and (vi) shall otherwise be in form and substance reasonably acceptable to Landlord. Notwithstanding the foregoing, the term of the Letter of Credit for the final period shall be for a term ending not earlier than the date forty-five (45) days after the last day of the Term. In the event that the issuer ceases to be reasonably acceptable to Landlord, due to a deterioration in its financial condition or change in status that threatens to compromise Landlord's ability to draw on the Letter of Credit as determined in good faith by Landlord or otherwise by its failure to be an Eligible Bank, then Tenant shall provide a replacement Letter of Credit from an issuer satisfying the terms of this Section 2.5.2 within thirty (30) days after Landlord's notice of such event. "**Eligible Bank**" shall mean shall mean a commercial or savings bank organized under the laws of the United States or any state thereof or the District of Columbia and having total assets in excess of $1,000,000,000.00 that shall be a financial institution having a rating of not less than BBB or its equivalent by Standard and Poors Corporation and subject to a Thompson Watch Rating of C or better.

2.5.3 The Letter of Credit shall be held by, or for the benefit of Landlord, as security for the performance of the provisions hereof by Tenant, including, without limitation, as provided in Section 6.4(a) of the Work Letter, and if the Letter of Credit or portion thereof is applied by Landlord for the payment of any Rent or any other sum in default or as provided in Section 6.4(a) of the Work Letter, then Tenant shall, upon demand therefor, restore the Letter of Credit to its original amount as provided in Section 2.5.1 above. Tenant hereby irrevocably waives and relinquishes any and all rights, benefits, or protections, if any, Tenant now has, or in the future may have under any provision of law which (i) establishes the time frame by which a landlord must refund a security deposit under a lease, or (ii) provides that a landlord may claim from a security deposit only those sums reasonably necessary to remedy defaults in the payment of rent, or to repair damage caused by a tenant or to clean the subject premises, as required and subject to the provisions of this Lease. Tenant acknowledges and agrees that (A) any statutory time frames for the return of a security deposit are superseded by the express period identified in this Section 2.5, and (B) rather than be so limited, Landlord may claim from the security deposit (i) any and all sums expressly identified in this Section 2.4, above, and (ii) any additional sums reasonably necessary to compensate Landlord for any and all losses or damages caused by Tenant's default of this Lease, including, but not limited to, all damages or rent due upon termination of this Lease.

2.5.4 Landlord shall be entitled to draw upon the Letter of Credit for its full amount or any portion thereof if (a) Tenant shall fail to perform any of its obligations under the Lease after the expiration of any applicable notice and cure period, or fail to perform any of its obligations under the Lease and transmittal of a default notice or the running of any cure period is barred or tolled by Applicable Law, or fail to perform any of its obligations under the Lease and any applicable notice and cure period would expire after the expiration of the Letter of Credit, (b) not less than thirty (30) days before the scheduled expiration of the Letter of Credit, Tenant has not delivered to Landlord a new Letter of Credit in accordance with this Section; provided no such delivery shall be required if the Letter of Credit provides for automatic renewals in compliance with Section 2.5.2, and the issuer of the Letter of Credit has not sent a notice of non-renewal, (c) as provided in Section 6.4(a) of the Work Letter attached as Exhibit B, or (d) as provided in Schedule 8 to the Work Letter attached as Exhibit B. Without limiting the generality of the foregoing, Landlord may, but shall not be obligated to, draw on the Letter of Credit from time to time in the event of a bankruptcy filing by or against Tenant and/or to compensate Landlord, in such order as Landlord may determine, for all or any part of any unpaid rent, any damages arising from any termination of the Lease in accordance with the terms of the Lease, and/or any damages arising from any rejection of the Lease in a bankruptcy proceeding commenced by or against Tenant. Landlord may, but shall not be obligated to, apply the amount so drawn to the extent necessary to cure Tenant's failure.

2.5.5 Any amount of the Letter of Credit drawn in excess of the amount applied by Landlord to cure any such failure, as provided in Section 6.4(a) of the Work Letter, or as provided on Schedule 8 to the Work Letter shall be held by Landlord as a cash security deposit for the performance by Tenant of its obligations under the Lease. If Tenant shall fail to perform any of its obligations under the Lease, Landlord may, but shall not be obliged to, apply the cash security deposit to the extent necessary to cure Tenant's failure. After any such application by Landlord of the Letter of Credit or cash security deposit, as the case may be, Tenant shall reinstate the Letter of Credit to the amount originally required to be maintained under the Lease, within ten (10) business days of Landlord's demand. Provided that Tenant is not then in default under the Lease, and no condition exists or event has occurred that after the expiration of any applicable notice or cure period would constitute such a default, within forty five (45) days after the later to occur of (i) the payment of the final Rent due from Tenant or (ii) the later to occur of the Term Expiration Date or the date on which Tenant surrenders the Premises to Landlord in compliance with Section 20 of the Lease, the Letter of Credit and any cash security deposit, to the extent not applied or held by Landlord for the purposes described in Section 6.4(a) of or Schedule 8 to the Work Letter, shall be returned to the Tenant, without interest, and Landlord, upon request, shall confirm termination of the Letter of Credit with the issuer thereof.

2.5.6 In the event of a sale of the Building or lease, conveyance or transfer of the Building, Landlord shall transfer the Letter of Credit or cash security deposit to the transferee. Upon such transfer, the transferring Landlord shall be released by Tenant from all liability for the return of such security, and Tenant agrees to look to the transferee solely for the return of said security. The provisions hereof shall apply to every transfer or assignment made of the security to such a transferee. Tenant further covenants that it will not assign or encumber or attempt to assign or encumber the Letter of Credit or the monies deposited herein as security, and that neither Landlord nor its successors or assigns shall be bound by any assignment, encumbrance, attempted assignment or attempted encumbrance.

2.5.7 Landlord and Tenant acknowledge and agree that in no event or circumstance shall the Letter of Credit, any renewal thereof or substitute therefor or the proceeds thereof be (i) deemed to be or treated as a security deposit within the meaning of California Civil Code Section 1950.7, (ii) subject to the terms of such Section 1950.7, or (iii) intended to serve as a security deposit within the meaning of such Section 1950.7. The parties hereto (A) recite that the Letter of Credit is not intended to serve as a security deposit and such Section 1950.7 and any and all other laws, rules and regulations applicable to security deposits in the commercial context ("**Security Deposit Laws**") shall have no applicability or relevancy thereto, and (B) waive any and all rights, duties and obligations either party may now or, in the future, will have relating to or arising from the Security Deposit Laws. Notwithstanding the foregoing, to the extent California Civil Code 1950.7 in any way: (a) is determined to be applicable to this Lease or the Letter of Credit (or any proceeds thereof); or (b) controls Landlord's rights to draw on the Letter of Credit or apply the proceeds of the Letter of Credit to any amounts due under this Lease or any damages Landlord may suffer following termination of this Lease, then Tenant fully and irrevocably waives the benefits and protections of Section 1950.7 of the California Civil Code, it being agreed that Landlord may recover from the Letter of Credit (or its proceeds) all of Landlord's damages under this Lease and California law including, but not limited to, any damages accruing upon the termination of this Lease in accordance with this Lease and Section 1951.2 of the California Civil Code.

ARTICLE 3
USE, COMPLIANCE WITH LAWS, HAZARDOUS MATERIALS, DOGS

3.1 Use. Tenant shall use the Premises solely for the Permitted Use, in a manner consistent with first-class life science buildings, and shall comply (and ensure that the Premises at all times comply) with all Applicable Laws. Tenant shall be solely responsible for the securing, modifying, maintaining, and compliance with any and all permits, licenses and approvals required or that may be required or otherwise in effect for the Permitted Use and under Environmental Laws in connection with Tenant's use and operation of the Premises. Tenant shall not commit, or allow to commit, any waste of or injury to the Premises or create, maintain or exacerbate any nuisance thereon or therefrom. Landlord agrees to reasonably cooperate with Tenant, at Tenant's sole cost and expense, in obtaining any permits, licenses and approvals required by Applicable Laws for the use of and operation at the Premises by Tenant for the Permitted Use, including, without limitation, by executing or joining in the execution of such applications and other documentation (the form and content of which shall be subject to Landlord's reasonable approval) in Landlord's name, solely as and because Landlord is the fee simple owner of the Premises, as may be necessary for obtaining such permits, licenses and approvals, all without cost or liability to Landlord. Tenant shall operate in a first-class manner and shall not exceed the density limit for the Building under Applicable Laws. Tenant shall not commit waste or cause a public nuisance.

3.2 Compliance with Applicable Laws. Tenant shall comply with all Applicable Laws and any agreements between Tenant and third parties with respect to the Premises and Tenant's operation at the Premises. It is intended that the Tenant bear the sole risk of all present or future Applicable Laws, regulations and orders affecting the Premises, and the Landlord shall not be liable for their enforcement. Should there be any material noncompliance or alleged material noncompliance by Tenant with Applicable Laws or agreements between Tenant and third parties with respect to the Premises and Tenant's operation at the Premises, Tenant shall promptly notify Landlord in writing of such actual or alleged noncompliance, which notice shall include (i) documentation that such actual or alleged noncompliance has been fully addressed and eliminated or, (ii) if such actual or alleged noncompliance has not been fully addressed and eliminated, a schedule to fully and expeditiously address and eliminate such actual or alleged noncompliance. The giving of such notice shall not relieve Tenant of any liability to Landlord or others for such actual or alleged noncompliance. To ensure Tenant's compliance with Applicable Laws and Tenant's performance of Tenant's management, repair, maintenance, and compliance obligations hereunder, upon reasonable notice to Tenant and subject to and in accordance with Applicable Laws and reasonable confidentiality requirements pertaining to Tenant's operations (provided such requirements do not impair or delay Landlord's rights under this Section), Landlord may inspect or cause non-invasive independent third party inspections of the facility and Tenant's operation to confirm compliance with Applicable Laws and Tenant's management, repair, maintenance, and compliance obligations hereunder, at Landlord's expense, except as otherwise provided in Section 3.3.7.

3.3 Hazardous Materials.

3.3.1 Tenant, and any of Tenant's assignees, sublessees, licensees, agents, servants, employees, invitees and contractors (or any of Tenant's assignees, sublessees and/or licensees respective agents, servants, employees, invitees and contractors) (collectively, "**Tenant Parties**"; any of them, a "**Tenant Party**") (a) shall not, and shall not permit at any time, the handling, use, manufacture, release, storage, or disposal of Hazardous Materials in or about any portion of the Premises in violation of Applicable Laws, (b) shall always manage, handle, use, store, and dispose of such Hazardous Materials in a safe manner, according to prudent industry practice, and in compliance with Applicable Laws, and (c) shall at all times have any and all required permits, licenses and approvals required for or in connection with, the use and handling of Hazardous Materials at the Premises and at all times be in compliance with such required permits, licenses and approvals. "**Hazardous Materials**" means (a) any and all substances (whether solid, liquid or gas) defined, listed or otherwise classified or regulated as "biological compounds", "bio-hazardous wastes", "radiological elements", "hazardous wastes," "hazardous materials," "hazardous substances," "toxic substances," "pollutants," "contaminants," "radioactive materials", "toxic pollutants", "solid wastes," or other similar designations in, or otherwise subject to regulation under Environmental Laws, and (b) any other substances, constituents or wastes that are deemed to have a negative impact on human health or the environment, whether or not naturally occurring, or that are subject to Environmental Law, now or hereafter in effect, including but not limited to (A) petroleum, (B) refined petroleum products, (C) waste oil, (D) waste aviation or motor vehicle fuel and their byproducts, (E) asbestos, (F) lead in water, paint or elsewhere, (G) radon, (H) Polychlorinated Biphenyls (PCBs), (I) urea formaldehyde, (J) volatile organic compounds (VOC), (K) total petroleum hydrocarbons (TPH), (L) benzene derivative (BTEX), (M) poly- and perfluoroalkyl substances and other emerging contaminants, and (N) petroleum byproducts. Hazardous Materials further includes flammables, explosives, corrosive materials, radioactive materials, materials capable of emitting toxic fumes, hazardous wastes, toxic wastes or materials, and other similar substances, petroleum products and derivatives, and any substance subject to regulation by or under any Environmental Law. As between Landlord and Tenant, Tenant is deemed to be the operator of the Premises, the generator of any Hazardous Materials waste present at or generated at the Premises or as part of Tenant's operations, and the owner of all Hazardous Materials at the Premises at any and all times during the Term. On or before the expiration or earlier termination of this Lease, Tenant shall remove from the Premises all Hazardous Materials introduced to the Premises by Tenant, any other Party or any other party other than Landlord during the Term of the Lease, regardless of whether such Hazardous Materials are included on the Hazardous Materials List or present at the Premises in concentrations which require removal under Applicable Laws. As used herein, the term "**Contamination**" means the presence of Hazardous Materials in the air, soil, surface and/or ground water in, on or under the Premises and/or any adjacent property at levels above those permitted by applicable Environmental Laws.

3.3.2 Landlord acknowledges that it is not the intent of this Section 3.3 to prohibit Tenant from using the Premises for the Permitted Use. Tenant may operate its business according to best industry practices so long as the use or presence of Hazardous Materials is strictly and properly monitored according to all then applicable Environmental Laws, all Hazardous Materials at the Premises are used in the operation of Tenant's business, and such use is consistent with similar first-class facilities engaged in the Permitted Use in the greater San Diego County area. Notwithstanding the foregoing, Tenant shall have no right to install any underground storage tanks at the Premises unless Landlord has given Tenant its written consent to do so, which consent may be withheld in Landlord's sole and absolute discretion. In conducting its research activities using Hazardous Materials, Tenant shall not perform work at or above the risk category Biosafety Level 3 as established by the Department of Health and Human Services publication Biosafety in Microbiological and Biomedical Laboratories (5th Edition) (as it may be or may have been further revised, the "**BMBL**") or such nationally recognized new or replacement standards as Landlord may reasonable designate, without the prior written approval of Landlord, which approval shall not be unreasonably withheld, conditioned, or delayed (and if such change in Tenant's operation requires the approval of Landlord's lender, the lender's denial of approval shall be deemed a reasonable basis for Landlord to deny its approval); provided, however, Landlord's approval of any operation above the risk category Biosafety Level 3 shall be in Landlord's sole discretion. Tenant shall comply with all applicable provisions of the standards of the BMBL to the extent applicable to Tenant's operations in the Premises.

3.3.3 As a material inducement to Landlord to allow Tenant to use Hazardous Materials in connection with its business, Tenant agrees to deliver to Landlord prior to the Commencement Date a list identifying each type of Hazardous Materials (other than ordinary office and cleaning supplies used in cleaning of the office spaces within the Building) to be brought upon, kept, used, stored, handled, treated, generated on, or released or disposed of from, the Premises and setting forth any and all governmental approvals or permits required in connection with the presence, use, storage, handling, treatment, generation, release or disposal of such Hazardous Materials on or from the Premises ("**Hazardous Materials List**"). Upon Landlord's request (not more than once per year, unless Landlord has a reasonable belief that Tenant is not in compliance with this Section 3.3, a release or threatened release of Hazardous Materials has occurred, or in connection with a sale, financing, refinancing, or recapitalization of Landlord's interest in the Premises), or any time that Tenant is required to deliver a Hazardous Materials List to any governmental authority (e.g., the fire department) or an insurer in connection with Tenant's use or occupancy of the Premises, Tenant shall deliver to Landlord a copy of such Hazardous Materials List. Tenant shall deliver to Landlord true and correct copies of the following documents (the "**Haz Mat Documents**") relating to the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials prior to the Commencement Date, or if unavailable at that time, concurrent with the receipt from or submission to a governmental authority: permits; licenses, approvals; reports and correspondence; storage and management plans; notice of violations of any Applicable Laws; fire safety plans; spill response plans; plans relating to the installation of any storage tanks to be installed in or under the Premises (provided, said installation of tanks shall only be permitted after Landlord has given Tenant its written consent to do so, which consent may be withheld in Landlord's sole and absolute discretion with respect to underground storage tanks); all closure plans or any other documents required by any and all governmental authorities for any storage tanks installed in, on or under the Premises for the closure of any such tanks; and a Surrender Plan (to the extent surrender in accordance with Section 3.3.9 cannot be accomplished in three (3) months). Tenant is not required, however, to provide Landlord with any portion(s) of the Haz Mat Documents containing proprietary information of a proprietary nature that, in and of themselves, do not contain a reference to any Hazardous Materials or hazardous activities. It is not the intent of this Section to provide Landlord with information that could be detrimental to Tenant's business should such information become possessed by Tenant's competitors.

3.3.4 Except to the extent caused by the gross negligence or willful misconduct of, or breach of contract by, Landlord or Landlord Parties, Tenant releases Landlord and Landlord Parties from and agrees to indemnify, defend and hold Landlord and Landlord Parties harmless for, from and against any and all actions (including, without limitation, remedial or enforcement actions of any kind, administrative or judicial proceedings, and orders or judgments arising out of or resulting therefrom), costs, claims, damages (including, without limitation, punitive damages and damages based upon diminution in value of the Premises, or the loss of, or restriction on, use of the Premises), expenses (including, without limitation, legal, consultants' and experts' fees, court costs and amounts paid in settlement of any claims or actions), fines, forfeitures or other civil, administrative or criminal penalties, injunctive or other relief (whether or not based upon personal injury, property damage, or Contamination of, or adverse effects upon, the environment, water tables or natural resources), liabilities or losses (i) that arise prior to, during, or after the Term, as a result of the presence, suspected presence, release, or suspected release of any Hazardous Materials in or into the environment, including the air, soil, surface water, or groundwater at, on, about, under, emanating to or from, having emanated to or from, or within the Premises, or any portion thereof caused or exacerbated by, or otherwise attributable to, Tenant or any other party (other than Landlord or Landlord Parties) prior to the date that Tenant vacates the Premises in the condition required following the termination or earlier expiration of the Term, or (ii) that arise prior to, during, or after the Term, as a result of the breach by Tenant of any of its obligations under this Section 3.3, including in each case, without limitation, the cost of assessment, containment and/or removal of any such Hazardous Materials, the reasonable and necessary cost of any actions taken in response to a release of any such Hazardous Materials so that it does not migrate or otherwise cause or threaten danger to present or future public health, safety, welfare or the environment, and costs incurred to comply with Environmental Laws in connection with all or any portion of the Premises or the operation thereof (or any surrounding areas for which Tenant or Landlord has any legal liability or obligation) during the Term.

3.3.5 EXCEPT AS OTHERWISE PROVIDED FOR HEREIN, LANDLORD LEASES AND WILL LEASE, AND TENANT TAKES AND WILL TAKE, THE PREMISES IN AN ENVIRONMENTALLY "AS IS" CONDITION, AND TENANT ACKNOWLEDGES THAT LANDLORD HAS NOT MADE AND WILL NOT MAKE, NOR SHALL LANDLORD BE DEEMED TO HAVE MADE, ANY WARRANTY OR REPRESENTATION, EXPRESS OR IMPLIED, WITH RESPECT TO THE ENVIRONMENTAL CONDITION OF THE PREMISES, INCLUDING ANY WARRANTY OR REPRESENTATION AS TO FITNESS OF THE PREMISES FOR ANY PARTICULAR USE OR PURPOSE, AS TO THE PRESENCE OR ABSENCE OF ANY HAZARDOUS MATERIALS, LATENT OR PATENT, ANY ENVIRONMENTAL CONDITION, KNOWN OR UNKNOWN, OR ANY AIR, SOIL, SOIL GAS, OR GROUNDWATER CONDITION, IT BEING AGREED THAT ALL RISKS AND LIABILITY INCIDENT TO ANY OF THE FOREGOING ARE TO BE BORNE BY TENANT

3.3.6 Tenant hereby represents and warrants to Landlord that (i) neither Tenant nor any of its legal predecessors has been required by any prior landlord, lender or governmental authority at any time to take remedial action in connection with Hazardous Materials contaminating the natural environment, which contamination was caused or permitted by Tenant or such predecessor or resulted from Tenant's or such predecessor's acts, omissions, or use or occupation of the property in question, and (ii) Tenant is not subject to any enforcement order issued, or regulatory proceedings or prosecution commenced, by any governmental authority in connection with the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials (including, without limitation, any order related to the failure to make a required reporting to any governmental authority).

3.3.7 Upon prior notice and using reasonable efforts to coordinate with Tenant, Landlord shall have the right but not the obligation to conduct annual tests (or at any time Landlord has a reasonable belief that Tenant is not in compliance with this Section 3.3) of the Premises including, without limitation, intrusive tests of the subsurface soil and/or ground water, to determine whether any Contamination of the Premises has occurred as a result of Tenant's use or occupation. Landlord shall pay the cost of such test of the Premises; provided, however, that if such tests show any Contamination of the Premises has occurred as a result of Tenant's use or occupation, Tenant shall pay the cost of such test. In connection with such testing, upon the request of Landlord, Tenant shall deliver to Landlord or its consultant such non-proprietary information concerning the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials in or about the Premises by Tenant or any Tenant Party as Landlord may reasonably request. If Contamination has occurred for which Tenant is liable under this Section 3.3, Tenant shall pay all costs to conduct such tests. Tenant shall, at its sole cost and expense, promptly and satisfactorily remediate any Contamination identified by such testing in accordance with all Environmental Laws. Landlord's receipt of or satisfaction with any environmental assessment in no way waives any rights that Landlord may have against Tenant.

3.3.8 Furthermore, upon the expiration of the Term or earlier termination of Tenant's right of possession, Tenant shall surrender the Premises to Landlord free of Hazardous Materials brought upon, kept, used, stored, handled, treated, generated in, or released or disposed of from, the Premises by any person other than Landlord (collectively, "**Tenant's Hazardous Materials**") and released of any license, clearance or other authorization or requirement of any kind required to enter into and restore the Premises issued by any governmental authority having jurisdiction over the use, storage, handling, treatment, generation, release, disposal, removal or remediation of Hazardous Materials in, on or about the Premises (collectively referred to herein as "**Hazardous Materials Clearances**"). At least three (3) months prior to the surrender of the Premises or such earlier date as Tenant may elect to cease operations at the Premises, Tenant shall deliver to Landlord a narrative description of the actions proposed (or required by any governmental authority) to be taken by Tenant in order to surrender the Premises (including any Alterations permitted by Landlord to remain in the Premises) at the expiration or earlier termination of the Term, free from any residual impact from Tenant's Hazardous Materials and otherwise released for unrestricted use and occupancy (the "**Surrender Plan**"). Such Surrender Plan shall be accompanied by a current listing of (i) all Hazardous Materials licenses and permits held by or on behalf of any Tenant Party with respect to the Premises, and (ii) all Hazardous Materials used, stored, handled, treated, generated, released or disposed of from the Premises, and shall be subject to the review and reasonable approval of Landlord's environmental consultant. In connection with the review and approval of the Surrender Plan, upon the request of Landlord, Tenant shall deliver to Landlord or its consultant such additional non-proprietary information concerning Tenant's Hazardous Materials as Landlord shall reasonably request. On or before such surrender, Tenant shall deliver to Landlord evidence that the approved Surrender Plan shall have been satisfactorily completed and Landlord shall have the right, subject to reimbursement at Tenant's expense as set forth below, to cause Landlord's environmental consultant to inspect the Premises and perform such additional procedures, including without limitation intrusive subsurface testing of soil and/or ground water, as may reasonably be deemed necessary to confirm that the Premises are, as of the effective date of such surrender or early termination of the Lease, free from any Tenant's Hazardous Materials. Tenant shall reimburse Landlord, as Additional Rent, for the actual out-of-pocket expense incurred by Landlord for Landlord's environmental consultant to review the Surrender Plan and to visit the Premises and verify satisfactory completion of the same, which cost shall not exceed $5,000 (which amount shall be increased by the same percentage as the Index as of each Adjustment Date). Landlord shall have the unrestricted right to deliver such Surrender Plan and any report by Landlord's environmental consultant with respect to the surrender of the Premises to third parties on a need-to-know basis.

3.3.9 If Tenant shall fail to prepare or submit a Surrender Plan approved by Landlord, or if Tenant shall fail to complete the approved Surrender Plan, or if such Surrender Plan, whether or not approved by Landlord, shall fail to adequately address any Tenant's Hazardous Materials in, on or about the Premises, Landlord shall have the right to take such actions as Landlord may reasonably deem appropriate to assure that the Premises are surrendered free from any Tenant's Hazardous Materials, the cost of which actions shall be reimbursed by Tenant as Additional Rent.

3.3.10 Tenant's obligations under this Section 3.3 shall survive the expiration or earlier termination of the Lease. During any period of time after the expiration or earlier termination of this Lease required by Tenant or Landlord to complete the removal from the Premises of any Hazardous Materials (including, without limitation, the release and termination of any licenses or permits restricting the use of the Premises and the completion of the approved Surrender Plan), Tenant shall continue to pay the full Rent in accordance with this Lease for any portion of the Premises not relet by Landlord in Landlord's sole discretion, which Rent shall be prorated daily.

3.4 Alterations.

3.4.1 Consent. Tenant may make any alterations, improvements, additions or changes to the Premises, including, without limitation, the Tenant Improvements as defined in the Work Letter, (collectively "**Alterations**") that meet all of the following criteria without first obtaining Landlord's Consent: (a) the Alterations are cosmetic, (b) the Alterations are non-structural and do not affect the mechanical systems of the Building, (c) the Alterations cost less than $1,000,000.00 per project (which amount shall be increased by the same percentage as the Index as of each Adjustment Date); and (d) after the Alterations, the Premises will continue to be used for the Permitted Use (collectively, Alterations meeting the criteria of (a)-(d), "Minor Alterations"). Any Alterations that are not Minor Alterations shall be subject to Landlord's approval, such approval not to be unreasonably withheld, conditioned or delayed. Tenant shall reimburse Landlord for any third-party expenses reasonably incurred by Landlord in connection with the review, inspection, and coordination of Tenant's plans for Alterations and Tenant's performance thereof. Tenant hereby agrees to provide copies of all plans of such Alterations, regardless of whether Landlord's consent is required. Tenant shall diligently and expeditiously complete any Alterations commenced. All Alterations shall become part of the realty constituting the Premises and shall belong to Landlord and shall not be removed by Tenant. If any Alteration is anticipated to cost more than $1,500,000, Landlord shall have the right to require Tenant to post a performance or payment bond in connection with any work or service done or purportedly done by or for the benefit of Tenant. Tenant acknowledges and agrees that all such work or service is being performed for the sole benefit of Tenant and not for the benefit of Landlord. Landlord shall, at the time it provides its approval for a proposed Alteration, advise Tenant whether the Alteration, or any portion thereof, is a Required Removable, as defined in Section 4.2.2. For the avoidance of doubt, with respect to the Tenant Improvements only, in the event of any conflict between the terms of this Section 3.4 and the terms of the Work Letter, the terms of the Work Letter shall control.

3.4.2 Liens. With respect to any Alterations, Tenant hereby agrees as follows: (a) Tenant shall not cause or permit any construction, mechanics' or other liens or encumbrances to be placed upon the Premises, or Tenant's leasehold interest hereunder, whether in connection with any work or service done or purportedly done by or for the benefit of Tenant, its subtenants, or any other party acting under or through Tenant, or otherwise, (b) Tenant shall cause all Alterations to be constructed free of all liens, in accordance with all Applicable Laws and shall, upon Landlord's request, deliver lien waivers to Landlord in the form required by Applicable Law, (c) Tenant shall pay the costs of the Alterations and so that Landlord, the Premises will be protected against any loss from any mechanic's, materialmen's, or other liens, and (d) prior to the commencement of the construction of any Alterations, Tenant shall give to Landlord evidence of the insurance required by Section 6.2.4. Notwithstanding the foregoing or anything to the contrary in this Lease, Tenant may contest any lien if (i) such lien is the subject of a bona fide dispute in which Tenant is contesting the amount or validity thereof, (ii) Tenant notifies Landlord of such dispute, and (iii) such lien is fully bonded by Tenant to the reasonable satisfaction of Landlord and any Mortgagee. Tenant shall give Landlord notice at least fifteen (15) days prior to the commencement of any work in the Premises, other than any Alterations that are purely cosmetic.

3.4.3 Requirements. Prior to starting work on any Alterations, Tenant shall furnish Landlord with two (2) complete sets of professionally prepared working drawings (which shall include any architectural, structural, electrical, mechanical, computer system wiring, and telecommunication plans, which shall all be in CAD or other electronic format if requested by Landlord), and will be consistent with the construction methods and procedures manual attached hereto as Exhibit I, as amended from time to time for the Premises (the "**Tenant Construction Manual**"); names of contractors reasonably acceptable to Landlord; required permits and approvals; and evidence of contractor's and subcontractor's insurance in amounts reasonably required by Landlord and naming as additional insureds the Landlord, the managing agent for the Premises, and such other Additional Insured Parties (as defined in Section 13) as Landlord may designate for such purposes. All Cable shall be clearly marked with adhesive plastic labels (or plastic tags attached to such Cable with wire) to show the purpose of such Cable (i) every six (6) feet in locations behind walls, beneath floors, and above ceilings (specifically including, but not limited to, the electrical room risers), and (ii) at the termination point(s) of such Cable. "**Cable**" shall mean and refer to any electronic, fiber, phone and data cabling and related equipment that is installed by or for the exclusive benefit of Tenant or any party acting under or through Tenant. Any changes to the plans and specifications, other than di minimus changes that are purely cosmetic, do not affect the Building structure or mechanical systems, and do not cause the cost of the Alterations to exceed $1,000,000 (which amount shall be increased by the same percentage as the Index as of each Adjustment Date), must also be submitted to Landlord for its approval. Prior to commencing Alterations, Tenant shall provide Landlord with a copy of the contract for the Alterations and evidence satisfactory to Landlord as to the existence of all necessary permits (to the extent not previously provided). Alterations shall be (a) constructed in a good and workmanlike manner, (b) consistent with first class standards, (c) consist of materials of a quality reasonably approved by Landlord, and Tenant shall ensure that no Alteration impairs any Building system, (d) performed by contractors or mechanics whose labor union affiliations are not incompatible with those of any workers, contractors or subcontractors who may be employed, retained or engaged by the Landlord for the development and making of any alterations at the Premises, and who are otherwise reasonably approved by Landlord, (e) in accordance with the Tenant Construction Manual, if any, and (f) designed and performed in accordance with all applicable Laws. It shall be deemed reasonable for Landlord to withhold its consent to any Alteration that adversely affects a Building's roof, structure, or systems, that is inconsistent with a first-class life science building, that results in an increase in gross floor area at the Premises or alteration of any Building footprint, that would violate any certificate of occupancy for the Building or any other permits or licenses relating to the Building, that would reduce the utility of the Premises for life sciences laboratory, research, and manufacturing purposes, or that is otherwise inconsistent with the requirements of this Section. Tenant shall reimburse Landlord for any third-party expenses incurred by Landlord in connection with the review, inspection, and coordination of Tenant's plans for Alterations and Tenant's performance thereof. Upon completion, Tenant shall furnish "as-built" plans (in CAD or other electronic format, if requested by Landlord) for Alterations, customary American Institute of Architects completion affidavits, full and final waivers of lien, any applicable certificate of occupancy for the space affected by such Alterations and other applicable municipal or local sign-offs and inspection reports, and any other items reasonably required by Landlord for closing out the particular work in question. Landlord's approval of an Alteration shall not be deemed to be a representation by Landlord that the Alteration complies with Law or will not adversely affect any Building system.

3.4.4 Construction Oversight Fee. With respect to any Alterations requiring Landlord's consent under Section 3.4.1, Tenant shall pay Landlord a construction oversight fee ("**Construction Oversight Fee**") equal to the sum of one percent (1%) of total hard and soft project costs, provided that Landlord's obligations in connection with the Alterations are limited to oversight only and not direct management of the project. The Construction Oversight Fee shall be calculated based on hard and soft project costs for the Alterations that were approved by Landlord for the portion of work that has been performed and invoiced and shall be payable monthly in arrears concurrent with the approved hard and soft project costs for the Alterations during the applicable month.

3.4.5 Completion. Upon the completion of any Alterations, Tenant shall, to the extent applicable, promptly give to Landlord (a) a reproducible copy of the "as-built" drawings of such Alterations, (b) a certificate of completion executed on behalf of Tenant's architect and/or engineering certifying completion of such Alterations in accordance with the respective plans and specifications, (c) a copy of the certificate of occupancy issued by the applicable governmental authorities with respect to such Alterations, and (d) copies of any warranties or guarantees with respect to such Alterations (and ensure that such warranties or guarantees are assignable to Landlord and/or run to both Landlord and Tenant's benefit).

3.4.6 Ownership of Alterations. Any Alterations shall belong to Tenant until the Termination Date, at which time the Alterations (other than Tenant's Trade Fixtures (as hereinafter defined)) shall belong to Landlord; provided, however, in no event shall the Alterations be removed by Tenant prior to the Termination Date, except as expressly provided herein. For purposes of this Lease, "**Trade Fixtures**" shall mean a piece of equipment placed on the Premises owned by Tenant and used in Tenant's trade or business. For the avoidance of doubt, Trade Fixtures shall not include, without limitation, Building systems and machinery, built-in cabinet work and/or lab benches, purpose-built mezzanine space, all HVAC, air handling, electrical, mechanical and plumbing equipment and related ducts, shafts, and conduits, all exterior venting fume hoods, walk-in freezers and refrigerators, clean-rooms, climatized rooms, electrical panels and power back-up distribution systems. The parties agree that Landlord will be treated for all purposes, including tax purposes, as the owner of (and will be the party entitled to claim depreciation or other cost recovery deductions for federal tax purposes with respect to) any improvements, equipment, or personal property that were paid for, or reimbursed by, Landlord, including any allowance provided by Landlord, and Tenant will be treated for all purposes, including tax purposes, as the owner of (and will be the party entitled to claim depreciation or other cost recovery deductions for federal tax purposes with respect to) any improvements to the extent that the cost for such improvements were paid for by Tenant and to the extent any such costs exceed any allowance provided by Landlord. Unless required to adopt a contrary position as a result of an administrative or judicial proceeding, the parties shall take no action inconsistent with, the intentions set forth in this paragraph. The parties will provide each other with such cooperation as is reasonably necessary to implement the intentions of this paragraph.

3.5 Jeopardy of Insurance. Tenant shall neither do nor omit to do anything that might result in the actual or threatened reduction or cancellation of or material adverse change in insurance carried by Landlord or Tenant on the Premises. If any such insurance is actually, or threatened to be, cancelled, reduced or materially adversely changed by an insurer as a result of the use or occupancy of the Premises or any article kept in or about the Premises or any act or omission of Tenant or any person for whom Tenant is in law responsible or any occupant of the Premises, and if Tenant fails to remedy the condition or the use or occupancy giving rise to such actual or threatened cancellation, reduction or change within three (3) business days after notice thereof, Landlord may, without limiting its other remedies for the default, enter upon the Premises and remedy the condition, use or occupancy giving rise to such actual or threatened cancellation, reduction or change, and Tenant shall pay to Landlord its cost of doing so within ten (10) days following invoice, plus an administrative fee equal to ten percent (10%) of such cost. Landlord shall not be liable for any damage to either the Premises or any property located on the Premises as a result of such entry.

3.6 Dogs. Tenant shall be permitted to bring a reasonable number of non-aggressive, fully domesticated, properly licensed, fully vaccinated, and well behaved dogs, kept by Tenant's employees as pets, into the Premises, provided and upon condition that: (a) all dogs shall be strictly controlled at all times, (b) dogs shall not be permitted to foul, damage or otherwise mar any part of the Building or Premises; and (c) while entering and exiting the Premises, all dogs shall be kept on leashes. Landlord may limit the number, weight, and breed of dogs that may be permitted in the Premises, and Landlord may implement other rules and regulations not inconsistent with this Section 3.6 that Landlord, in its sole discretion, deems reasonable or prudent. Tenant shall be responsible for any damage and additional cleaning costs and all other costs which may arise from the dogs' presence in the Building and on the Premises. Tenant shall be liable for, and hereby agrees to indemnify, defend and hold Landlord harmless from any and all claims arising from any and all acts (including but not limited to biting and causing bodily injury to, or damage to the property of, another lessee, sublessee, occupant, licensee, invitee, Landlord or an employee of Landlord) of, or the presence of, any dog in or about the Premises or the Building. Tenant shall promptly remove any dog waste and excrement from the Premises and Building. Dogs shall be strictly controlled and supervised at all times (including, without limitation, by being on leashes) by Tenant's employees, with no less than one (1) such employee responsible for so controlling and supervising no more than two (2) dogs apiece. Within three (3) business days following Landlord's request therefor, Tenant shall provide Landlord with reasonably satisfactory evidence showing that all current vaccinations have been received by any dogs permitted on the Premises. No dog shall be brought to the Premises if such dog is ill or contracts a disease that could potentially threaten the health or wellbeing of any person on the Premises (which diseases may include, without limitation, rabies, leptospirosis and lyme disease). Tenant shall not permit any objectionable dog related noises or odors to emanate from the Premises (as determined by Landlord in its sole discretion), and in no event shall any dog be at the Premises overnight or for any extended period of time. Tenant shall install and maintain dog waste bag dispensers in outdoor areas of the Premises, and all waste generated by any dogs in or about the Premises shall be promptly removed and disposed of (on no less than a daily basis) in trash receptacles. Any areas of the Premises affected by such waste shall be immediately cleaned and otherwise sanitized. Landlord may require Tenant to permanently ban any dog from the Premises if (i) any such dog exhibits aggressive behavior, damages or destroys property in the Premises, violates specific provisions of this Section, defecates or urinates in any non-outdoor area of the Project, or defecates in any outdoor area of the Project and Tenant fails to remove such waste in accordance with the terms of this Section, and (ii) any such dog is found by Landlord in its sole but good faith discretion to be a substantial, repeated nuisance to the Premises, and, in any such event, such substantial, repeated nuisance persists after at least two (2) written notices to Tenant from Landlord in any twelve (12) month period), then Landlord may terminate Tenant's rights under this Section. Tenant shall promptly pay to Landlord, within thirty (30) days after demand, all costs incurred by Landlord that directly result from the presence of any of dogs in the Premises. Tenant's right provided in this Section is personal only to the original named Tenant and/or any Permitted Transferee, shall not be exercisable by any other assignee, subtenant or other transferee of or successor to any portion of Tenant's interest under the Lease or to the Premises.

3.7 LEED Standards. Landlord and Tenant each acknowledge that the Building has been designed to meet the standard for at least a "Gold" rating under the U.S. Green Building Council's Leadership in Energy and Environmental Design ("**LEED**") rating system. Tenant shall reasonably cooperate with Landlord to obtain and maintain LEED Gold certification for the Building, including, without limitation, cooperating with Landlord in its submission of all filings and applications for LEED Gold certification, at Tenant's cost and expense. All Alterations, and any lighting installed by Tenant in the Premises, shall be designed, maintained, and installed in accordance with the requirements for at least LEED Gold, as the same may change from time to time. If necessary to ensure compliance with LEED Gold or such other standards, Tenant further agrees to engage a qualified third party LEED or Green Globe Accredited Professional or similarly qualified professional during the design phase of any Alterations, in order to review all plans, material procurement, demolition, construction and waste management procedures to ensure they are in full conformance with the requirements to maintain a LEED Gold or such other rating.

ARTICLE 4
REPAIR AND MAINTENANCE; SERVICES

4.1 Tenant Repair and Maintenance Obligations. The parties intend for this Lease to be absolutely triple net. Tenant shall be responsible for all repairs, replacements and maintenance of the Premises. Landlord shall have no obligation whatsoever to repair or maintain the Premises. Tenant shall repair and maintain the Premises in substantially the condition as exists as of the Commencement Date of this Lease (and as it may be improved or altered thereafter, including, without limitation, pursuant to the Work Letter), keep same in good order, condition and repair, and in compliance with Applicable Laws, ordinary wear and tear and casualty excepted, to the extent Tenant is not otherwise obligated to restore the same.

4.2 Condition of Premises on Surrender

4.2.1 Except as otherwise provided in this Section 4.2, upon the Termination Date, all Alterations (other than Tenant's Trade Fixtures) shall belong to Landlord without compensation, and title shall pass to Landlord under this Lease. On the Termination Date, Tenant shall give Landlord possession of the Premises, together with all such Alterations (other than Tenant's Trade Fixtures) and the LCW by Tenant, in the good, broom clean condition, free of all debris, excepting only ordinary wear and tear and damage that Tenant is not required to repair or restore under this Lease. On or prior to the Termination Date, Tenant shall also (a) remove all of Tenant's furniture, Trade Fixtures, furnishings, equipment belonging to the Tenant, and other personal property (collectively, the "**Personalty**"), and (b) repair any damage caused by the removal of such Personalty. All of Tenant's Personalty not so removed by Tenant, may be removed from the Premises by Landlord and stored, at Tenant's sole risk and expense, and in any event, Landlord shall not be responsible for the value, preservation, or safekeeping thereof. Tenant shall pay to Landlord, upon demand, all reasonable expenses so incurred by Landlord, including the cost of repairing any damage caused by removal and storing such Personalty (collectively, "**Tenant's Property**"). Any such Tenant's Property not claimed by Tenant within sixty (60) days after Tenant's surrender of the Premises shall, at Landlord's option, be deemed either abandoned or conveyed by Tenant to Landlord under this Lease without further payment or credit by Landlord to Tenant. On the Termination Date, Tenant shall assign to Landlord all manufacturers' and contractors' warranties with respect to the Premises and the Alterations (including all fixtures therein or thereon but excluding Tenant's Trade Fixtures) and Tenant shall use commercially reasonable efforts obtain the consent of the issuers of such warranties (which may include, without limitation, the payment of an assignment fee), to the extent that such consent is required for the assignment to Landlord.

4.2.2 Landlord, at the time required by Section 3.4.1, by written notice to Tenant may require Tenant, at Tenant's expense, to remove any Alterations or other affixed installations that, in Landlord's reasonable judgment, are of a nature that are not customary office or life science improvements and would require removal and repair costs that are materially in excess of the removal and repair costs associated with standard improvements for the Permitted Use ("**Required Removables**"). Required Removables shall include, without limitation, internal stairways, raised floors, vaults, rolling file systems, structural alterations and modifications (including any slab penetrations) other than de minimis alterations and modifications associated with connection of other improvements to the structure of the Building or relocation of demising walls provided that the same are otherwise consistent with first class life science buildings, Tenant's signage, supplemental systems (including HVAC), vivariums, and any Cable installed by or on behalf of Tenant that is not necessary for the proper functioning of any Alterations remaining in the Premises in accordance with this Lease. Notwithstanding the foregoing, any fixtures or improvements existing within the Premises on the Effective Date shall not be deemed Required Removables. The Required Removables shall be removed by Tenant before the expiration or earlier termination of this Lease in accordance with Section this Section 4.2, unless otherwise directed by Landlord. Landlord shall be treated as the owner of all Alterations (but, subject to Section 4.2.1, not any of Tenant's Property, including any trade fixtures and equipment that are installed in a manner that will not damage the Premises when removed) during the term of the Lease, including for tax and depreciation purposes, but Tenant shall have the exclusive right to use the same subject to the terms of this Lease. In no event shall the LCW by Tenant be considered Required Removables.

4.3 Services and Utilities. Landlord shall not be obligated to furnish to the Premises any services or utilities (including, without limitation, janitorial services), and Tenant shall contract directly with the providers of all services and utilities Tenant desires to receive at the Premises, at Tenant's sole cost and expense. Tenant shall have the right to add alternative electricity sources such as additional solar panels, the installation of which shall be subject to Section 3.4. Landlord is not responsible for the furnishing of, or any interruption, diminishment or termination of, services or utilities, whether due to the application of Laws, the failure of any equipment, the performance of maintenance, repairs, improvements or alterations, or utility interruptions, and no such interruption, diminishment, or termination shall render Landlord liable to Tenant, give rise to an abatement of Rent, or relieve Tenant from the obligation to fulfill any covenant or agreement. Except as expressly set forth in Article 9, below, Landlord shall in no event be required under any provision of this Lease or applicable Law to maintain or repair or to make any alterations, rebuildings, replacements, changes, additions or improvements on or off the Premises during the Term of this Lease. Tenant acknowledges that it shall be responsible for providing and procuring all other services necessary to its operations in and on the Premises. If Tenant (or any party claiming by, through or under Tenant) pays directly to the provider for any energy consumed at the Building, Tenant, promptly upon request, shall deliver to Landlord (or, at Landlord's option, execute and deliver to Landlord an instrument enabling Landlord to obtain from such provider) any data about consumption that Landlord, in its reasonable judgment, is required to disclose to a prospective buyer, tenant or mortgage lender under California Public Resources Code §25402.10 or any similar law. Further, Tenant hereby waives and releases its right to make repairs at Landlord's expense under Sections 1932(1), 1933(4), 1941 and 1942 of the California Civil Code or any similar or successor laws now or hereinafter in effect. At Landlord's request, Tenant shall provide Landlord information regarding Tenant's energy usage at the Premises from time to time (provided that Landlord shall hold such information confidential to the extent Landlord is not required to disclose such information pursuant to Applicable Law, nothing in this sentence being deemed to prohibit Landlord from utilizing such information to make public statements about the sustainability profile or "green" nature of Landlord, or Landlord's affiliates, properties).

ARTICLE 5
ASSIGNMENT AND SUBLETTING

5.1 General Prohibition on Transfers.

5.1.1 Transfers Generally. Tenant shall not, directly or indirectly, make a Transfer (as defined below), without Landlord's consent, except as expressly set forth in this Article 5, and any purported Transfer that does not comply with the provisions of this Article 5 shall, at Landlord's option, be deemed an Event of Default by Tenant and shall be voidable by Landlord. Tenant hereby waives the provisions of Section 1995.310 of the California Civil Code, or any similar or successor laws, now or hereinafter in effect, and all other remedies, including any right at law or equity to terminate this Lease in connection with Landlord's withholding its consent to any Transfer, on its own behalf and on behalf of the proposed transferee. Landlord shall not unreasonably withhold, condition, or delay its consent to an assignment of this Lease or any sublet of the Premises, subject to the terms and conditions of this Article 5. Without limitation, it is agreed that Landlord's consent shall not be considered unreasonably withheld if the proposed Transferee (defined below) (a) is a governmental entity, (b) is incompatible with the character of occupancy of a first class life sciences building, (c) is an entity with which the payment for the sublease or assignment is determined in whole or in part based upon its net income or profits, (d) would subject the Premises to a use that would: (i) involve increased personnel or wear upon the Building in a manner inconsistent with first-class life science buildings; (ii) require any addition to or material modification of the Premises or the Building in order to comply with building code or other governmental requirements; or (iii) involve a violation of the Permitted Use clauses of this Lease, or (e) if there is any other reasonable ground not stated above for withholding consent.

(a) "**Clients and Business Partners**" means persons or entities who are not employees or agents of Tenant or its Affiliates but are occupying or using portions of the Premises and are either (i) performing services for Tenant as subcontractors under Tenant's contracts, (ii) personnel employed by persons or entities for whom Tenant is performing services on a contractual basis, or (iii) personnel employed by persons or entities with whom Tenant is engaged in a joint venture or joint teaming effort.

(b) "**Office Sharing**" means the use of portions of the Premises by Clients and Business Partners, if, with respect to such Clients and Business Partners, such use is in connection with the services being provided to Tenant by the applicable Clients and Business Partners, the services being provided to the applicable Clients and Business Partners by Tenant, or the services being jointly provided by Tenant and the applicable Clients and Business Partners.

(c) "**Transfer**" means any assignment, pledge, mortgage, charge, debenture (floating or otherwise), hypothecation, encumbrance, lien attaching to, collateral assignment, or other transfer of this Lease or the leasehold created hereby, or any sublet or other transfer of any portion of the Premises, or any Interest Transfer (as defined below), in any case whether voluntarily, by operation of law, or otherwise, or permitting the Premises to be used or occupied by anyone other than Tenant.

(d) "**Transferee**" means the party to which a Transfer is made.

(e) "**Interest Transfer**" means if Tenant is a corporation, trust, partnership, limited liability company or other entity, (i) the transfer of a Controlling Interest or a majority of the voting stock, beneficial interest, partnership interests, membership interests or other ownership interests therein (whether at one time or in the aggregate) or (ii) the sale, mortgage, hypothecation, or pledge of more than 50% of Tenant's net assets. A "**Controlling Interest**" means the effective control over the management of such entity.

5.1.2 Consent Requests. If Tenant desires to effect a Transfer and such Transfer requires Landlord's consent, then Tenant shall give to Landlord Notice thereof at least thirty (30) days, but not more than sixty (60) days, prior to the proposed effective date of the Transfer, which Notice shall include (a) the name and address of the proposed Transferee, (b) the relevant terms of the Transfer, (c) copies of financial reports and other relevant financial information for the proposed Transferee, (d) information regarding the nature of the business the proposed Transferee intends to operate in the Premises and how long the proposed Transferee has operated such business, (e) a fully executed copy of the proposed assignment, sublease, or other document to be used to effect the Transfer (the "**Transfer Document**"), and (f) payment to Landlord of One Thousand and No/100 Dollars ($1,000.00) as a transfer review fee. In addition, Tenant shall reimburse Landlord for any third-party expenses reasonably incurred by Landlord in connection with the review, inspection, and coordination of Tenant's request for Landlord's consent to a Transfer, not to exceed $5,000 per request (which amount shall be increased by the same percentage as the Index as of each Adjustment Date). Landlord shall not unreasonably withhold, condition or delay its consent to a Transfer. If Landlord's consent is required with respect to a Transfer, and Landlord fails to respond to Tenant's request for consent within thirty (30) days of Tenant's request and submission of the documents required by this Section 5.1.2, Tenant may send a second written request, which request shall contain, in bold, capital letters, the following: "THIS NOTICE CONSTITUTES TENANT'S SECOND NOTICE OF ITS REQUEST FOR CONSENT TO A TRANSFER PURSUANT TO SECTION 5.1.2 OF THE LEASE; LANDLORD'S FAILURE TO RESPOND TO THIS NOTICE WITHIN FIVE (5) BUSINESS DAYS SHALL BE DEEMED LANDLORD'S CONSENT TO THE REQUESTED TRANSFER." If Landlord fails to respond to such second notice within five (5) business days of receipt, Tenant's request for the applicable Transfer shall be deemed approved. Tenant hereby waives the provisions of Section 1995.310 of the California Civil Code, or any similar or successor laws, now or hereinafter in effect, and all other remedies, including, without limitation, any right at law or in equity to terminate this Lease, on its own behalf and, to the extent permitted under all Applicable Laws, on behalf of the proposed transferee.

5.1.3 Permitted Transfer. Notwithstanding anything in this Article 5 to the contrary, Tenant may assign its interest in this Lease or sublease all or any part of the Premises (each a "**Permitted Transfer**") to a Permitted Transferee (defined below) with notice to Landlord (delivered prior to the Transfer, or in the event Tenant is prohibited from doing so by Applicable Laws or contractual obligations, then as soon as reasonably practical) but without Landlord's prior written consent; provided, that (i) with respect to a Permitted Transfer involving an assignment of this Lease, the Permitted Transferee assumes this Lease by a written assumption agreement delivered to Landlord prior to the effective date of such Permitted Transfer (unless such prior delivery is prohibited by Applicable Laws, in which event Tenant shall deliver such assumption agreement as soon as allowed), (ii) the Permitted Transferee shall use the Premises only for the Permitted Use, (iii) the use of the Premises by the Permitted Transferee shall not violate any other agreements or leases affecting the Property, (iv) the occurrence of a Permitted Transfer shall not waive Landlord's rights as to any subsequent Transfer, (v) the Permitted Transferee shall satisfy the Credit Requirement (defined below), and (vi) Tenant shall have given Landlord written notice at least thirty (30) day before such Transfer (unless such notice is prohibited by applicable Law, in which event Tenant shall give such notice within ten days following such Transfer). As used herein, (A) "**Affiliate**" means any person or entity who or which controls, is controlled by, or is under common control with Tenant, (ii) a corporation or other entity which shall be a wholly owned subsidiary of the Tenant, (iii) the parent corporation or other entity that wholly owns Tenant, or (iv) a subsidiary of such parent corporation or other entity that wholly owns Tenant, or a corporation or other entity having a majority of its ownership in common with the ownership of Tenant, or (v) a Successor corporation, limited liability company or other entity; (B) "**Successor**" means any (i) business entity in which or with which Tenant is merged or consolidated in accordance with applicable statutory provisions governing merger and consolidation of business entities, so long as Tenant's obligations under this Lease are assumed by the Successor, or (ii) the successor or surviving corporation or other entity in the event of a merger or consolidation of the Tenant with another corporation, so long as Tenant's obligations under this Lease are assumed by the Successor; (C) "**Purchaser**" means any person or entity who or which acquires all or substantially all of the assets or equity interests of Tenant; (D) "**Permitted Transferee**" means an Affiliate, Successor or Purchaser. The "**Credit Requirement**" shall be deemed satisfied if, as of the effective date of the Permitted Transfer, the resulting tenant under this Lease meets or exceeds all of following minimum criteria immediately following the Transfer: (i) cash on hand equal to at least Two Billion Dollars ($2,000,000,000) according to the Permitted Transferee's most recent financial statement, determined in accordance with generally accepted accounting principles ("**GAAP**"), (ii) outstanding debt of not more than sixty (60%) of the Permitted Transferee's available cash on hand (as determined pursuant to the foregoing subsection (i) according to the Permitted Transferee's most recent financial statement, determined in accordance with GAAP, and (iii) a market capitalization equal to at least Five Billion Three Hundred Million Dollars ($5,300,000,000).

5.2 Other Permitted Transfers.

5.2.1 Office Sharing. Notwithstanding anything in this Article 5 to the contrary, provided no Event of Default has occurred and is continuing, Tenant may, without Landlord's consent but upon at least ten (10) days' prior notice to Landlord, permit up to ten percent (10%) of the total leasable area of the Premises to be used for Office Sharing by Clients and Business Partners, without the same constituting a Transfer. Tenant agrees to notify Landlord, promptly upon Landlord's written request therefor, as to the approximate amount of Office Sharing by Clients and Business Partners and to certify to Landlord that such use or occupancy constitutes Office Sharing by Clients and Business Partners and does not constitute a sublease, assignment or other leasehold interest. Notwithstanding the foregoing, Tenant shall not have the right to engage in Office Sharing with respect to any particular Clients and Business Partners as aforesaid if such Clients and Business Partners are engaged in a business, or the Premises will be used in a manner, that is inconsistent with the Permitted Use. For purposes of this Lease, the acts or omissions of the employees or other personnel of Clients and Business Partners shall be deemed to be the acts or omissions (as applicable) of Tenant. Upon Landlord's request, Clients and Business Partners who are Office Sharing shall provide to Landlord satisfactory evidence of insurance covering their activities within the Premises.

5.3 Non-Transfers. For so long as Tenant is a corporation whose ownership equity is available through the free trade of shares of stock on nationally recognized stock exchanges or over-the-counter (OTC) markets that are subject to the oversight of the United States Securities and Exchange Commission (a "**Public Company**"), any transfer of Tenant's equity interests (or those of its Affiliates) whatsoever shall not be deemed a Transfer under this Lease and, for the avoidance of doubt, shall not require Landlord's consent.

5.4 Conditions to Effectiveness. As conditions precedent to any Transfer becoming effective and binding on Landlord:

5.4.1 except as otherwise specified herein, prior to the proposed effective date of the Transfer, Tenant shall give to Landlord a copy of the fully executed Transfer Document, which shall (i) be in form and substance reasonably acceptable to Landlord, and (ii) for an assignment of this Lease, contain Transferee's express assumption of Tenant's obligations under this Lease and waivers by Tenant, for the benefit of Landlord, of all applicable suretyship defenses (unless such prior delivery is prohibited by Applicable Laws, in which event Tenant shall deliver such documents as soon as allowed); and

5.4.2 as of the proposed effective date of the Transfer, there shall exist no Event of Default.

5.5 Miscellaneous.

5.5.1 Notwithstanding any Transfer, permitted or otherwise, including without limitation a Permitted Transfer, (a) Tenant shall not be released and shall at all times remain directly, primarily, and fully responsible and liable for the payment of Rent and for compliance with all of the other obligations to be performed by Tenant under the terms, provisions and covenants of this Lease, and (b) if any Transferee defaults under this Lease, then Landlord may proceed directly against Tenant without the necessity of exhausting remedies against such Transferee. Notwithstanding the foregoing, Tenant shall be automatically released from all liability under the Lease accruing from and after the date of a Transfer if the Transfer is a Permitted Transfer that is a merger or consolidation whereby the named Tenant herein is not the surviving entity; provided, however, as conditions of the foregoing release: (i) the surviving entity shall assume, either expressly or by operation of law, all of the obligations of the preceding entity for liabilities accruing before and after the Transfer, and (ii) the surviving entity must retain ownership of substantially all of the assets of the preceding entity.

5.5.2 Upon the occurrence of an Event of Default, if all or any portion of the Premises is then subject to one or more subleases, then Landlord, in addition to any other remedies provided in this Lease or at law or in equity, may collect directly from the subtenants under such subleases all rents due and becoming due to Tenant or a Transferee under such subleases and apply such rent against any sums due to Landlord from Tenant under this Lease, and no such collection shall be construed to constitute a novation or release of Tenant from the further performance of Tenant's obligations under this Lease.

5.5.3 Except for any Permitted Transfer, if the proposed Transfer is an assignment or a sublease of more than seventy five percent (75%) of the Premises for a term longer than seventy five percent (75%) of the then remaining Term, then Landlord shall have the right in its sole and absolute discretion to terminate this Lease by sending Tenant written notice of such termination within thirty (30) days after Landlord's receipt of Tenant's notice requesting consent to the Transfer. If Landlord elects to terminate this Lease, Tenant may withdraw its notice requesting consent to the Transfer by providing written notice within five (5) business days after Landlord's termination (with time being of the essence), in which case Landlord's termination shall be negated, and the Lease shall continue pursuant to its terms. If Landlord elects to terminate this Lease, then Tenant shall tender the Premises to Landlord in the condition required by this Lease at the end of the Term, and this Lease shall terminate, on the proposed effective date of the requested Transfer, and Tenant shall have no further obligations under this Lease except for those accruing prior to the termination date and those that, pursuant to the terms of the Lease, survive the expiration or early termination of the Lease.

5.5.4 Except for a Permitted Transfer, in the event, if any, that (i) all rent and other consideration that Tenant receives as a result of a Transfer exceeds (ii) the Rent payable to Landlord for the portion of the Premises and Term covered by the Transfer (allocated on a per square foot basis), then Tenant shall, at Landlord's election, pay to Landlord an amount equal to fifty percent (50%) of such excess, from time to time on a monthly basis upon Tenant's receipt of such excess; provided that in determining any such excess, Tenant may deduct from the excess all reasonable and customary expenses directly incurred by Tenant in connection with such Transfer, except that any construction costs incurred by Tenant in connection with such Transfer shall be deducted on a straight-line basis over the term of the applicable Transfer. If Tenant is in Default, Landlord may require that all sublease payments be made directly to Landlord, in which case Tenant shall receive a credit against Rent in the amount of Tenant's share of payments received by Landlord.

5.5.5 Without limiting Landlord's right to withhold its consent to any transfer by Tenant, and regardless of whether Landlord shall have consented to any such transfer, neither Tenant nor any other person having an interest in the possession, use or occupancy of the Premises or any part thereof shall enter into any lease, sublease, license, concession, assignment or other transfer or agreement for possession, use or occupancy of all or any portion of the Premises that provides for rent or other payment for such use, occupancy or utilization based, in whole or in part, on the net income or profits derived by any person or entity from the space so leased, used or occupied, and any such purported lease, sublease, license, concession, assignment or other transfer or agreement shall be absolutely void and ineffective as a conveyance of any right or interest in the possession, use or occupancy of all or any part of the Premises..

5.5.6 This Section 5.5 shall survive the expiration or earlier termination of this Lease.

ARTICLE 6
INDEMNIFICATION; RELEASE; INSURANCE

6.1 Indemnification and Release.

6.1.1 To the extent permitted by Applicable Law, Tenant shall protect, indemnify, release, defend and hold Landlord (and the Landlord Parties) harmless from and against any and all Claims to the extent caused by or incurred by reason of: (a) any damage to any property (including the property of Landlord), or any injury (including death) to any person, occurring in, on, or about any portion of the Premises, except to the extent caused by or arising from the gross negligence or willful misconduct of Landlord or the Landlord Parties; (b) any Alterations, work, or other thing done by Tenant or any Tenant Parties in or about any portion of the Premises, or from transactions of Tenant concerning any portion of the Premises; (c) Tenant's failure to comply with any Applicable Laws; (d) any breach or default by Tenant of any representation, covenant or other term of this Lease; provided that Tenant shall not be obligated to so indemnify Landlord to the extent any such matter arises from, or is caused by, the willful misconduct or gross negligence of Landlord or the Landlord Parties; or (e) Tenant's use and occupancy of the Premises. Tenant's agreement to indemnify, defend and hold the Landlord and the Landlord Parties (the "**Indemnitees**") harmless is conditioned upon the Indemnitees (i) providing written notice to Tenant of any claim, demand or action arising out of the indemnified activities within thirty (30) days after Landlord has actual knowledge of such claim, demand or action, provided that the failure to so notify Tenant will not relieve Tenant of its obligations hereunder except to the extent such failure has actually materially prejudiced Tenant; (ii) permitting Tenant to assume full responsibility to investigate, prepare for and defend against any such claim or demand, subject to Landlord's reasonable approval of any counsel used in the defense of such claim or demand; (iii) assisting Tenant, at Tenant's expense, in the reasonable investigation of, preparation of and defense of any such claim or demand; and (iv) not settling such claim or demand that would result in a payment in excess of $100,000 (individually or in the aggregate) without Tenants' prior written consent, which shall not be unreasonably withheld, conditioned, or delayed. "**Claims**" mean claims, demands, losses, penalties, fines, liabilities, actions (including informal proceedings), settlements, judgments, damages, reasonable costs, and reasonable expenses (including reasonable attorneys' fees and consultants' fees, court costs, and other litigation expenses) of whatever kind or nature, known or unknown, contingent or otherwise, incurred or suffered by, or asserted against, the party in question.

6.1.2 Tenant hereby releases Landlord and the Landlord Parties from any and all liability for any loss or claim, including all economic losses and all consequential and indirect losses, as a result of loss, damage or injury to the property and persons of Tenant and its employees, as a result of any occurrence in, upon or at the Premises or the occupancy or use by the Tenant of the Premises, including damage to the Building or loss of access to the Premises, whether or not such loss or claim may have arisen out of the acts, omissions or negligence of Landlord, the Landlord Parties or those for whom Landlord or the Landlord Parties are in law responsible. Except with respect to Sections 1.3 and 3.3.4, Landlord hereby releases Tenant from any and all liability for consequential or special damages, including lost profits (which shall not limit the rights and remedies of Landlord expressly provided in this Lease).

6.2 Insurance.

6.2.1 Landlord's Insurance. Landlord shall obtain and keep in force throughout the Term the following coverages in the following amounts: (a) commercial general liability insurance on an "occurrence" basis on the current ISO CG 00 01 occurrence form or its equivalent with a deductible reasonably acceptable to Landlord with a limit of not less than $5,000,000 per occurrence, (b) property damage insurance covering the core and shell of the Building and structural elements of other improvements situated upon the Premises on a replacement cost basis against loss or damage as provided by the standard fire and extended coverage policy, including, without limitation, earthquake and terrorism, and all other risks of direct physical loss as insured against under a special extended coverage endorsement in amounts and with a deductible determined by Landlord in its commercially reasonable discretion, (c) boiler and machinery insurance on a repair or replace basis, (d) business interruption insurance with respect to insurance required under (b) and (c) above with an indemnity period determined by Landlord, and (e) any such other insurance as Landlord's lender may require. Tenant shall provide Landlord with such information from time to time as Landlord may reasonably require in connection with Landlord's determination of the insurance required pursuant to clause (b), above.

6.2.2 Tenant's Insurance. Tenant shall procure and maintain during the Lease Term, at its sole cost and expense, a policy or policies of insurance protecting Landlord and Tenant against each of the following:

(a) Commercial general liability insurance with respect to the operations of Tenant insuring against bodily injury or death and property damage in amounts (i) not less than $10,000,000 in the aggregate,(ii) not less than $2,000,000 per occurrence and (iii) not less than $10,000,000 of excess umbrella liability insurance. Such insurance shall contain separation of insured clauses and separation of insureds, with Landlord and any third party now or hereafter providing financing to Landlord where such third party has a security interest in the Premises under such financing shall be included as additional insureds. Tenant may satisfy the foregoing limits through any combination of primary and umbrella/excess policies, provided the combined total coverage is not less than $20,000,000 in the aggregate. The amount of such commercial general liability insurance shall be increased from time to time as Landlord may reasonably determine. All such bodily injury and property damage insurance shall insure Tenant's exposure with respect to the indemnity agreement as to personal injury or property damage contained in Section 6.1 herein.

(b) Insurance covering Tenant's construction, alterations, additions or improvements permitted herein (other than the core and shell of the Building and structural elements of other improvements, except for the LCW by Tenant, which shall be insured by Tenant), existing tenant improvements, trade fixtures and personal property, in an amount not less than 100% of their full replacement cost from time to time during the Lease Term, providing protection on an all risk basis, including, without limitation, coverage for earthquakes with coverage commencing on or prior to the commencement of Tenant's construction, for the repair or replacement of the property damaged or destroyed.

(c) Pollution Legal Liability that provides first party coverage for clean-up costs and third party coverage for bodily injury and property damage resulting from pre-existing and future contamination conditions, of at least Five Million Dollars ($5,000,000.00) per pollution event; such coverage shall specifically include this lease as an insured contract.

(d) The minimum limits of insurance required to be carried by Tenant shall not limit Tenant's liability. All policies of insurance to be provided by Tenant shall be issued by insurance companies, with general policy holder's rating of not less than A and a financial rating of not less than Class VIII as rated in the most current available "Best's" Insurance Reports, and admitted to do business in the State of California. Such policies shall be issued in the name of Tenant, with Landlord, Landlord's managing agent, lenders, and any other party designated by Landlord ("**Additional Insured Parties**") included as an additional insured. Tenant's property insurance and any builder's risk policy carried by Tenant or its contractors shall identify Landlord or, at Landlord's direction, Landlord's lender, as a loss payee. The full replacement cost of improvements under Tenant's property insurance may be designated by Landlord in the good faith exercise of Landlord's judgment. In the event that Tenant does not agree with Landlord's designation, Tenant shall have the right to submit the matter to an insurance appraiser reasonably selected by Landlord and paid for by Tenant. The insurance appraiser shall submit a written report of his appraisal, and if said report discloses that the improvements are not insured as therein required, Tenant shall promptly obtain the insurance required. The policies provided by Tenant shall be for the mutual and joint benefit and protection of Landlord and Tenant, and certificates of insurance shall be delivered to the Landlord within ten (10) days after the Lease Commencement Date and, thereafter, within thirty (30) days after to the expiration of the term of each such policy. Upon Landlord's request, Tenant shall deliver to Landlord, in lieu of such certificates, copies of the policies of insurance required to be carried under Section 6.2.2 showing that the Additional Insured Parties are named as additional insureds (with respect to the applicable policies). Upon the expiration or termination of any such policy, renewal or additional policies shall be procured and maintained by the Tenant to provide the required coverage. All policies of insurance delivered to Landlord must contain a provision that the company writing said policy will provide Landlord with thirty (30) days' notice in writing in advance of any cancellation or lapse or the effective date of any reduction in the amounts of insurance (except in the event of non-payment of premium, in which case ten (10) days' written notice shall be given). Notwithstanding the foregoing, if the foregoing requirement that the insurance company provide prior notice to Landlord of cancellation or material change of the applicable policy cannot reasonably be obtained based on then-prevailing insurance industry practices, Tenant shall so advise Landlord of such unavailability and shall instead shall use reasonable efforts to cause its insurer to provide Landlord, and in any event Tenant shall provide Landlord with, notice of any such cancellation of any of Tenant's insurance policies. All of Tenant's commercial general liability, property damage and other casualty policies shall be written as primary policies, not contributing with and not in excess of coverage which Landlord may carry. Tenant agrees that if, after the Commencement Date, Tenant does not take out and maintain the insurance required under this Section 6.2, Landlord may (but shall not be required to) procure, and thereafter maintain, said insurance on Tenant's behalf, and any costs or expenses incurred by Landlord in connection therewith, plus an administration fee of ten percent (10%) of the cost, shall promptly be paid by Tenant to Landlord as Additional Rent.

(e) Notwithstanding anything to the contrary, Tenant's obligation to carry the insurance described in this Section 6.2.2 may be brought within the coverage of a so-called blanket policy or policies of insurance carried and maintained by the Tenant, provided that (i) Landlord will be an additional insured thereunder as its interests may appear; (ii) the coverage afforded Landlord will not be reduced or diminished by reason of the use of such blanket policy of insurance; and (iii) the requirements set forth herein are otherwise satisfied. In the event of any Claims covered by Tenant's insurance, Tenant shall, within 10 days following Landlord's written request, provide Tenant with copies of the applicable insurance policies carried by Tenant pursuant to this Lease.

6.2.3 Release of Subrogation Rights. Tenant and Landlord each hereby releases the other from liability and waives all right to recover against the other for any loss from perils insured against under their property insurance policies, including any extended coverage and special form endorsements to said policies; provided, however, this Section 6.2.3 shall be inapplicable if it would have the effect, but only to the extent that it would have the effect of invalidating any insurance coverage of Landlord or Tenant. Tenant and Landlord's property damage policies shall contain, if available, a waiver of subrogation clause.

6.2.4 Insurance for Alterations. During the performance of any Alterations by Tenant, (a) the insurance required under this Section 6.2 shall extend to all of Tenant's consultants and contractors (and subcontractors of any tier) and shall include injuries to persons and damage to property arising in connection with such Alterations and (b) Tenant shall also maintain such other insurance as Landlord may reasonably require, including all-risk builder's insurance, each of which policies shall name Landlord and Landlord's lender as additional insureds and loss payees. Tenant shall give to Landlord copies of the policies of such insurance prior to commencing construction of such Alterations.

ARTICLE 7
THIRD PARTIES

7.1 Subordination, Attornment and Non-Disturbance. This Lease shall be automatically subject and subordinate at all times to the lien of any first priority mortgages or deeds of trust on, against, or affecting any portion of the Premises, or Landlord's interest or estate in any portion of the Premises, and to all renewals, modifications, consolidations, replacements, and extensions thereof (each, a "**Mortgage**"); provided that, as a condition precedent to such subordination, Tenant must receive a fully executed subordination, non-disturbance and attornment agreement substantially in the form attached as Exhibit E hereto, or in such other commercially reasonable form as required by Landlord's Mortgagee (as hereinafter defined) (a "**SNDA**") from any current and future encumbrance holder (each, a "**Mortgagee**") with such changes as reasonably requested by Tenant. Landlord shall request a SNDA from each present and any future Mortgagee seeking to subordinate this Lease to the lien of its Mortgage and deliver the same to Tenant. In the event Mortgagee enforces it rights under the Mortgage, Tenant, at Mortgagee's option, will attorn to Mortgagee or its successor; provided, however, that, subject to the terms of any SNDA between Tenant and such Mortgagee (which shall govern in the event of any conflicts with the provisions of this Section 7.1), Mortgagee or its successor shall not be liable for or bound by (i) any payment of any Rent installment that may have been made more than thirty (30) days before the due date of such installment, (ii) any act or omission of or default by Landlord under this Lease (but Mortgagee, or such successor, shall be subject to the continuing obligations of landlord under the Lease arising from and after such succession, but only to the extent of Mortgagee's, or such successor's, interest in the Premises as provided in Article 12), (iii) any then-exercisable credits, claims, setoffs or defenses that Tenant may have against Landlord, or (iv) any obligation to provide tenant improvements allowances or perform tenant improvements to be provided by Landlord hereunder.

7.2 Mortgagee's Right to Cure. Notwithstanding anything to the contrary in this Lease, before exercising any right (a) of offset, counterclaim, reduction, deduction, or abatement against Tenant's payment of Rent under this Lease or (b) to terminate the Lease or to claim a partial or total eviction, in each case arising from Landlord's default under this Lease, (i) Tenant shall provide to each Mortgagee whose name and address has been furnished in writing to Tenant with written notice of the default by Landlord giving rise to same, and (ii) Mortgagee shall have a period of thirty (30) days after the last date on which Landlord could have cured such default within which such Mortgagee will be permitted, but not be obligated, to cure such default. If such default cannot be cured within such thirty-(30)-day period, then such Mortgagee shall have such additional time as may be necessary to cure such default, if prior to the end of such thirty-(30)-day period such Mortgagee has commenced and is diligently pursuing such cure or the remedies under the Mortgage necessary for Mortgagee to be able to effect such cure, in which event Tenant shall have no right with respect to such default while such cure and remedies are being diligently pursued by such Mortgagee. Notwithstanding the foregoing, such Mortgagee shall have no obligation to cure (and shall have no liability or obligation for not curing) any default by Landlord. In addition, as to any default by Landlord the cure of which requires possession and control of the Premises, provided that such Mortgagee undertakes by written notice to Tenant to exercise reasonable efforts to cure or cause to be cured by a receiver such default within the period permitted by this Section 7.2, such Mortgagee's cure period shall continue for such additional time as such Mortgagee may reasonably require to either: (A) obtain possession and control of the Premises with due diligence and thereafter cure the default with reasonable diligence and continuity; or (B) obtain the appointment of a receiver and give such receiver a reasonable period of time in which to cure the default.

7.3 Sale of the Premises. Subject to the provisions of Article 11, if Landlord sells or conveys the Premises, such sale or conveyance shall release Landlord from any liability from and after such sale or conveyance upon any of the covenants or conditions, expressed or implied, contained in this Lease in favor of Tenant (to the extent such liability is expressly assumed by such transferee), and in such event, Tenant agrees to look solely to the successor-in-interest of Landlord in and to this Lease with respect to such liabilities that are incurred from and after such sale or conveyance. In the event Landlord enters into a purchase and sale agreement for the sale or conveyance of the Premises, in the event such purchaser is an entity engaged primarily in the business of research, development, manufacturing, sale, or marketing of a biopharmaceutical product (a "**Pharma Competitor**"), then the Pharma Competitor shall execute a non-disclosure and confidentiality agreement substantially in the form attached hereto as Exhibit F; provided, however, that Tenant shall negotiate in good faith in the event the Pharma Competitor wishes to deviate from the form attached as Exhibit F. Except as set forth in this Section 7.3, this Lease shall not be affected by any such sale or conveyance and Tenant agrees to attorn to the purchaser or assignee. Landlord shall transfer or deliver the Security Deposit to Landlord's successor-in-interest and thereupon Landlord shall be discharged from any further liability with regard thereto.

7.4 Estoppel Certificates. Within ten (10) business days after Landlord's written request, Tenant shall execute and deliver to Landlord and any of Landlord's then existing or prospective lenders, investors, or purchasers of any portion of the Premises, a certificate substantially in the form attached as Exhibit C, or in such other commercially reasonable form and containing such other information as Landlord or any such lenders, investors, or purchasers, may reasonably require. Any certificate delivered in accordance with this Section 7.4 may be relied upon by any such lender, investor, or purchaser. Within ten (10) business days after Tenant's request, Landlord shall execute and deliver to Tenant and any of Tenant's then existing or prospective lenders, investors, or purchasers, a statement in writing certifying that Tenant is in possession of the Premises under the terms of this Lease, that this Lease is unmodified and in full force and effect (or, if there have been modifications, that this Lease is in full force and effect, as modified, and setting forth such modifications), stating the dates to which rent has been paid, and either stating that no defaults exist hereunder, or specifying each such default of which Landlord may have knowledge, and such other matters as may be reasonably requested by Tenant.

7.5 Liens. Tenant shall, within fifteen (15) business days of written notice of filing, discharge (either by payment or by filing of the necessary bond, insure over, or otherwise) any mechanic's, materialman's or other lien or encumbrance against any portion of the Premises that arises out of any payment due for, or purported to be due for, any labor, services, materials, supplies or equipment alleged to have been furnished to or for Tenant. If Tenant shall fail to so discharge such lien or encumbrance (either by payment or by filing of the necessary bond, insure over or otherwise) then, such failure shall be an Event of Default under this Lease and, in addition to any other right or remedy of Landlord, Landlord may discharge the same (either by payment or by filing of the necessary bond or otherwise), and any payment, costs and expenses incurred by Landlord in connection therewith, including reasonable attorneys' fees, shall be repaid together with interest thereon at the rate set forth in Section 2.3 from the date of payment. Notwithstanding the foregoing or anything to the contrary in this Lease, Tenant may contest any lien (and Landlord shall not discharge such lien at Tenant's expense for so long as Tenant is diligently pursuing such contest) if (i) such lien is the subject of a bona fide dispute in which Tenant is contesting the amount or validity thereof, (ii) Tenant notifies Landlord in writing of such dispute, (iii) Tenant has or establishes unrestricted cash reserves to in an amount equal to 125% of (x) the amount of Tenant's obligations being contested plus (y) any additional interest, charge or penalty arising from such contested lien and (iv) such lien is fully bonded by Tenant to the reasonable satisfaction of Landlord and any Mortgagee.

ARTICLE 8
EVENTS OF DEFAULT & REMEDIES

8.1 Events of Default. "**Event of Default**" means any of the following:

(a) Tenant fails to pay when due any Rent, and such failure continues for five (5) business days after Landlord delivers to Tenant notice thereof; provided, however, Landlord shall not be required to provide prior notice of Tenant's failure to pay any recurring obligation to pay any Base Rent or any monthly payment of estimated Taxes or Insurance Expenses more than twice during any twelve (12) month period, after which Tenant's failure to pay such amount shall be an Event of Default if Tenant fails to pay the amount when due and such failure continues for five (5) business days after the due date;

(b) except as otherwise provided in this Lease, Tenant fails to comply with any term, provision, or covenant of this Lease and such failure continues for thirty (30) days after Landlord gives to Tenant Notice thereof (but if such failure is curable but cannot reasonably be cured during such 30-day period, and if Tenant has commenced such cure promptly and in any case within such 30-day period and thereafter has diligently pursued such cure to completion, then such 30-day period shall be extended to ninety (90) days);

(c) Tenant fails to obtain and keep in force at all times any insurance required under this Lease, and such failure continues for five (5) days after Landlord gives to Tenant Notice thereof;

(d) Tenant fails to deliver to Landlord, within fifteen (15) business days after Landlord gives Tenant Notice thereof, any instrument or assurance required under this Lease;

(e) The filing by Tenant in any court pursuant to any statute or petition in bankruptcy or insolvency or for reorganization or arrangement for the appointment of a receiver or all of a portion of Tenant's property the filing against Tenant of any such petition, or the commencement of a proceeding for the appointment of a trustee, receiver or liquidator for Tenant, or of any property of Tenant, or a proceeding by any governmental authority for the dissolution or liquidation of Tenant, if such proceeding shall not be dismissed or trusteeship discontinued within sixty (60) days of commencement of such proceeding or the appointment of such trustee or receiver; or the making by Tenant of an assignment for the benefit of creditors. Tenant hereby stipulates to the lifting of the automatic stay in effect and relief from such stay for Landlord in the event Tenant files a petition under the United States Bankruptcy Laws, for the purpose of landlord pursuing its rights and remedies against Tenant;

(f) Tenant's failure to cause to be released any mechanics liens filed against the Premises within twenty (20) days after the date Tenant is notified that the same shall have been filed or recorded, subject to Tenant's right to dispute liens as set forth in Section 7.5;

(g) Abandonment of the Premises pursuant to California Civil Code Section 1951.3, or failure by Tenant or a transferee permitted pursuant to Article 5 to occupy at least sixty percent (60%) of the Premises for a period of ninety (90) consecutive days or more for any reason other than restoration following a casualty or condemnation, Force Majeure affecting Tenant's ability to operate within the Premises, and temporary cessations in order to complete Alterations in accordance with this Lease, provided that it shall not be deemed to be a failure to occupy for purposes of this clause (ii) if the applicable portion of the Premises remains fully furnished with the necessary equipment to conduct business operations consistent with the Permitted Use as it was undertaken prior to such failure to occupy, with regular repair, maintenance, and cleaning occurring in accordance with the terms of this Lease, no other Event of Default has occurred, and Tenant is actively marketing the applicable portion of the Premises for sublease (or marketing this Lease for assignment);

(h) Tenant's failure to provide a SNDA within the period required by Section 7.1 or Tenant's failure to provide a certificate within the time period required by Section 7.4 and such failure continues for five (5) business days after Landlord delivers to Tenant notice thereof;

(i) Tenant performs a Transfer in violation of Article 5, or

(j) Tenant fails to deliver the Letter of Credit in the form approved by Landlord as and when required by Section 2.5.1 of the Lease, or

(k) If Landlord elects, in its sole discretion, the occurrence of any "Event of Default" under the Companion Lease.

8.2 Remedies.

8.2.1 Upon Event of Default. Upon the occurrence of any Event of Default, Landlord shall have the option to pursue any one or more of the following remedies without any Notice or demand whatsoever (except as expressly provided herein), concurrently or consecutively and not alternatively (in addition to any other remedies available to Landlord at law or in equity), all of which remedies shall be distinct, separate and cumulative:

(a) Termination. Landlord may terminate this Lease upon notice to Tenant, in which event Tenant shall vacate the Premises immediately and deliver possession of the Premises to Landlord in the condition which Tenant is required to surrender the Premises at the expiration of the Term (Tenant hereby waives, relinquishes and releases for itself and for all those claiming under Tenant any right of occupancy of the Premises following termination of this Lease, and any right to redeem or reinstate this Lease by order or judgment of any court or by any legal process or writ under Applicable Laws, including, without limitation, California Code of Civil Procedure Sections 473 and 1179, and California Civil Code Section 3275), and if Tenant fails to do so, then Landlord may, after due process of law, enter upon and take possession of the Premises, and expel or remove Tenant and any other person who may be occupying the Premises or any portion thereof, without being liable for prosecution or any claim or damages therefor. Upon termination of the Lease as provided in this Section, Landlord may recover from Tenant the following: (i) the worth at the time of award of any unpaid rent which has been earned at the time of such termination; plus (ii) the worth at the time of award of the amount by which the unpaid rent which would have been earned after termination until the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus (iii) the worth at the time of award of the amount by which the unpaid rent for the balance of the Term after the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus (iv) any other amount necessary to compensate Landlord for all the detriment proximately caused by Tenant's failure to perform its obligations under this Lease or which in the ordinary course of things would be likely to result therefrom, specifically including but not limited to, attorneys' fees, brokerage commissions and advertising expenses incurred, expenses of remodeling the Premises or any portion thereof for a new tenant, whether for the same or a different use, and any special concessions made to obtain a new tenant; plus (v) at Landlord's election, such other amounts in addition to or in lieu of the foregoing as may be permitted from time to time by Applicable Law. The term "rent" as used in this Section 8.2.1(a) shall be deemed to be and to mean all sums of every nature required to be paid by Tenant pursuant to the terms of this Lease, whether to Landlord or to others, including, without limitation, late charges and interest. As used in Sections 8.2.1(a)(i) and (ii), the "worth at the time of award" shall be computed by allowing interest at the rate set forth in Section 2.4 above, but in no case greater than the maximum amount of such interest permitted by Applicable Law. As used in Section 8.2.1(a)(iii), the "worth at the time of award" shall be computed by discounting such amount at the discount rate of the Federal Reserve Bank of San Francisco at the time of award plus one percent (1%). Landlord shall have no obligation to relet the Premises or any part thereof and shall in no event be liable for failure to relet the Premises or any part thereof, or, in the event of any such reletting, for refusal or failure to collect any rent due upon such reletting. No such refusal or failure shall operate to relieve Tenant of any liability under this Lease. Tenant shall instead remain liable for all unpaid Rent and for all such expenses. This paragraph is expressly intended to afford Landlord the remedies provided for in California Civil Code § 1951.2. Possession. Landlord may re-enter the Premises without terminating this Lease by Notice to Tenant and sublet the whole or any part thereof for the account of Tenant upon as favorable terms and conditions as the market will allow; provided, however, that Tenant shall have not less than thirty (30) days following such re-entry to remove Tenant's Personalty from the Premises. In the latter event (a) Landlord shall have the right to collect any Rent which may thereafter become due and payable under such sublease and to apply the same first, to the payment of any expenses incurred by Landlord in dispossessing Tenant and in subletting the Premises, and second, to the payment of the Rent herein reserved and to the fulfillment of Tenant's other covenants hereunder, and (b) Tenant shall be liable for amounts equal to the Rent as the same would under the terms of this Lease become due, less any amounts actually received by Landlord and applied on account of Rent as aforesaid. Landlord shall have the remedy described in California Civil Code Section 1951.4 (lessor may continue lease in effect after lessee's breach and abandonment and recover rent as it becomes due, if lessee has the right to sublet or assign, subject only to reasonable limitations). Accordingly, if Landlord does not elect to terminate this Lease due to any Event of Default, Landlord may, from time to time, without terminating this Lease, enforce all of its rights and remedies under this Lease, including, without limitation, the right to recover all Rent as it becomes due.

(c) Subleases of Tenant. Whether or not Landlord elects to terminate this Lease, Landlord may terminate any and all subleases or other consensual arrangements for possession or occupancy of the Premises entered into by Tenant or any subtenant of Tenant, or may succeed to Tenant's or Tenant's subtenant's interest in such subleases or other arrangements. If Landlord elects to succeed to Tenant's or Tenant's subtenant's interest in any such subleases or other arrangements, then as of the date of Notice by Landlord of such election (i) Tenant shall have no further right to, or interest in, the rent or other consideration receivable thereunder, and (ii) any sublessee or other occupant of the Premises shall attorn to and recognize Landlord as its landlord.

(d) Right to Perform Tenant's Covenants. If Tenant shall at any time fail to pay any Taxes or to take out, pay for, maintain or deliver any of the insurance provided for in this Lease, or shall fail to make any other payment or perform any obligation under this Lease, and such failure continues beyond applicable notice and cure periods (or without any notice and right to cure where required to protect life or property), then Landlord may, without waiving or releasing Tenant from any obligations of Tenant in this Lease contained, pay any such Tax, effect any such insurance coverage and pay premiums therefor, and make any other payment or perform any other act which Tenant is obligated to perform under this Lease, in such manner and to such extent as Landlord shall, in its sole discretion, deem necessary. In exercising any such rights, Landlord may pay necessary and incidental costs and expenses including reasonable attorneys' fees. All sums so paid by Landlord and all necessary and incidental costs and expenses in connection with the performance of any such act by Landlord, together with interest thereon at the Interest Rate, shall be payable to Landlord on demand. If Landlord incurs any third-party expenses to cure a breach of any non-monetary obligation of Tenant, Tenant shall also pay an administrative charge equal to ten percent (10%) of the cost of the work performed by Landlord. Landlord shall have no obligation to perform on Tenant's behalf and if Landlord does so, Landlord shall not be liable to Tenant for any damage resulting from its actions.

(e) Other Remedies. In addition to the remedies set forth in this Lease, Landlord shall have all other remedies provided by law or statute to the same extent as if fully set forth herein word for word (including, without limitation, the right to enforce Tenant's specific performance of each and every covenant, condition and other provisions of this Lease). No remedy herein conferred upon, or reserved to Landlord shall exclude any other remedy herein or by law provided, but each shall be cumulative.

8.2.2 Form of Payment Following Event of Default. Following the occurrence of a monetary Event of Default, Landlord shall have the right to require that any or all subsequent amounts paid by Tenant to Landlord under this Lease, whether relating to the Event of Default in question or otherwise, be paid in the form of wire transfer or immediately available funds, or by other means approved by Landlord, notwithstanding any prior acceptance by Landlord of payments from Tenant in any different form.

8.2.3 Mitigation of Damages. Except as required by law, Landlord shall have no obligation to mitigate its damages. If Landlord is required by law to mitigate its damages under this Lease, then (a) Landlord shall be required only to use reasonable efforts to so mitigate, which shall not exceed such efforts as commercial landlords generally use to lease similar premises in the vicinity of the tri-city area (Oceanside, Carlsbad and Vista) of the State of California; (b) Landlord shall not be deemed to have failed to so mitigate if Landlord leases less than all of the Premises; and (c) Landlord's failure to so mitigate shall only reduce the Rent to which Landlord is entitled. Tenant acknowledges that Landlord's rejection of a prospective replacement tenant based on an offer of rentals below published rates for new leases of similar premises in the vicinity of the tri-city area (Oceanside, Carlsbad and Vista) of the State of California at the time in question, or containing terms less favorable than those contained herein, shall not give rise to a claim by Tenant that Landlord failed to so mitigate.

8.2.4 Waiver of Right of Redemption. Tenant (for itself and all others claiming through Tenant) irrevocably waives and releases any rights under any law now or hereafter existing to redeem or reinstate this Lease or Tenant's right of occupancy of the Premises after termination of this Lease, including, without limitation, any and all rights conferred by Section 3275 of the Civil Code of California and by Sections 1174(c) and 1179 of the Code of Civil Procedure of California..

8.2.5 Reimbursement of Expenses. In the case of termination of this Lease pursuant to this Section 8.2, Tenant shall reimburse Landlord for all expenses arising out of such termination, including without limitation, all costs incurred in collecting amounts due from Tenant under this Lease (including legal fees, costs of litigation and the like); all expenses incurred by Landlord in attempting to relet the Premises or parts thereof (including advertisements, brokerage commissions, Tenant's allowances, costs of preparing space, and the like); all of Landlord's then unamortized costs of any work allowances provided to Tenant for the Premises; and all Landlord's other reasonable expenditures necessitated by the termination. The reimbursement from Tenant shall be due and payable immediately from time to time upon notice from Landlord that an expense has been incurred, without regard to whether the expense was incurred before or after the termination.

8.2.6 Claims in Bankruptcy. Nothing herein shall limit or prejudice the right of Landlord to prove and obtain in a proceeding for bankruptcy, insolvency, arrangement or reorganization, by reason of the termination, an amount equal to the maximum allowed by a statute or Applicable Law in effect at the time when, and governing the proceedings in which, the damages are to be proved, whether or not the amount is greater to, equal to, or less than the amount of the loss or damage that Landlord has suffered.

8.3 Landlord Default. If Landlord shall fail to perform any material obligation under this Lease required to be performed by Landlord, Landlord shall not be deemed to be in default hereunder nor subject to claims for damages of any kind, unless such failure shall have continued for a period of thirty (30) days after written notice thereof by Tenant or, if such failure is curable but cannot reasonably be cured during such 30-day period, such additional time as it would reasonably take to cure. If Landlord shall fail to cure within the time permitted for cure herein, Landlord shall be liable to Tenant for those actual damages sustained by Tenant as a result of Landlord's default and Tenant shall also have the right to pursue injunctive relief against Landlord, to the extent available under Applicable Laws. Except as may be expressly provided in this Lease, in no event shall Tenant have the right to terminate the Lease nor shall Tenant's obligation to pay Base Rent or other charges under this Lease abate based upon any default by Landlord of its obligations under the Lease. In no event shall Landlord or any Landlord Related Party ever be liable to Tenant for loss of profits, loss of business, or indirect or consequential damages suffered by Tenant from whatever cause.

8.4 Non-Waiver. The failure of Landlord to insist upon strict performance of any of the terms, covenants, conditions or agreements contained herein shall not be deemed a waiver of any rights or remedies that Landlord may have, and shall not be deemed a waiver of any subsequent breach or default in the performance of any of the terms, covenants, conditions or agreements contained herein. The performance of each and every term, covenant, condition and agreement to be performed by Landlord pursuant to this Lease shall not be a condition precedent to Landlord's right to collect Rent or to enforce this Lease. Further, pursuant to the requirements of California Code of Civil Procedure Section 1161.1(c), Tenant is hereby placed on actual notice that Landlord's acceptance of Rent shall not constitute a waiver by Landlord of (a) any preceding breach by Tenant of any provision of this Lease, other than the failure of Tenant to pay the particular Rent so accepted; or (b) any of Landlord's rights, including, without limitation, any rights Landlord may have to recover possession of the Premises or to sue for any remaining Rent owed by Tenant.

ARTICLE 9
CASUALTY & CONDEMNATION

9.1 Casualty.

9.1.1 Generally. Subject to Section 9.1.2 below, if the Premises are damaged by fire, the elements or other casualty (collectively a "**Casualty**"), Tenant shall promptly notify Landlord of the same. Except as expressly set forth below, this Lease shall not terminate in the event of damage to the Premises by other casualty, nor any other obligation of Tenant hereunder be abated or affected in any way. If all or any portion of the Premises becomes untenantable or inaccessible by a Casualty, Landlord shall cause a general contractor selected by Landlord to provide Landlord and Tenant with a written estimate of the amount of time required, using standard working methods, to substantially complete the repair and restoration of the affected portion of the Premises ("**Completion Estimate**"). Landlord shall promptly forward a copy of the Completion Estimate to Tenant. Notwithstanding anything to the contrary contained in this Lease, Landlord and Tenant hereby waive the provisions of any Law relating to the matters addressed in this Section, and agree that their respective rights for damage to or destruction of the Premises shall be those specifically provided in this Lease, which shall constitute an express agreement between the parties with respect thereto, and Landlord and Tenant hereby agree that any Applicable Law, including Sections 1932(2) and 1933(4) of the California Civil Code, with respect to any rights or obligations concerning damage or destruction of leased or hired property, shall have no application to this Lease or to any damage or destruction to all or any part of the Premises.

9.1.2 Termination. Notwithstanding Section 9.1.1, if the Completion Estimate indicates that the Premises cannot be made tenantable within twenty-four (24) months from the date the repair is started, then either party shall have the right to terminate this Lease upon written notice to the other within ten (10) days after Tenant's receipt of the Completion Estimate, which notice, if sent by Tenant, shall be accompanied by a sum equal to all Rent due from Tenant to Landlord to the date of termination. Tenant, however, shall not have the right to terminate this Lease if the Casualty was caused by the negligence or intentional misconduct of Tenant or any Tenant Parties. If (i) the Completion Estimate indicates that the Premises can be made tenantable within thirty-six (36) months from the date the repair is started, and (ii) Tenant terminates this Lease pursuant to the first sentence of this Section 9.1.2., then, within thirty (30) days after receipt of Tenant's termination notice, Landlord may, in its sole and absolute discretion, negate Tenant's termination by providing notice to Tenant that Landlord agrees to an abatement of Base Rent beginning immediately following the twenty-fourth (24th) month after the date the repair is started and ending on the date when Landlord has substantially completed the repair and restoration of the affected portion of the Premises. In addition, if the Premises are damaged by fire, the elements or other casualty during the last twelve (12) months of the Term, and the Completion Estimate shows that the restoration cannot be completed within one hundred twenty (120) days after the Casualty, then either party shall have the right, in lieu of Tenant fulfilling its obligations under Section 9.1.1 above, to terminate this Lease as of the date of the Casualty by notice to the other party within ten (10) business days after the delivery of the Completion Estimate, which notice, if sent by Tenant, shall be accompanied by a sum equal to all Rent due from Tenant to Landlord to the date of termination. If Tenant elects to terminate the Lease pursuant to this Section 9.1.2, Tenant shall (1) assign to Landlord all of Tenant's right, title and interest in and to any property insurance proceeds received in connection with such casualty for the Tenant Improvements and LCW by Tenant (each as defined below) and (2) pay to Landlord an amount equal to Tenant's deductible under any insurance and/or any applicable self-insured retention amount covering the Tenant Improvements and LCW by Tenant. In addition, Landlord, by notice to Tenant within ninety (90) days after the date of the Casualty, shall have the right to terminate this Lease if (1) any Mortgagee requires that the insurance proceeds be applied to the payment of the mortgage debt; or (2) a material uninsured loss to the Building or Premises occurs, and, in either case, Tenant does not provide Landlord with sufficient funds (or evidence of the same satisfactory to Landlord) to complete such restoration within thirty (30) days after Landlord's termination notice.

9.1.3 Restoration. If this Lease is not terminated, Landlord shall promptly and diligently, subject to reasonable delays for insurance adjustment or other matters beyond Landlord's reasonable control, restore the core and shell of the Building and structural elements of other improvements situated upon the Premises, subject to the following provisions. Such restoration shall be to substantially the same condition that existed prior to the Casualty, except for modifications required by Applicable Law or any other modifications deemed desirable by Landlord ("**Landlord's Restoration**"). Landlord shall be paid a construction management fee equal to three percent (3%) of the hard and soft costs of construction in connection with Landlord's Restoration. In no event shall Landlord be required to spend more for the Landlord's Restoration than the proceeds received by Landlord, whether from Landlord's insurance proceeds or proceeds from Tenant. Landlord shall not be liable for any inconvenience to Tenant, or injury to Tenant's business resulting in any way from the Casualty or the repair thereof. Landlord shall not be responsible for restoration of any portion of the non-structural tenant improvements, any improvements or fixtures installed for Tenant's specific business operations, the TI by Landlord (as defined in Exhibit B), the LCW by Tenant (as defined in Exhibit B), or any Alterations (collectively, the "**Tenant Improvements**"). If this Lease is not terminated, upon the substantial completion of Landlord's Restoration, Tenant shall diligently and promptly repair all such damage and restore the Tenant's Improvements (the "**Tenant's Restoration**") to substantially the same quality, use and usability to the Building and related improvements that existed immediately prior to the Casualty.

9.1.4 No abatement of Rent. If the Premises are damaged or destroyed by casualty, then the Rent shall not be abated and Tenant shall not be entitled to any compensation or damages from Landlord for loss of the use of the Premises, damage to Tenant's Personalty or to any Alterations, or any inconvenience occasioned by any damage, repair, or restoration.

9.1.5 Insurance Proceeds. Tenant shall be entitled to any and all of the insurance proceeds payable for the damage to the Tenant Improvements and LCW by Tenant, provided, however, that if Tenant elects to terminate this Lease pursuant to Section 9.1.2, then Tenant shall assign and pay over to Landlord all insurance proceeds received by or payable to Tenant with respect to damage to the core and shell of the Building and structural elements of other improvements situated upon the Premises, including the LCW by Tenant (but not Tenant Improvements and Tenant's Personalty). Whether or not Tenant so elects to terminate this Lease, Tenant shall be entitled to any and all of the insurance proceeds payable for the damage to Tenant's Personalty.

9.2 Waiver. Tenant (for itself and all others claiming through Tenant) irrevocably waives and releases its rights to make repairs at Landlord's expense. The provisions of this Lease, including this Section 9.2, constitute an express agreement between Landlord and Tenant with respect to any damage to, or destruction of, any portion of the Premises. Any law in respect of any rights or obligations concerning any such damage or destruction in the absence of an express agreement between the parties, and any other law relating to damage or destruction of leased premises, whether in effect on the date of this Lease or thereafter, shall have no application to this Lease or any damage or destruction of any part of the Premises.

9.3 Total Condemnation. If after the execution of this Lease and prior to the expiration of the Term, all or a significant portion of the Premises shall be permanently taken under power of eminent domain by any public or private authority, or conveyed by Landlord to said authority in lieu of such taking (collectively, a "**Taking**"), and if as a result of such Taking: (a) access to the Premises to and from the publicly dedicated roads adjacent to the Premises as of the Effective Date is permanently and materially impaired such that Tenant no longer has access to such dedicated road; (b) there is insufficient parking to operate the Premises under Applicable Laws and replacement parking cannot be constructed or provided elsewhere on the Premises; or (c) the taking includes a portion of the Building such that the remaining portions are unsuitable for the Permitted Use and the remaining portions of the Premises cannot, in the reasonable opinion of a contractor mutually agreed upon by Landlord and Tenant, be restored to useful condition within eighteen (18) months after the Taking (such event, a "**Total Condemnation**"), then, in such event:

9.3.1 Termination. On the date of the Total Condemnation, this Lease shall automatically terminate; provided, however, that Tenant's obligations under any indemnification provisions of this Lease and Tenant's obligation to pay Rent and all other monetary obligations (whether payable to Landlord or a third party) accruing under this Lease prior to the date of termination shall survive such termination. If the date of such Total Condemnation is other than the first day of a month, the Base Rent for the month in which such Total Condemnation occurs shall be apportioned based on the date of the Total Condemnation

9.3.2 Award . Landlord shall be entitled to receive the entire award payable in connection with a Total Condemnation without deduction for any estate vested in Tenant by this Lease, and Tenant hereby expressly assigns to Landlord all of its right, title and interest in and to every such award and agrees that Tenant shall not be entitled to any such award or other payment for the value of Tenant's leasehold interest in this Lease; provided, however, that Tenant shall have the right to file any separate claim available to Tenant for any taking of Tenant's

Personalty, loss of goodwill, and for moving and relocation expenses (but only if such payment to Tenant does not reduce any award available to Landlord).

9.4 Partial Condemnation. In the event of a Taking which is not a Total Condemnation, neither party shall have the right to terminate this Lease and Landlord shall, using proceeds therefor from the condemning authority, restore the core and shell of the Building and structural elements of other improvements situated upon the Premises reasonably sufficient to make a functional unit of the remaining portion of the Premises, and Tenant shall proceed with restoration of the Tenant Improvements and LCW by Tenant to the extent possible to make a functional unit of the remaining portion of the Premises. In the event any partial taking materially affects Tenant's operations in the Building for the Permitted Use, such that the Premises no longer provides sufficient space for Tenant to carry out its business without material interference with the Permitted Use, then, commencing on the date on which Tenant's operations are materially affected, the Base Rent shall be abated in proportion to the square footage of the portion of the Building taken.

ARTICLE 10
MISCELLANEOUS

10.1 Notices. Any notice, consent, demand, or other communication or document required or permitted to be given under this Lease or pursuant to any law ("**Notice(s)**"), shall be (a) in writing (except as otherwise provided in this Lease), (b) addressed to the intended recipient at its address set forth in the Basic Lease Information (provided that each of Landlord and Tenant may change its addresses for the giving of notices by giving written notice thereof to the other party), (c) sent by fully prepaid registered or certified United States Mail return receipt requested, or by any nationally recognized overnight courier service furnishing a written record of attempted or actual delivery, and (d) deemed to have been delivered upon actually delivery or rejection of delivery. Any Notice may be given by an attorney on behalf of Landlord or Tenant.

10.2 Certain Representations

10.2.1 Neither of Tenant nor any wholly-owned subsidiary of Tenant is (i) in violation of any OFAC Law or Regulation, the U.S. Patriot Act or Anti-Corruption Legislation, (ii) is named by any Executive Order (including the September 23, 2001, Executive Order Blocking Property and Prohibiting Transactions With Persons Who Commit, Threaten to Commit, or Support Terrorism) or the United States Treasury Department as a terrorist, "Specially Designated National and Blocked Person," or (iii) (to the Tenant's knowledge) acting, directly or indirectly, on behalf of any such person. To Tenant's actual knowledge, no such person, group, entity or nation owns 20% or more Tenant's voting securities. To the Tenant's knowledge, the monies used in connection with this Lease and amounts committed with respect thereto, were not and are not derived from any activities that contravene any applicable OFAC Laws and Regulations, the U.S. Patriot Act, AML Legislation or Anti-Corruption Legislation, each as defined below.

10.2.2 As used herein, the term "**AML Legislation**" means United States anti-money laundering-related and anti-terrorism financing laws, regulations, and codes of practice applicable to the Tenant, its affiliates, and their operations from time to time, including, any regulations, guidelines or orders thereunder. As used herein, the term "**Anti-Corruption Legislation**" means U.S. Foreign Corrupt Practices Act and similar anticorruption and anti-bribery laws of the United States. As used herein, the term "**OFAC Laws and Regulations**" means (i) any lists, laws, rules, sanctions and regulations maintained by OFAC pursuant to any authorizing statute, Executive Order or regulation, including the Trading with the Enemy Act, 50 U.S.C. App. § 1 et seq., the International Emergency Economic Powers Act, 50 U.S.C. § 1701 et seq., the Iraq Sanctions Act, Pub. L. 101-513, Title V, §§ 586 to 586J, 104 Stat. 2047, the National Emergencies Act, 50 U.S.C. §§ 1601 et seq., the Antiterrorism and Effective Death Penalty Act of 1996, Pub. L. 104- 132, 110 Stat. 1214-1319, the United Nations Participation Act, 22 U.S.C. § 287c, the International Security and Development Cooperation Act, 22 U.S.C. § 2349aa-9, the Nuclear Proliferation Prevention Act of 1994, Pub. L. 103-236, 108 Stat. 507, the Foreign Narcotics Kingpin Designation Act, 21 U.S.C. §§ 1901 et seq., the Iran and Libya Sanctions Act of 1996, Pub. L. 104-172, 110 Stat. 1541, the Cuban Democracy Act, 22 U.S.C. §§ 6001 et seq., the Cuban Liberty and Democratic Solidarity Act, 22 U.S.C. §§ 6021-91, and the Foreign Operations, Export Financing and Related Programs Appropriations Act, 1997, Pub. L. 104-208, 110 Stat. 3009-172; (ii) all regulations, executive orders, or administrative orders of any kind issued under these statutes, including 31 C.F.R., Subtitle B, Chapter V; and (iii) any other applicable United States civil or criminal federal or state laws, regulations, or orders that (1) limit the use of and/or seek the forfeiture of proceeds from illegal transactions; (2) limit commercial transactions with designated countries or individuals believed to be terrorists, narcotics dealers or otherwise engaged in activities contrary to the interests of the United States; or (3) are designed to disrupt the flow of funds to terrorist organizations, as all of the foregoing laws may be amended from time to time.

10.3 Brokers. Each of Landlord and Tenant represents and warrants to the other that such party has not dealt with any broker or finder in connection with this Lease. Each party shall indemnify the other and hold it harmless from any cost, expense, or liability (including costs of suit and reasonable attorneys' fees) for any compensation, commission or fees claimed by any other real estate broker or agent in connection with this Lease or its negotiation by reason of any act or statement of the indemnifying party.

10.4 No Waivers. No provision of this Lease shall be deemed waived by either party unless expressly waived in a writing signed by the waiving party (and then only to the extent so expressly waived). No waiver shall be implied by delay or any other act or omission of either party. No waiver by either party of any provision of this Lease shall be deemed a waiver of such provision with respect to any subsequent matter relating to such provision, and Landlord's consent or approval respecting any action by Tenant shall not constitute a waiver of the requirement for obtaining Landlord's consent or approval respecting any subsequent action. No act or thing done by Landlord or its agents during the Term shall be deemed a termination of this Lease, an acceleration of the Termination Date, or an acceptance of the surrender of the Premises, and no agreement to terminate this Lease, accelerate the Termination Date, or accept a surrender of the Premises shall be valid, unless expressly provided in a writing signed by Landlord. Acceptance of the full or any partial payment of Rent shall not be deemed Landlord's waiver of any breach by Tenant of any provision of this Lease and Landlord's acceptance of a lesser amount than the Rent due under this Lease shall not be deemed Landlord's waiver of Landlord's right to receive the full amount of Rent due, nor shall any endorsement or statement on any check or payment or any letter accompanying such check or payment be deemed an accord and satisfaction, and Landlord may accept such partial payment without prejudice to Landlord's right to recover the full amount of Rent due. Tenant acknowledges that this Section 10.4 imparts actual notice to Tenant that Landlord's acceptance of partial payment of Rent does not constitute a waiver of any of Landlord's rights, including any right Landlord may have to recover possession of the Premises. Forbearance by Landlord in enforcing one or more of the remedies provided in this Lease upon an Event of Default shall not be deemed a waiver of such Event of Default or of Landlord's right to enforce any such remedies with respect to such Event of Default or any subsequent Event of Default. Landlord's acceptance of any Rent or of the performance of any other provision of this Lease from any person other than Tenant, including any Transferee, shall not be deemed a waiver of Landlord's right to approve any Transfer in accordance with Article 5.

10.5 Future Development. Provided the Tenant is Ionis Pharmaceuticals, Inc., or an affiliate, and Tenant is operating for the Permitted Use, in no event shall Landlord take any action or permit any actions to be taken that may or will increase or decrease, modify, change or alter the zoning or entitlements of the Premises, alter the Building, change the site amenities, or add additional improvements without the express written consent of Tenant. Notwithstanding the foregoing, subject to the terms of this Section 10.5, Landlord reserves all rights as may be necessary or desirable to construct additional improvements serving the Premises, the Companion Premises, or both, in connection with the construction of the improvements under the Companion Lease, including, without limitation, pedestrian walkways, installation of utilities and utility connections, structured parking, a pedestrian bridge, and site improvements at the Premises, and to modify the Building in connection with any such additional development, all as required by the Companion Lease and consistent with the plans and specifications for the construction of the Companion Premises ("**Future Development**"). In connection with any such Future Development, facilities at the Premises may be eliminated, altered, or relocated and may also be utilized to serve the Companion Premises. The rights set forth above shall include rights to use portions of the Premises for the purpose of temporary construction staging and related activities and to implement valet parking for reserved and unreserved parking spaces for the purpose of facilitating construction during such activities.

10.5.1 Landlord and its representatives, contractors, agents, employees and licensees shall have the right during any construction period to enter the Premises to undertake such work; to shore up the foundations, walls, and other improvements at the Premises; to erect scaffolding and protective barricades around the Premises; and to do any other act necessary for the safety of the improvements at the Premises or the expeditious completion of such construction. Landlord shall use reasonable efforts not to interfere with the conduct of Tenant's business and to minimize the extent and duration of any inconvenience, annoyance or disturbance to Tenant resulting from any work pursuant to this Section in or about the Premises, consistent with accepted construction practice, and so long as Landlord uses such reasonable efforts Landlord shall not be liable to Tenant for any compensation or reduction of Rent by reason of inconvenience or annoyance or for loss of business resulting from any act by Landlord pursuant to this Section.

10.5.2 Tenant agrees to enter into any instruments reasonably requested by Landlord in connection with the Future Improvements, and for the continued maintenance of such Future Improvements, so long as the same do not materially decrease the rights or materially and adversely increase the obligations of Tenant under this Lease, including reciprocal easement agreements, declarations of covenants, and other agreements to facilitate use of the improvements between the Premises and Companion Premises. Tenant agrees not to take any action to oppose any application by Landlord for any permits, consents or approvals from any governmental authorities for any redevelopment or additional development of all or any part of the Companion Premises, and will use all commercially reasonable efforts to prevent any of Tenant's subtenants or assigns, and Tenant's and their respective officers, directors, employees, agents, contractors and consultants from doing so. For purposes hereof, action to oppose any such application shall include, without limitation, communications with any governmental authorities requesting that any such application be limited or altered. Also for purposes hereof, commercially reasonable efforts shall include, without limitation, commercially reasonable efforts, upon receiving notice of any such action to oppose any application on the part of any Tenant Parties, to obtain injunctive relief, and, in the case of a subtenant, exercising remedies against the subtenant under its sublease.

10.6 Other Provisions.

10.6.1 Covenant of Quiet Enjoyment. Landlord covenants that Tenant, while no Event of Default has occurred and be continuing, shall peaceably and quietly have, hold, and enjoy the Premises for the Term without hindrance from Landlord, but not otherwise, subject to all matters of record and to the terms and provisions of this Lease.

10.6.2 Survival. All obligations of Tenant under this Lease not fully performed as of the Termination Date shall survive the Termination Date.

10.6.3 Entire Agreement. This Lease, together with the Exhibits, contains all of the agreements of Landlord and Tenant in respect of this Lease and supersedes any previous negotiations. There have been no representations made by Landlord or any of Landlord's representatives, or understandings made between Landlord and Tenant, other than those set forth in this Lease and the Exhibits. This Lease may not be modified except by a written instrument duly executed by the party to be bound. Landlord and Tenant each represent to the other, that is has the individuals executing this Lease have been properly authorized by proper action of the Landlord and Tenant, as the case may be.

10.6.4 Execution in Counterparts. This Lease may be executed in counterparts, each of which shall be deemed an original and all of which together shall constitute one and the same instrument.

10.6.5 Recording. Tenant shall not record this Lease, but may record a short form memorandum of this Lease in the form attached hereto as Exhibit D.

10.6.6 Non-Discrimination. Tenant shall not (and Tenant shall not permit any person claiming through or under Tenant to) discriminate against or segregate any person or group of persons on account of race, color, creed, sex, religion, marital status, ancestry, or national origin, whether in the use, occupancy, subleasing, transferring, or enjoyment of the Premises, or otherwise.

10.6.7 Attorneys' Fees. In any action or proceeding that Landlord or Tenant initiates against the other party declaratory or otherwise, arising out of this Lease, the unsuccessful party in such action or proceeding shall reimburse the prevailing party for its costs, including reasonable attorneys' fees (at trial and appellate levels).

10.6.8 Waiver of Consequential Damages. Except as set forth in Section 1.3 and Section 3.3, neither Landlord nor Tenant shall be liable to the other for any form of special, indirect, consequential, or punitive damages.

10.6.9 Tenant Information. Upon Landlord's request from time to time, Tenant shall provide to Landlord the financial statements for Tenant for its most recent fiscal year and fiscal quarter. Financial statements for each fiscal year shall be prepared and certified by a certified public accountant; financial statements for each quarter shall be prepared and certified by Tenant's chief financial officer. In addition, if so requested, and provided that Landlord may not require such information more than once in any calendar year except where Landlord has reasonable grounds for concern, details of the financial and credit standing and details of the corporate organization of Tenant and any Indemnitor, including copies of financial statements for the last three (3) fiscal years of Tenant. If requested by Tenant, such financial statements shall be furnished pursuant to a confidentiality agreement in a form reasonably provided by Landlord for such purpose. The provisions of this Section 10.6.9 shall not apply to Tenant if it is a Public Company and its financial statements are publicly available.

10.6.10 REIT Provisions. Tenant and Landlord intend that all amounts payable by Tenant to Landlord shall qualify as "rents from real property," and will otherwise not constitute "unrelated business taxable income" or "impermissible tenant services income," all within the meaning of Section 856(d) of the Internal Revenue Code of 1986, as amended (the "**Code**") and the U.S. Department of Treasury Regulations promulgated thereunder (the "**Regulations**"). In the event that Landlord determines that there is any risk that any amount payable under this Lease may not qualify as "rents from real property" or will otherwise constitute impermissible tenant services income within the meaning of Section 856(d) of the Code and the Regulations, Tenant agrees to (a) cooperate with Landlord by entering into such amendment or amendments as Landlord deems necessary to qualify all amounts payable under this Lease as "rents from real property" and (b) permit (and, upon request, to acknowledge in writing) an assignment of the obligation to provide certain services under the Lease, and, upon request, to enter into direct agreements with the parties furnishing such services (which shall include but not be limited to a taxable REIT subsidiary of Landlord). Notwithstanding the foregoing, Tenant shall not be required to take any action pursuant to the preceding sentence (including acknowledging in writing an assignment of services pursuant thereto) if such action would result in (A) Tenant's incurring more than de minimis additional liability under this Lease or (B) more than a de minimis negative change in the quality or level of Building operations or services rendered to Tenant under this Lease. For the avoidance of doubt, (i) if Tenant does not acknowledge in writing an assignment as described in clause (b) above (it being agreed that Tenant shall not unreasonably withhold, condition or delay such acknowledgment so long as the criteria in clauses (A) and (B), above, are satisfied), then Landlord shall not be released from liability under this Lease with respect to the services so assigned; and (ii) nothing in this Section 10.6.10 shall limit or otherwise affect Landlord's ability to assign its entire interest in this Lease to any party as part of a conveyance of Landlord's ownership interest in the Building.

10.7 Interpretation.

10.7.1 Captions. The captions in this Lease are for convenience of reference and shall not define, increase, limit, or describe the scope or intent of any provision of this Lease.

10.7.2 Landlord and Tenant. The terms "Tenant" and "Landlord", and any pronoun used in place thereof, shall indicate and include each of the parties' and respective successors, executors, administrators, and permitted assigns, according to the context, provided that, for the purposes of any provisions indemnifying or waiving claims against, Landlord, the term "Landlord" shall also include Landlord's present and future investment manager, and property management company, and all of their trustees, directors, officers, partners, beneficiaries, principals, members, managers, investors, stockholders, employees, Affiliates, agents, representatives, contractors (and subcontractors of any tier), successors and assigns.

10.7.3 Non-Exclusivity. Whenever the words "including", "include", or "includes" are used in this Lease, they shall be interpreted in a non-exclusive manner as though the words "without limitation" immediately followed the same. Any reference to "any part" or "any portion of" the Premises or any other property shall be construed to refer to all or any part of the same.

10.7.4 Covenants Independent. This Lease shall be construed as though the covenants herein between Landlord and Tenant are independent.

10.7.5 Joint and Several Liability. In any case where either Landlord or Tenant consists of more than one person, the obligations of such party under this Lease shall be joint and several.

10.7.6 Time of the Essence. Time is of the essence of this Lease and all of its provisions.

10.7.7 Governing Law. This Lease shall in all respects be governed by the laws of the State of California without giving effect to the principles of conflicts of law thereof or of any other jurisdiction that would result in the application of the Applicable Laws of any other jurisdiction. Tenant's obligation to pay Rent shall not be discharged or otherwise affected by any Applicable Law or regulation now or hereafter applicable to the Premises, or any other restriction on Tenant's use, or (except as expressly provided in this Lease) any Casualty or Taking, or any failure by Landlord to perform any covenant contained herein, or any other occurrence; and no termination or abatement remedy that is not expressly provided for in this Lease for any breach or failure by Landlord to perform any obligation under this Lease shall be implied or applicable as a matter of Applicable Law.

10.7.8 Successors and Assigns. Subject to the provisions of Article 5, the provisions of this Lease shall be binding upon and inure to the benefit of the heirs, successors, executors, administrators, and assigns of Landlord and Tenant.

10.7.9 Submission. The submission of this Lease to Tenant or a summary of some or all of its provisions for examination does not constitute a reservation of or option for the Premises or an offer to lease, and no legal obligations shall arise with respect to the Premises or other matters herein unless and until such time as this Lease is executed and delivered by Landlord and Tenant and approved by the holder of any mortgage on the Building having the right to approve this Lease.

10.8 Tenant's Signage. Tenant shall have the right to install such signage at or upon the Premises as permitted by Applicable Laws. Tenant, at its sole expense, shall maintain Tenant's Signage in good condition and repair during the Term. Should Tenant's Signage require maintenance or repairs as determined in Landlord's reasonable judgment, Landlord shall have the right to provide notice thereof to Tenant and Tenant shall cause such repairs and/or maintenance to be performed within thirty (30) days after receipt of such notice from Landlord at Tenant's sole cost and expense. Should Tenant fail to perform such maintenance and repairs within the period described in the immediately preceding sentence, then, in addition to all of Landlord's other rights and remedies, Landlord may, but need not, perform the required maintenance and repairs, and Tenant shall pay Landlord the cost thereof, plus a fee for Landlord's oversight and coordination of such work equal to five percent (5%) of its cost, within thirty (30) days after receipt of Landlord's request for payment, together with reasonable, supporting backup documentation. Landlord shall have the right to maintain one or more signs at the Premises in a prominent location near the entrance to the Building identifying the property manager and the identity of Landlord or its direct or indirect ownership group in a manner similar to that shown on Exhibit G attached, subject to Tenant's approval of the size and location of such signage, such approval not to be unreasonably withheld, conditioned or delayed.

10.9 Choice of Law. This Lease shall be governed by the Applicable Laws of the State of California.

10.10 CASp Inspection. For purposes of Section 1938(a) of the California Civil Code, Landlord hereby discloses to Tenant, and Tenant hereby acknowledges, that neither the Building nor any portion of the Premises has undergone inspection by a Certified Access Specialist (CASp) (defined by California Civil Code Section 55.52). Pursuant to California Civil Code Section 1938, Tenant is hereby notified as follows: "A Certified Access Specialist (CASp) can inspect the subject premises and determine whether the subject premises comply with all of the applicable construction-related accessibility standards under state law. Although state law does not require a CASp inspection of the subject premises, the commercial property owner or lessor may not prohibit the lessee or tenant from obtaining a CASp inspection of the subject premises for the occupancy of the lessee or tenant, if requested by lessee or tenant. The parties shall mutually agree on the arrangements for the time and manner of any CASp inspection, the payment of the fee for the CASp inspection and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the premises." If Tenant requests to perform a CASp inspection of the Premises, Tenant shall, at its cost, retain a CASp approved by Landlord to perform the inspection of the Premises at a time agreed upon by the parties. Tenant shall provide Landlord with a copy of any report or certificate issued by the CASp (the "**CASp Report**"). Landlord and Tenant agree that any modifications necessary to correct violations of construction related accessibility standards identified in the CASp Report shall be the responsibility of Tenant. Tenant agrees to keep the information in the CASp Report confidential except as necessary for the Tenant to complete such modifications.

10.11 Landlord Access. Landlord, its affiliates, and their respective contractors and agents, subject to the terms of this Section 10.11, may, (a) at any and all reasonable times during normal business hours (or during non-business hours, if Landlord so requests and Tenant consents), and upon at least two (2) business days' prior notice (which may be oral or by email to the office manager or other Tenant-designated individual at the Premises; but provided that no time restrictions shall apply or advance notice be required if a bona fide emergency with an immediate threat to property damage or personal injury necessitates immediate entry and any oral notice will be followed immediately by email notice as provided above prior to entry), enter the Premises to (i) inspect the same and to determine whether Tenant is in compliance with its obligations hereunder, (ii) supply any service Landlord is required to provide hereunder, (iii) alter, improve or repair any portion of the premises under the Companion Lease for which access to or through the Premises is reasonably necessary, (iv) post notices of non-responsibility, (v) show the Premises to current and prospective investors, lenders and purchasers, and (vi) show the Premises, other than the Secure Access Areas, during the final eighteen (18) months of the Term (provided that Tenant has not timely exercised an Extension Option to extend the Term pursuant to Section 1.4) to prospective tenants, and (b) notwithstanding the foregoing, at any and all reasonable times during business and non-business hours and upon at least two (2) business days' prior notice enter the Premises for the purposes of performing any repairs or maintenance that Landlord is obligated or entitled to perform pursuant to this Lease (provided that no time restrictions shall apply if a bona fide emergency with an immediate threat to property damage or personal injury necessitates immediate entry); provided, however, that Landlord shall comply with Tenant's reasonable safety procedures and protocols with respect to the Premises, and with respect to portions of the Premises (if any) that are reasonably designated in writing by Tenant to Landlord as controlled or having restricted access (the "**Secure Access Areas**"), shall comply with Tenant's reasonable additional security and safety procedures and protocols related to such portions of the Premises including only entering such designated Secure Access Areas when accompanied by a Tenant representative (provided further, that Tenant shall provide a Tenant representative to accompany Landlord upon written request from Landlord at least two (2) business days' in advance). In no event shall Tenant's Base Rent abate as a result of Landlord's activities pursuant to this Section; provided, however, that all such activities shall be conducted in such a manner so as to cause as little interference to Tenant as is reasonably possible. Landlord shall at all times retain keys, key cards and access codes with which to unlock all of the doors in the Premises. Landlord acknowledges that the standard operating procedures set forth on Exhibit J shall apply to the issuance to Landlord of any key cards, electronic keypad codes, or door keys to any Secure Access Areas for any unaccompanied access too the Premises by Landlord, provided, however, that Tenant shall identify a single designee to act as Landlord's point of contact to administer the requirements of Tenant's standard operating procedures on behalf of Landlord and that in no event shall any such requirements prohibit Landlord's entry into Secure Access Areas (i) in the event of a bona fide emergency with an immediate threat to property damage or personal injury that necessitates immediate entry or (ii) when accompanied by a representative of Tenant. If an emergency necessitates immediate access to the Premises, Landlord may use whatever force is necessary to enter the Premises, and any such entry to the Premises shall not constitute a forcible or unlawful entry to the Premises, a detainer of the Premises, an eviction of Tenant from the Premises or any portion thereof, or a violation of the provisions of this Section 10.11. Notwithstanding anything herein to the contrary, in the event Tenant notifies Landlord within one (1) business day (which may be oral or by email to the Landlord-designated individual) following Landlord's request for access that the proposed day and/or time for entry will cause a disruption to a planned event, meeting or other programming for Tenant, Landlord and Tenant shall cooperate with one another to identify a better date and/or time Landlord's entry of the Premises.

ARTICLE 11
TENANT'S RIGHT OF FIRST OFFER

11.1 Right of First Offer.

11.1.1 Notwithstanding anything contained in this Lease to the contrary, provided that (i) no Event of Default by Tenant has occurred under this Lease, and (ii) the Tenant is Ionis Pharmaceuticals, Inc., or its affiliate, if Landlord intends to offer the Premises (or any portion thereof) for sale to an unaffiliated third party, Landlord shall promptly notify Tenant of the same in writing (the "**Offer Notice**") and indicate the terms and conditions upon which Landlord is willing to accept for the sale of the Premises to a third party. Tenant may elect to purchase the Premises (or portion thereof) on the terms and conditions set forth in the Offer Notice by notifying Landlord in writing (the "**Election Notice**") of its election no later than fifteen (15) days after the Offer Notice, which notice shall be accompanied by the Option Deposit (defined herein), and the sale of the Premises shall be consummated pursuant to the terms hereof on a date (the "**Closing Date**") within sixty (60) days after the Election Notice, such date to be mutually agreed upon by Landlord or Tenant. In the event of any of the following: (x) Tenant fails to deliver the Election Notice or the Option Deposit to Landlord on or before the expiration of the 15-day period set forth above, (y) Tenant fails to close on its acquisition of the Premises on or before the Closing Date, or (z) Landlord provides an Offer Notice to Tenant and Tenant does not exercise its right to purchase the Premises, then in each case Tenant shall be deemed to have waived its right to purchase the Premises and thereafter Tenant's rights under this Article 11 shall be null and void and of no further force or effect. The term "**Option Deposit**" shall mean the amount of cash deposit required in the Offer Notice or, if no cash deposit is specified in the Offer Notice, a sum equal to five percent (5%) of the purchase price for the Premises set forth in the Offer Notice.

11.1.2 If the Premises is not sold to Tenant pursuant to Section 11.1.1 above, Landlord shall have the right to direct the marketing of the Premises (including the unilateral right to select any broker to be utilized), and to take all actions in furtherance thereof, including, without limitation, the right and authority to execute, such agreements, documents, instruments and applications, including a purchase and sale agreement and a deed, assignment of leases, bills of sale and other conveyance documents conveying the Premises (collectively, "**Sale Documents**") as Landlord, may reasonably deem necessary or desirable in order consummate such sale, and, subject to Section 11.1.1 above and Section 11.2 below, Landlord shall be authorized to accept an offer for the sale of the Premises. If Landlord modifies the terms of its offer such that the purchase price is less than ninety-five percent (95%) of the consideration provided in the Offer Notice, then the proposed transaction shall again be subject to Tenant's rights under this Article 11, and Landlord shall deliver an amended Offer Notice to Tenant.

11.1.3 Tenant shall, at no material out-of-pocket cost to Tenant, reasonably cooperate with Landlord's efforts to sell the Premises, including by providing information with respect to the Premises, and by allowing and facilitating physical access to the Premises to prospective purchasers and their lenders and consultants, but such cooperation and execution by the Tenant shall not be a condition to the effectiveness of any actions taken by Landlord with respect to such sale or to the effectiveness of Sale Documents.

11.2 Tenant's Competitors. Provided that (i) no Event of Default by Tenant has occurred under this Lease, and (ii) the Tenant is Ionis Pharmaceuticals, Inc., or an affiliate, and such Tenant remains in possession of the Premises and operating for the Permitted Use, Landlord shall not sell the Premises (or any portion thereof, or all or substantially all of Landlord's interest therein) or enter into an agreement to that would transfer Landlord's interest in the Premises to a Competitor during the Term; provided, however, this Section 11.2 shall not prohibit Landlord from entering into an agreement to sell or transfer the Premises to a Competitor if the effective date of the transfer would occur after the expiration of the Term. As used herein, "**Competitor**" or "**Competitors**" means the companies expressly listed as competitors in Tenant's most recent publicly filed Annual Report (10-K); provided, however, (1) such companies shall be directly engaged in the development, manufacturing, or commercializing a medicine or other life sciences product, and "Competitor" shall not mean any affiliates, investors, parents, or other stake-holders of such companies, and (2) there shall not be more than twenty (20) Competitors at any one time. If Tenant's most recent publicly filed Annual Report (10-K) includes more than twenty (20) companies that would otherwise be deemed Competitors, only those companies that were previously listed in Tenant's Annual Report (10-K) shall be deemed a Competitor unless Tenant provides a written notice to Landlord specifying which companies listed in Tenant's most recent Annual Report (10-K) shall be included in the list of twenty (20) Competitors for the purposes of this Lease.

11.3 Transfers. Notwithstanding anything to the contrary herein, Tenant's rights under this Article 11 shall not apply to any transaction that meets at least one of the following criteria:

11.3.1 any sale/leaseback transaction made in connection with a bona fide financing, provided that the seller/lessee under any such transaction shall be bound by the provisions of this Article 11 at such time, if any, as such seller/lessee reacquires title to the Premises;

11.3.2 any sale or transfer of the Premises to a partnership, corporation, limited liability company, trust or other entity that is under control by, common control with, or controls Landlord or any direct or indirect owner of Landlord, but any such transferee shall hold title subject to Tenant's rights under this Article 11;

11.3.3 any transfer in the nature of a financing transaction with a financial institution that is made for a bona fide business purpose (i.e., other than in order to allow a transfer of the Premises in avoidance of Tenant's rights under this Article 11), including without limitation the granting of, foreclosure under, or giving of a deed-in-lieu of foreclosure under, a mortgage or the granting or exercise of any pledge of ownership interests; provided that, following any foreclosure of the Premises, deed in lieu thereof, or similar acquisition of title by a mortgagee, lender, or their affiliates, following the first sale of the Premises by such mortgagee, lender or their affiliates, the subsequent Landlord shall be bound by Tenant's rights under this Article 11;

11.3.4 any issuance or transfer of a direct or indirect interest in Landlord that represents a transfer of less than 80% of such interests (so long as such transfer does not also include the ability to control the day-to-day operations of Landlord); provided that any transferee of direct interests in Landlord otherwise described in this Section 11.3.4 is not a Competitor;

11.3.5 any issuance or transfer of a direct or indirect interest in Landlord on a nationally recognized stock exchange; and

11.3.6 any bona fide portfolio transaction that includes at least two other real estate assets (excluding the Premises and, if the Companion Lease is in effect, the Companion Premises) that in the aggregate have rentable space at least equal to 416,000 square feet of rentable space.

11.4 Termination. Upon (x) any sale of the Premises, (y) any portfolio transaction sale that includes the Premises, or (z) any foreclosure of a Mortgage on the Premises or conveyance by deed-in-lieu of foreclosure, in each case to a third-party person or entity in accordance with the terms of this Article 11, Tenant's right of first offer to purchase the Premises under this Article 11 shall forever terminate.

11.5 Confidentiality. Any Offer Notice and information in connection therewith, and any information regarding a sale of the Premises, provided to Tenant by Landlord pursuant to this Article 11 shall be held confidential by Tenant and not disclosed to any third party except as required by law or in connection with any dispute between Landlord and Tenant regarding this Article 11 and for disclosures to Tenant's legal advisors and third-party consultants to the extent such legal advisors and consultants are reasonably required for Tenant to evaluate such information and, in each case, provided that such legal advisors and consultants are made subject to the provisions of this paragraph or are otherwise bound by provisional obligations of confidentiality. Any such information shall be returned by Tenant to Landlord if Tenant's rights under this Article 11 terminate in accordance with the terms hereof. Nothing in this Section 11.5 shall prevent Tenant from making disclosures required by applicable public company disclosure laws, provided, however, such disclosures shall include no more information than what is minimally necessary to satisfy the legal requirement, and provided further that Landlord shall have the right to reasonably approve any disclosure that exceeds what is minimally necessary to satisfy the legal requirement, and provided further that Landlord shall have the right to review any disclosure prior to the filing of the same for purposes of confirming compliance with the terms of this sentence, to the extent that such review is permitted pursuant to Applicable Law.

ARTICLE 12
LIMITATION OF LIABILITY

12.1 Landlord's Liability. Tenant agrees from time to time to look only to Landlord's interest in the Premises for satisfaction of any claim against Landlord hereunder or under any other instrument related to the Lease (including any separate agreements among the parties and any notices or certificates delivered by Landlord) and not to any other property or assets of Landlord. If Landlord from time to time transfers its interest in the Premises, then from and after each such transfer Tenant shall look solely to the interests in the Premises of Landlord's transferees for the performance of all of the obligations of Landlord hereunder (or under any related instrument). The obligations of Landlord shall not be binding on any direct or indirect partners (or members, trustees, or beneficiaries) of Landlord or of any successor, individually, but only upon Landlord's or such successor's interest described above. Further, if Landlord is, or one of the parties comprising Landlord is, or the Lease is assigned to, a real estate investment trust ("**REIT**"), the parties acknowledge and agree that the obligations of the REIT hereunder and under all documents delivered pursuant hereto (and all documents to which the Lease may be pursuant) or which give effect to, or amend or supplement, the terms of the Lease are not personally binding upon any trustee thereof, any registered or beneficial holder of units (a "**Unitholder**") or any annuitant under a plan of which a Unitholder acts as a trustee or carrier, or any officers, employees or agents of the REIT and resort shall not be had to, nor shall recourse or satisfaction be sought from, any of the foregoing or the private property of any of the foregoing.

12.2 Assignment of Rents.

12.2.1 With reference to any assignment by Landlord of Landlord's interest in this Lease, or the rents payable hereunder, conditional in nature or otherwise, which assignment is made to the holder of a mortgage on property that includes the Premises, Tenant agrees that the execution thereof by Landlord, and the acceptance thereof by the holder of such mortgage shall never be treated as an assumption by such holder of any of the obligations of Landlord hereunder unless such holder shall, by notice sent to Tenant, specifically otherwise elect and, except as aforesaid, such holder shall be treated as having assumed Landlord's obligations hereunder only upon foreclosure of such holder's mortgage and the taking of possession of the Premises.

12.2.2 In no event shall the acquisition of Landlord's interest in the Premises by a purchaser that, simultaneously therewith, leases Landlord's entire interest in the Premises back to the seller thereof be treated as an assumption by operation of Law or otherwise, of Landlord's obligations hereunder, but Tenant shall look solely to such seller-lessee, and its successors from time to time in title, for performance of Landlord's obligations hereunder. In any such event, this Lease shall be subject and subordinate to the lease to such purchaser. For all purposes, such seller-lessee, and its successors in title, shall be the Landlord hereunder unless and until Landlord's position shall have been assumed by such purchaser-lessor.

12.2.3 Except as provided in Section 12.2.2, in the event of any transfer of title to the Premises by Landlord, the transferring Landlord shall thereafter be entirely freed and relieved from the performance and observance of all covenants and obligations hereunder, and Tenant shall only look to any subsequent party becoming Landlord hereunder the same. Tenant hereby agrees to enter into such agreements or instruments as may, from time to time, be requested in confirmation of the foregoing.

(SIGNATURES APPEAR ON NEXT PAGE)

IN WITNESS WHEREOF, the parties hereto have duly executed this Lease on the day and year first above written.

LANDLORD:

LOTS 21 & 22 OWNER (DE) LLC, a Delaware limited liability company

By: /s/ Tycho Suter
Name: Tycho Suter
Title: Vice President

By: /s/ Kristen Binck
Name: Kristen Binck
Title: Vice President

TENANT:

IONIS PHARMACEUTICALS, INC., a Delaware corporation

By: /s/ Elizabeth L. Hougen
Name: Elizabeth L. Hougen
Title: CFO

SCHEDULE 1

EXAMPLE SHOWING CALCULATION OF BASE RENT

Cost Item	Ref	Estimate	$PSF
Land Acquisition		33,000,000	200
Closing Costs Allocation		495,000	3
Soft Costs		12,955,502	79
Hard Costs		87,782,086	533
Landlord Tenant Improvement Allowance		41,208,250	250
Development Fee[(1)]		3,434,210	21
Operating Shortfall		2,352,572	14
Financing Costs		17,812,408	108
Total Budget	**(A)**	**199,040,029**	**1,208**
Yield-on-Cost	**(B)**	6.35%	
Annual Rent at Commencement	**(A * B)**	**12,639,042**	**76.71**
Monthly Rent at Commencement	**(A * B) / 12**	**1,053,253**	**6.39**

(1) Calculated based on sum of (a) 3.0% of Hard and Soft Costs, and (b) 1.0% of Tenant Improvement Allowance

EXHIBIT A

LEGAL DESCRIPTION OF THE PREMISES

Real property in the City of CARLSBAD, County of San Diego, State of California, described as follows:

LOTS 21 AND 22 OF CARLSBAD TRACT NO. 97-13-03, CARLSBAD OAKS NORTH PHASE 3, IN THE CITY OF CARLSBAD, COUNTY OF SAN DIEGO, STATE OF CALIFORNIA, ACCORDING TO MAP THEREOF NO. 16145, FILED IN THE OFFICE OF THE COUNTY RECORDER OF SAN DIEGO COUNTY, OCTOBER 13, 2016 AS DOCUMENT 2016-7000438 OF OFFICIAL RECORDS.

APN: 209-120-23-00 (Affects: Lot 21) and 209-120-24-00 (Affects: Lot 22)

EXHIBIT B

WORK LETTER

This Work Letter (this "**Work Letter**") is made and entered into as of the date of the Lease to which it is attached ("**Effective Date**") and is attached to and made a part of that certain Lease by and by and between **LOTS 21 & 22 OWNER (DE) LLC**, a Delaware limited liability company as landlord ("**Landlord**") and **IONIS GAZELLE, LLC**, a Delaware limited liability company as tenant ("**Tenant**") for the development of approximately 8.37 acres (the "**Land**") known as Lots 21 and 22 with approximately 164,757 gross square feet, which shall be comprised of a three (3) level lab and office building (the "**Building**"), a three (3) (inclusive of the rooftop deck) level parking structure ("**Parking Structure**") and a pedestrian bridge connecting the Building to an adjacent building leased by Tenant from an affiliate of Landlord (the "**Bridge**"). Capitalized terms not otherwise defined in this Work Letter shall have the meanings set forth in the Lease. In the event of any conflict between the terms hereof and the terms of the Lease, the terms hereof shall prevail for the purposes of design and construction of the Improvements (hereinafter defined).

1. Permits and Approvals. Prior to the Effective Date, Tenant has applied for and obtained (or Landlord has obtained by use of its self-help rights under the PSA, as defined below) the discretionary zoning and planning approvals and approvals by the Architecture Committee under the covenants, conditions and restrictions of the Carlsbad Oaks North Business Park Owners Association necessary to obtain a building permit for Landlord's Construction Work by right (as identified on Schedule 1, attached, the "**Entitlements**"), and, prior to commencement of construction, has obtained or will obtain the other ministerial permits necessary for the development and construction of the Landlord's Construction Work (as defined below) (as identified on Schedule 1, attached, the "**Ministerial Approvals**"; collectively, together with the Entitlements, the "**Permits and Approvals**"), which Permits and Approvals Tenant acknowledges and agrees are all of the permits, licenses, and approvals necessary for the commencement of construction of all of the Landlord's Construction Work, provided, however, that following the Effective Date, (x) to the extent Tenant has not yet prepared and/or submitted applications for Ministerial Permits in accordance with the Development Schedule, Landlord (or General Contractor) shall be responsible for preparing and/or submitting such Ministerial Permits and (y) to the extent that Tenant has not yet obtained the building permit referenced on Schedule 1, Landlord shall assume the responsibility for obtaining the same (and the parties shall cooperate to the extent reasonably required for Landlord to do so). The parties acknowledge that certain Permits and Approvals are necessary solely for commencing a particular aspect of the Landlord's Construction Work (e.g., the grading permit and lot line adjustment between lots 21 & 22). The parties further acknowledge that, following the commencement of vertical construction of the Building and Parking Structure, certain ministerial permits will be obtained by Landlord (or the General Contractor) in the ordinary course as normally obtained in the course of construction.

Tenant shall use diligent, best efforts to pursue the Entitlements on or before the Outside Satisfaction Date as defined in (and subject to extensions expressly permitted under) that certain Purchase and Sale Agreement dated October 20, 2022, by and between Tenant and an affiliate of Landlord (as it may have been amended, the "**PSA**"). Tenant shall provide Landlord with updates regarding the status of the Permits and Approvals from time to time (and in any event no less often than once per month) and otherwise upon the written request of Landlord. Tenant shall not amend or modify the Entitlements, or submit any new applications for Entitlements, without the prior written consent of Landlord, and, in any event, the final Entitlements shall be subject to the final written approval of Landlord, in each case such consent and approval not to be unreasonably withheld, conditioned, or delayed, provided that it shall be reasonable for Landlord to disapprove of the Entitlements, amendments to them, or applications for any new Entitlements for Landlord's Construction Work, if they (a) contain conditions (i) the cost of which are not (A) includable within the Construction Costs (unless Tenant agrees in writing to pay such costs directly and such Entitlements, amendments, or applications for new Entitlements otherwise comply with the provisions of clause (ii)) or (B) otherwise the responsibility of Tenant pursuant to the terms of the Lease (unless Tenant agrees in writing to perform the same and such Entitlements, amendments, or applications for new Entitlements otherwise comply with the provisions of clause (ii)), or (ii) that are not customary for similar first class lab and office projects in the applicable leasing market (including without limitation with respect to costs or obligations resulting from the same that are recurring beyond the termination or earlier expiration of the Term), or (b) are inconsistent with the Approved Concept Plans (as defined below).

The Permits and Approvals shall provide for (a), at a minimum, as-of-right use of the Premises for the Permitted Use, (b) improvements with a lab to office ratio of no less than 35% to 65%, the calculation of which shall be made in good faith by Landlord and Tenant in consultation with the Architect (with any dispute being resolved pursuant to Article 13, below), (c) at least 164,757 square feet of gross floor area (as measured by the applicable zoning codes and ordinances), (d) no fewer than 426 parking stalls, floor-to-floor heights of at least 16 feet, (e) a floor load of at least 125 pounds per square foot live load, 15 pounds per square foot dead load and, in any event, on areas of the roof within areas of mechanical screening or otherwise intended for mechanical equipment installations, at least 150 pounds per square foot, (f) vertical MEP infrastructure sufficient to support a lab to office ratio of at least 50% to 50% (incorporating the minimum standards set forth on Schedule 8, attached), (g) building construction type of II-B, (h) MEP capacities consistent with Schedule 8 and MEP infrastructure consistent with the allocation of responsibility attached as part of Schedule 2, and (j) otherwise be consistent with first class life sciences use, generally (the "**Fundamental Requirements**"). Landlord shall approve or provide detailed objections to the Entitlements within ten (10) business days of its receipt of the same. If Landlord fails to respond within such ten (10) business day period, Tenant may provide a written reminder notice to Landlord. Landlord's failure to respond to such reminder notice within three (3) business days after delivery of such notice shall be deemed to be Landlord's approval of the Entitlements. Prior to making any material submission to a permitting or other governmental authority, committee, association, or other regulatory committee, agency or governing body having jurisdiction over the over the Landlord's Construction Work (collectively, "**governmental authorities**"), Tenant shall give the Landlord the opportunity to review and comment on the same, and Tenant shall give Landlord reasonable prior notice of any material meetings, hearings, or conversations with governmental authorities related the Permits and Approvals and give Landlord the reasonable opportunity to participate in the same. Furthermore, to the extent Tenant is responsible for Ministerial Approvals pursuant to this Section 1, Tenant shall submit such applications for Ministerial Approvals to Landlord for its review and comment prior to Tenant submitting the same to the applicable governmental authorities, but such review by Landlord is solely for the purpose of confirming that such applications are consistent with the terms and conditions of this Work Letter. Tenant shall cooperate with Landlord as reasonably required to facilitate obtaining the Ministerial Approvals in an orderly and timely manner to the extent the same have not been obtained by Tenant prior to the Effective Date, including by providing Landlord with such information as is necessary with respect to prior and pending applications.

If Tenant is unable to obtain the grading permit listed on Schedule 1 by August 21, 2023 subject to extension due to Landlord Fault (the "**Grading Permit Deadline**"), then the Delivery Date shall be deemed to occur one-half day earlier for each day following the Grading Permit Deadline until the grading permit has been received (which half-day shall be increased to one day per day of delay in issuance of the grading permit following the Grading Permit Deadline if any failure to obtain the grading permit results in whole or part from the acts or omissions of Tenant or its agents, employees, or representatives, referred to herein as "**Tenant Fault**"). Landlord agrees to provided notice to Tenant if Landlord is aware of any delay in issuance of the grading permit that results from Tenant Fault. "**Landlord Fault**" means any actual delay in the Tenant's ability to obtain the grading permit to the extent resulting from the acts or omissions of Landlord or any its agents, employees, or representatives. Tenant agrees to provide notice to Landlord if Tenant is aware of any delay in the issuance of the grading permit that results from Landlord Fault.

2. Design of the Landlord's Construction Work. Prior to the Effective Date, Tenant has caused the Architect to prepare, and the Landlord and Tenant have approved, the conceptual plans and the allocation of responsibility for the Landlord's Construction Work as further described on Schedule 2, attached (collectively, the "**Approved Concept Plans**"). The Approved Concept Plans will be developed into Approved Core and Shell Plans as further provided in Section 5.2, below.

3. Landlord's Construction. Promptly following the date on which the Permits and Approvals have been received and are no longer subject to any potential appeal or challenge and the execution of the GMP Contract as set forth in Section 4.3 below (but in no event prior to the Effective Date), or on such earlier date as Landlord may elect in its discretion, Landlord shall cause the General Contractor (hereinafter defined) to commence and diligently prosecute the construction of the shell and core of the Building to completion pursuant to the Approved Shell and Core Plans (the "**Shell and Core**"), in accordance with the terms and conditions set forth in this Work Letter subject only to Shell and Core Permitted Changes and any other changes authorized pursuant to this Work Letter (all such construction, the "**Landlord's Construction Work**"). Tenant shall construct the tenant improvements in the Building pursuant to the Approved TI Plans (the "**Tenant Improvements**") as further provided below**.** The Landlord's Construction Work, together with the Tenant Improvements shall collectively be referred to herein as the "**Building Improvements**"**.** Landlord's Construction Work shall be constructed in a good and workmanlike manner, and in accordance with Applicable Laws (subject only to such incomplete work as will not materially adversely impact Tenant's continuous and uninterrupted use of the Premises for Tenant's Permitted Use). The allocation of responsibility for completion of the Building Improvements is included as part of Schedule 2. The parties acknowledge and agree that Landlord has agreed to perform certain Tenant Improvements on behalf of the Tenant (the "**TI by Landlord**") in coordination with the Landlord's Construction Work and Tenant has agreed to perform certain Landlord's Construction Work in coordination with the Tenant Improvements (the "LCW by Tenant") as further described on Schedule 9, attached. Following the completion of the Approved TI Plans for the TI by Landlord, the parties shall cooperate to make such adjustments as are necessary to the allocation of responsibility included in Schedule 2 to reflect the full scope of the LCW by Tenant and the TI by Landlord

3.1. Substantial Completion of Landlord's Construction Work. Landlord's Construction Work shall be deemed "**Substantially Complete**" or there shall be "**Substantial Completion**" at such time as (a) Landlord has received an AIA form certificate from the Architect confirming that the Landlord's Construction Work is substantially complete substantially in accordance with the Approved Shell and Core Plans, other than seasonal items such as balancing and landscaping, and other Punchlist Items (as defined below), and (b) all certifications and approvals with respect to the completion of the Landlord's Construction Work that may be required from any governmental authority to permit occupancy of the Premises for the Permitted Use, generally (as opposed to Tenant's use, specifically) have been obtained by Landlord (to the extent they may be obtained prior to the completion of the Tenant Improvements). The date on which Landlord's Construction Work is deemed Substantially Complete pursuant to the foregoing shall be referred to herein as the "**Substantial Completion Date.**" As used herein, the "**Delivery Date**" means the date that is the earlier to occur of (x) the date (i) the Landlord's Construction Work is in the condition required by Schedule 7 (the "**Delivery Condition**"), and (ii) Landlord has provided Tenant with reasonably continuous and uninterrupted access to the Project for the construction of Tenant Improvements, subject to the reasonable requirements necessary for, and established by, Landlord's General Contractor to allow it to obtain Substantial Completion, complete the Punchlist Items and exercise any of its other rights or obligations under this Work Letter and the Lease within the time periods set forth herein and (y) 60 days after the date that Tenant enters any portion of the Premises for the commencement of substantial work in connection with the Tenant Improvements; provided, however, in no event shall minor work such as the MEP deck inserts/hangers or other minor work that is installed early in the interest of efficiency be considered the commencement of the Tenant Improvements. Notwithstanding anything to the contrary in this Work Letter or the Lease, neither the LCW by Tenant nor the TI by Landlord is included for purposes of the determination of Substantial Completion, Delivery Condition, or the Delivery Date (the completion of the TI by Landlord being addressed in Section 11, below).

On a date or dates reasonably specified by Landlord (but not later than five (5) business days following Substantial Completion of the Landlord's Construction Work), Landlord and Tenant and each of their architects shall inspect the Landlord's Construction Work for the purpose of preparing a list of the punchlist type items, and any items of a seasonal nature such as balancing and landscaping, then remaining to be completed for the Landlord's Construction Work (the items on such list being referred to as "**Punchlist Items**"). Landlord shall, within ten (10) business days after the date of such inspection, submit a final punchlist to Tenant, and Tenant shall sign and return the final punchlist to Landlord within five (5) business days of Landlord's delivery of such final punchlist to Tenant (or, if earlier, by the day before Tenant takes occupancy of the Premises for the Permitted Use), noting any items that Tenant reasonably believes should be added thereto. Items shall not be added to the final punchlist by Tenant after it is delivered to Landlord and the expiration of such five (5) business day period. If the final punchlist is not executed by Tenant and returned to Landlord within such five (5) business day period, then Tenant shall be deemed to have accepted the final punchlist as submitted to Tenant by Landlord without modification and, except as set forth on the final punchlist, Landlord shall have no further obligation to cause any other Landlord's Construction Work to be completed. With respect to items on the final punchlist not in dispute, Landlord shall cause such items to be completed as soon as reasonably practicable in a diligent manner during regular business hours, but in a manner that will seek to minimize interruption of Tenant's construction of the Tenant Improvements. In any event, Landlord shall use commercially reasonable efforts to complete all punchlist work within 60 days (or such longer period as is reasonably required with respect to applicable items), other than matters that cannot be completed owing to their seasonal nature (which shall be completed as soon as reasonably practicable in a diligent manner), and subject to extension for Force Majeure and Tenant Delays. With respect to any disputed final punchlist items, Landlord shall cause such items to be completed in like manner, but Landlord may nevertheless reserve Landlord's rights to require Tenant to pay the costs therefor as Construction Costs. In the event of a dispute between Landlord and Tenant over Punchlist Items, the parties shall submit such dispute to resolution pursuant to Section 13, below. A separate process for the determination of substantial completion, punchlist, and completion of the same will apply with respect to the TI by Landlord, to be performed in the manner set forth above.

3.2. Schedule and Budget. As of the date hereof, Landlord and Tenant estimate that (a) the Delivery Date will occur on or before February 21, 2025 (the "**Target Delivery Date**"), and (b) the Substantial Completion Date of Landlord's Construction Work will occur on or before December 21, 2025 (the "**Target Substantial Completion Date**"). The final GMP agreement with the Contractor shall set forth an updated, estimated Delivery Date (the "**Estimated Delivery Condition Date**") and Substantial Completion Date (the "**Estimated Substantial Completion Date**") based on the initial construction of the Landlord's Construction Work (excluding the TI by Landlord and the LCW by Tenant). If Landlord reasonably believes the costs and expenses of achieving Substantial Completion of Landlord's Construction Work (excluding the TI by Landlord and the LCW by Tenant) will exceed the contemplated costs and expenses thereof as set forth in the Budget, then Landlord will promptly notify Tenant's Authorized Representative (by telephone, fax, email, or letter) thereof. All books and records for the Landlord's Construction Work and the TI by Landlord will be made available to Tenant on an "open book" basis (and Landlord's contract with the General Contractor shall require that the General Contractor shall also make available all of its books and records on the same "open book" basis, and, in coordination with the Landlord's final closeout of the construction contract with the General Contractor, Tenant may reasonably request that Landlord enforce its rights to audit the General Contractor's books and records to the full extent allowed by the Landlord's contract with the General Contractor, the costs of which audit shall be included in Construction Costs as a soft cost). Landlord's contract with the General Contractor for the Landlord's Construction Work shall be substantially in the form submitted to Tenant by e-mail delivery from Geoff Howell of DLA Piper LLP (US) to David Crawford of Cooley LLP and Mallorie Klemens of Ionis Pharmaceuticals, Inc. on August 22, 2022 and otherwise subject to Tenant's review and comment. Tenant shall have five (5) business days to review and reasonably comment on the final form of construction contract after delivery to Tenant. If Tenant fails to respond within such five (5) business day period, Landlord may provide a written reminder notice to Tenant. Tenant's failure to respond to such reminder notice within two (2) business days after delivery of such notice shall be deemed to be a waiver of Tenant's right to comment.

3.3. Construction Costs. Subject to the terms and provisions of this Work Letter, Landlord shall pay the costs to construct the Landlord's Construction Work in accordance with this Work Letter. As further provided in the definition of Base Rent within the Basic Lease Information section of the Lease, the Base Rent for the Premises shall be determined based on the costs of Landlord to acquire, design, construct, finance, and otherwise develop the Landlord's Construction Work ("**Construction Costs**") with a return-on-cost interest rate of 6.35%. Construction Costs include the costs and expenses of (a) Landlord's acquisition of the Land, including all closing costs and expenses thereof, (b) reimbursements to Tenant for the TI Allowance (hereinafter defined), (c) the General Contractor and other contractors and subcontractors, (d) space planning, architectural services, engineering and other related services, (e) building and other permits and other taxes, fees, charges and levies by any governmental authority for the entitlements (including without limitation pursuant to the Permits and Approvals) or for inspections of the Building Improvements, (f) labor, material, buildings, building systems, equipment, fixtures, additions and decorations, (g) all Taxes assessed or imposed and other carrying costs (including interest on debt) for the period from the Effective Date through the Commencement Date, (h) any association fees, (i) all utilities and other out-of-pocket operating costs necessary for development and construction, or deficiencies necessary to be paid in order to reconstruct the Landlord's Construction Work following any damage or destruction that occurs prior to the Lease Commencement Date, (j) insurance costs payable to the General Contractor and any other insurance obtained by Landlord pursuant to the terms of this Work Letter or otherwise required by any lender, (k) legal fees incurred in connection with the Landlord's Construction Work; (l) any costs incurred with respect to off-site improvements and mitigation such as traffic improvements, sidewalk improvements, and the like; (m) so-called linkage fees and other fees and payments in the nature of mitigation for project impacts as required by Applicable Law or the Permits and Approvals, (n) utility connection fees and deposits, (o) off-site improvements required by Permits and Approvals or to complete the Landlord's Construction Work in accordance with the Approved Core and Shell Plans, (p) pre-construction fees and payments to the General Contractor and other consultants, including any so-called design-assist fees and payments to subcontractors, (q) costs (including interests and fees thereon) incurred by Landlord or any holder of a direct or indirect interest in Landlord in connection with obtaining, negotiating and closing the financing of the acquisition and development of the Premises or the Landlord's obligations hereunder (including without limitation any construction loan for the Landlord's Construction Work), (r) any sales and use taxes on materials included within the Landlord's Construction Work, (s) the Developer Fee (as defined below), (t) costs to remove, store, remediate, and otherwise handle any Hazardous Materials, (u) reasonably allocated costs of the gross salary and wages or pro rata share thereof, federal and state unemployment taxes, social security taxes, group medical and health insurance premiums, worker's compensation insurance and other benefits of Landlord and its affiliates engaged in the design, construction, financing, and development of the Landlord's Construction Work, not to exceed $1,300,000.00 unless resulting from unusually frequent (when judged in accordance with industry custom and practice) change requests, unusually frequent (when judged in accordance with industry custom and practice) requests for information, or other acts or omissions of Tenant, Tenant Delays, Shell and Core Tenant Change Order Requests, or delays in the Landlord's Construction Work caused by Force Majeure, (v) costs to complete work and enforce warranties and indemnities during the Corrective Period (as defined below), (w) any other costs and expenses necessary for the acquisition, design, development, financing, and construction of the Project as determined by Landlord in its reasonable discretion, and (x) all the foregoing paid by Landlord with respect to the LCW by Tenant in accordance with Section 6(c), below. Construction Costs shall not include any "project management" fees payable to Landlord or its affiliates, other than the Developer Fee, and Landlord acknowledges that it shall not include a third-party project management consultant in addition to the general contractor as part of Construction Costs. For purposes of this Lease, any funds delivered by Landlord to pay any Construction Costs shall be deemed to constitute "**Disbursements**"**,** and "**Aggregate Disbursements**" will mean the aggregate amount of funds disbursed by Landlord for the Landlord's Costs. To the extent that Tenant has paid or does pay any design or pre-development costs directly prior to the Effective Date that would otherwise be an eligible Construction Cost if incurred by Landlord pursuant to this paragraph, such cost shall not be a Construction Cost or otherwise included in the determination of Base Rent. For purposes of clarity, it is acknowledged and agreed that Landlord shall (by assumption from Tenant in accordance with this Work Letter or directly) hold all contracts for the design and (except for the LCW by Tenant) construction of the Landlord's Construction Work from and after the Effective Date, and Tenant shall hold all contracts for the design and (except for the TI by Landlord) construction of the Tenant Improvements. The parties acknowledge that there will be separate Corrective Periods for the Landlord's Construction Work and TI by Landlord.

3.4. For a period commencing, and not to exceed, sixty (60) days prior to the occurrence of Delivery Condition for the Premises, Tenant shall have the right, upon at least seventy-two (72) hours' prior written notice via e-mail to Landlord's Authorized Representatives, to commence the Tenant Improvements and prosecute the same on a schedule to be mutually agreed upon with Landlord and the General Contractor (the "**Early Access Schedule**") subject to Landlord's and the General Contractor's reasonable security and safety precautions; provided, however, that prior to any such entry, Tenant shall furnish to Landlord evidence reasonably satisfactory to Landlord in advance that insurance coverages required of Tenant under the provisions of Section 8.3, below are in effect. Such entry shall be at Tenant's sole risk and subject to all the terms and conditions of the Lease, except for the payment of Rent. In the course of such entry, Tenant and its contractors shall not interfere with or delay the occurrence of Delivery Condition or Landlord's completion of the Landlord's Construction Work. Tenant and any Tenant contractor shall not damage, the Landlord's Construction Work. Tenant shall be responsible for the costs to repair any Landlord's Construction Work to the extent damaged by Tenant's contractors during the early access period. Following the Effective Date, Landlord and Tenant shall review the Early Access Schedule monthly with the General Contractor to determine with the General Contractor whether updates are needed to reflect the actual progress of the Landlord's Construction Work (e.g., including to allow access on an earlier date than originally set forth in the Early Access Schedule if Landlord's Construction Work is ahead of schedule).

Any requirements of any such Tenant contractor for services from Landlord or the General Contractor, such as hoisting, electrical or mechanical needs, shall be paid for by Tenant and arranged between such Tenant contractor and Landlord or Landlord's Contractor. Should the Tenant Improvements depend on the installed field conditions of any item of Landlord's Construction Work, such Tenant contractor shall ascertain such field conditions after installation of such item of Landlord's Construction Work. Neither Landlord nor the General Contractor shall be required or obliged to alter the method, time or manner for performing Landlord's Construction Work on account of the Tenant Improvements, but Landlord's General Contractor shall cooperate with Tenant to allow Tenant access to prosecute its work in accordance with the Early Access Schedule. Tenant shall cause each Tenant contractor performing Tenant Improvements on the Premises prior to the occurrence of Delivery Condition to substantially clean up regularly and remove its debris from the Premises and Building to the extent reasonably required by the Landlord's General Contractor.

4. General Requirements.

4.1. Authorized Representatives.

(a) Landlord designates, as Landlord's authorized representative ("**Landlord's Authorized Representative**"), Michael Haverty (e-mail: [***], phone: [***]) as the person authorized to initial plans, drawings, change orders, and provide consents and approvals pursuant to this Work Letter. Tenant shall not be obligated to respond to or act upon any such item until such item has been initialed or signed (as applicable) by the appropriate Landlord's Authorized Representative. Landlord may change Landlord's Authorized Representative upon one (1) business day's prior written notice to Tenant. Deliveries to Landlord's Authorized Representative by e-mail will be sufficient for purposes of delivery of notices and submissions required under this Work Letter, provided that an e-mail delivery made after 5 p.m. shall be treated as having been delivered on the next business day.

(b) Tenant designates Wayne Sanders (e-mail: [***], phone: [***]) ("**Tenant's Authorized Representative**") as the person authorized to initial all plans, drawings, change orders and provide consent and approvals pursuant to this Work Letter. Landlord shall not be obligated to respond to or act upon any such item until such item has been initialed or signed (as applicable) by Tenant's Authorized Representative. Tenant may change Tenant's Authorized Representative upon one (1) business day's prior written notice to Landlord. Deliveries to Tenant's Authorized Representative by e-mail will be sufficient for purposes of delivery of notices and submissions required under this Work Letter, provided that an e-mail delivery made after 5 p.m. shall be treated as having been delivered on the next business day.

4.2. Architects, Contractors and Consultants. The architect, engineering consultants, general contractor and major subcontractors responsible for the design and construction of the Landlord's Construction Work shall be selected by Landlord and approved by Tenant, which approval Tenant shall not unreasonably withhold, condition or delay. Landlord's request for approval of any design or construction professional shall be approved or disapproved by Tenant within five (5) business days after delivery to Tenant. If Tenant fails to respond within such five (5) business day period, Landlord shall provide a written reminder notice to Tenant. Tenant's failure to respond to such reminder notice within three (3) business days after delivery of such notice shall be deemed approval by Tenant of the applicable consultant. The parties acknowledge that DG Architects, Inc., dba DGA is approved as the architect, Spurlok is approved as the landscape architect, and EXP (mechanical, electrical and plumbing engineering, inclusive of Fire Alarm and Fire Sprinkler Basis of Design), KPFF (structural engineering), Pasco, Laret Suiter & Associates (civil engineering), Waveguide (acoustics/vibration consultant), Forsyth Consulting (building envelope consulting and waterproofing) are approved as engineers and consultants, and BNBuilders is approved as General Contractor. Except as pre-approved in this Section 4.2, Tenant may refuse to use any architects, consultants, contractors, subcontractors or material suppliers that Tenant reasonably believes could cause labor disharmony during the construction of the Tenant Improvements. The approved architect is referred to herein as the "**Architect**". Tenant shall enter into an architect's agreement with Architect (the "**Architect's Contract**") on a form provided by Landlord and approved by Landlord. Tenant shall use diligent, good faith efforts to enter into the Architect's Contract on or before November 1, 2022, and in any event shall enter into the Architect's Contract prior to the submission of schematic design plans to Landlord for its review.. As of the Effective Date, Landlord shall assume the Architect's Contract. Prior to the Effective Date, Tenant shall not modify or amend the Architect's Contract or approve any changes in the personnel providing services under the Architect's Contract without the prior consent of Landlord, which may be withheld in its sole discretion, and Tenant shall copy Landlord on all written communications with, and submissions to, the Architect. Landlord acknowledges that Tenant may hire, at its sole cost (subject to reimbursement as a soft cost out of the TI Allowance), an "owner's representative" in connection with the Project (a "**Project Manager**"), which Project Manager shall be reasonably approved by Landlord and be entitled to participate in meetings and receive any information to which Tenant is entitled under this Work Letter. Landlord acknowledges that it has approved Project Management Advisors, Inc. dba PMA as Tenant's Project Manager. The "**General Contractor**" for the Landlord's Construction Work means BNBuilders (or such other general contractor as may be proposed by either party and approved by the other in writing, such approval not to be unreasonably withheld, conditioned, or delayed), the parties acknowledging that such selection took place prior to the Effective Date through a collaborative process based on Tenant's request for proposal submitted to the General Contractor candidates, a copy of which has been provided to Landlord. Tenant provided Landlord with copies of responses to the request for proposal as well as all material communications between Tenant and any general contractor candidates. As used in this Work Letter, **"significant subcontractors and material suppliers"** means those subcontractors and suppliers (including the General Contractor, with respect to any self-performed work) that the parties agree fall within the category of "material" based on the final list of trades needed to bid on the Landlord's Construction Work, as reasonably agreed to by the parties. Notwithstanding the forgoing to the contrary, the LCW by Tenant shall be performed by Tenant's approved contractor and subcontractors as part of the Tenant Improvements and the TI by Landlord shall be performed by the General Contractor as part of the Landlord's Construction Work (but responsibility for the design of such work shall remain with the Architect or Tenant's architect responsible for the Tenant Improvements (with respect to the TI by Landlord) and the Landlord's Construction Work (with respect to the LCW by Tenant).

4.3. Landlord shall endeavor to cause Tenant to be designated as a third party beneficiary with respect to each warranty and/or indemnity with respect to the Landlord's Construction Work and the TI by Landlord that is made by the General Contractor or any "significant subcontractors and material suppliers" against which Landlord is able to exercise remedies pursuant to a contractual right (each, a "**Material Contractor**"**,** and each such warranty/indemnity, a "**Third Party Beneficiary Warranty**"**)**, including without limitation Landlord's rights during the Corrective Period (as defined below); provided, however, that it shall not be a default of Landlord hereunder if Landlord is unable to do so. Tenant shall not exercise its rights with respect to any Third Party Beneficiary Warranty until Substantial Completion has occurred and then only if (a) Tenant identifies any part of the Landlord's Construction Work that violates such Third Party Beneficiary Warranty (a "**Warranty Issue**"*),* (b) Tenant provides Landlord with written notice of any Warranty Issue, (c) the GMP Contract does not prohibit Landlord as the owner or Tenant as the third party beneficiary from exercising its rights with respect to such warranty/indemnity, and (d) either (i) within fifteen (15) business days after receiving such notice from Tenant, Landlord has not requested that the respective Material Contractor address such Warranty Issue, or (ii) Landlord fails to diligently endeavor to cause the Material Contractor to address such Warranty Issue (the parties acknowledging that, from and after the Corrective Period (as defined below), Landlord has no obligation to pursue any such Warranty Issue). Subject to the immediately preceding sentence, in any event during the Corrective Period Landlord shall use reasonable efforts to cause the General Contractor to repair any latent defects discovered by Tenant in the Landlord's Construction Work and the TI by Landlord and of which Landlord receives timely notice from Tenant during the Corrective Period. Following the Corrective Period, Landlord shall assign all warranties and indemnities for the Landlord's Construction Work and the TI by Landlord to Tenant, to the extent assignable, and, whether or not assignable, shall cooperate with Tenant, at Tenant's sole cost, to the extent necessary in pursuing any warranty or indemnity claim under the third-party contracts for the Landlord's Construction Work. The provisions of this paragraph shall be the Tenant's sole remedy in the event of any defect in the Landlord's Construction Work and the TI by Landlord. In no event shall Landlord have any responsibility with respect to defects in the LCW by Tenant, it being understood and agreed that such work shall be treated in the manner of Tenant Improvements following the substantial completion of the same (e.g., Tenant will be responsible for final completion and correction of any defects in the LCW by Tenant and insuring the LCW by Tenant).

4.4. GMP Contract. Following the completion of the Approved Core and Shell Plans, Landlord shall cause the General Contractor to solicit bids from at least three subcontractors for each significant subcontract and material supplier (unless fewer than three qualified bidders are available) and shall provide to, and review the bids with, Tenant. In the event that the General Contractor desires to self-perform a significant subcontract scope of work, either Landlord shall require the General Contractor to obtain at least two subcontractor bids for each trade to be self-performed, or Landlord shall engage a third-party cost estimator (as a Construction Cost) to provide an estimate of the same scope of work, and cause such cost estimator and General Contractor to reconcile estimates within +/-5% prior to approving the General Contractor's bid. Landlord shall select the lowest qualified bid unless otherwise instructed by Tenant. Landlord covenants that it will, within thirty (30) days following the completion of bidding, enter into a guaranteed maximum price contract between Landlord and General Contractor, which shall provide for the one hundred percent (100%) lien-free completion of the Landlord's Construction Work, provide for a correction period for defective work of at least twelve (12) (and not more than twenty-four (24)) months (as set forth in the contract, the "**Corrective Period**"), and be based on the final bids and otherwise approved terms of the form of construction contract ((the "**GMP Contract**"). The GMP Contract shall contain a complete line item budget to complete the Landlord's Construction Work in a manner consistent with similar projects. The parties acknowledge that certain long lead packages may be bid and procured separately by Landlord prior to the execution of the GMP Contract. The parties further acknowledge that it may be prudent, on the advice of the General Contractor or any other consultant providing pre-construction services, to procure some long lead items contained within the Landlord's Construction Work prior the execution of the GMP Contract or to place deposits for the acquisition of the same, in each case as a means to mitigate against potential supply chain issues during construction. The parties shall collaborate and cooperate in discussing opportunities for such mitigation. In connection with any agreement to spend such amounts prior to the Effective Date, the parties shall agree on how such sums shall be treated for the purposes of Construction Costs (with the understanding that amounts spent by Landlord on any such items shall be considered part of Construction Costs, Landlord having no obligation to incur any such costs prior to the Effective Date). The parties further acknowledge that the GMP Contract shall reflect strategies developed with the General Contractor to mitigate against risks of supply chain delays; Landlord shall use reasonable efforts, in collaboration with Tenant, to minimize the right of the General Contractor under the GC Contract to claim extensions for Force Majeure resulting from supply chain delays, consistent with similar projects in the same market. The TI by Landlord shall be priced separately from the remainder of the GMP Contract as a change order on either a lump sum or cost-plus-fee, not to exceed, basis, and Landlord shall cause the General Contractor to segregate the accounting of the same. Landlord shall consult with Tenant in the finalization of such change order to provide Tenant with the opportunity to institute TI Changes related to the TI by Landlord as appropriate for Tenant's value-engineering purposes.

4.5. Schedule. The currently anticipated schedule for the development, and completion of the Landlord's Construction Work is attached hereto as Schedule 3 to the Work Letter (the "**Schedule**"). Following the Effective Date, the Landlord shall update the Schedule from time to time to reflect the actual status of the Landlord's Construction Work (other than the LCW by Tenant) and to the extent applicable, the TI by Landlord. Landlord will provide Tenant with regular updates to the Schedule; provided at a minimum, Landlord shall provide Tenant with a monthly updated Schedule and a reconciliation of the actual progress of Landlord's Construction Work (other than the LCW by Tenant) against the Schedule. Landlord shall use commercially reasonable efforts to complete the Landlord's Construction Work (other than the LCW by Tenant) and the TI by Landlord in accordance with the Schedule, but Tenant acknowledges that such Schedule is subject to change from time to time to reflect the actual progress of the Landlord's Construction Work and the TI by Landlord and that failure to comply with the same shall not result in a default under this Lease. Following the commencement of construction, Landlord shall hold weekly a construction meeting that includes Tenant's Project Manager, the General Contractor, and the Architect.

5. Shell and Core. Landlord's Construction Work related to the Shell and Core shall be performed by Landlord at Landlord's sole cost and expense substantially in accordance with the Approved Shell and Core Plans, subject only to changes made in accordance with this Work Letter. The LCW by Tenant shall be performed by Tenant at Landlord's sole cost and expense substantially in accordance with the Approved Shell and Core Plans, subject only to changes made in accordance with this Work Letter.

5.1. Approved Design Development Plans. As noted above, the parties have approved the Approved Concept Plans. Prior to the Effective Date, Landlord acknowledges that Tenant shall have the right to make changes to the Approved Concept Plans as required to comply with the requirements of the City of Carlsbad, subject to Landlord's reasonable approval, such approval not to be unreasonably withheld, conditioned, or delayed (it being reasonable for Landlord to disapprove of such changes if such change will result in the Landlord's Construction Work not complying with the Fundamental Requirements). Once approved, any such change shall be incorporated into the Approved Concept Plans by the Architect.

5.2. Approved Shell and Core Plans. Prior to the Effective Date, and in any event no later than October 17, 2022, Tenant shall cause the Architect to develop full schematic design documents for the entire Premises that are consistent with the Approved Concept Plans, which schematic design documents shall be subject to Landlord's written approval, such approval not to be unreasonably withheld, conditioned or delayed provided that the same are consistent with the Concept Plans, the requirements of the Permits and Approvals, and the Fundamental Requirements, and achievement of Delivery Condition and Substantial Completion by the Target Delivery Condition Date and Target Substantial Completion Date, respectively (as approved, the "**Approved Schematic Plans**"). Following the Effective Date, Landlord shall cause the Architect to prepare design development documents and final 100% construction documents for the Landlord's Construction Work (including the LCW by Tenant) that (a) are consistent with and are logical evolutions of the Approved Schematic Plans or reasonably inferable therefrom, and (b) incorporate any Shell and Core Permitted Changes, and (c) incorporate any other Landlord-requested (and Tenant approved) Shell and Core Changes. As soon as such design development documents and the final construction documents (collectively, **"Landlord's Shell and Core Plans"**) are completed, Landlord shall deliver the same to Tenant for Tenant's approval, which approval may be withheld only if: (i) the applicable Landlord's Shell and Core Work Plans are neither consistent with nor logical evolutions of the Approved Schematic Plans or the previously approved design development documents, as applicable, or (ii) such plans are otherwise inconsistent with the requirements of this paragraph**.** Such Landlord's Shell and Core Plans shall be approved or disapproved by Tenant within ten (10) business days after delivery to Tenant (or five (5) business days with respect to any resubmission of plans to Tenant). If Tenant fails to respond within such ten (10) (or (five (5), as applicable) business day period, Landlord may provide a written reminder notice to Tenant. Tenant's failure to respond to such reminder notice within five (5) business days after delivery of such notice shall be deemed approval by Tenant of the applicable Landlord's Shell and Core Plans. If the applicable Landlord's Shell and Core Plans are disapproved by Tenant, then Tenant shall notify Landlord in writing of its detailed objections to such Landlord's Shell and Core Plans, and Landlord shall revise the applicable Landlord's Shell and Core Plans accordingly unless it disputes the basis of such objections, in which case such dispute shall be resolved as provided in Section 13, below. The final Landlord's Shell and Core Plans so approved, and all change orders and other changes thereto specifically permitted by this Work Letter, are referred to herein as the "**Approved Shell and Core Plans.**" If the Approved Schematic Plans are completed and finally approved by Landlord prior to the Effective Date, the parties acknowledge that they shall collaborate and cooperate to have Tenant cause the Architect to proceed with generating design development documents for the Landlord's Construction Work, with the intent of completing the same for submission to the parties on or about December 9, 2022. The approval of the design development documents by Landlord, to the extent occurring prior to the Effective Date, shall be handled in the manner applicable to the schematic design documents. As a condition to the authorization of the architect to proceed with the design development phase prior to the Effective Date, the parties shall agree on how such sums shall be treated for the purposes of Construction Costs. The parties acknowledge and agree that the Approved Shell and Core Plans shall be designed to meet at least LEED Gold certification standards and Tenant shall, prior to the Effective Date, submit the Building for pre-certification under LEED Gold standards and diligently pursue pre-certification. The parties shall cooperate as reasonable required to obtain LEED Gold (or such better standard as has been designed) certification for the Building, Landlord and Tenant acknowledging that the inability to obtain such certification for matters not within the control of Landlord and Tenant (such as the failure of the LEED program to continue to exist) shall not be deemed to be a default hereunder.

The parties shall cooperate to schedule periodic design and construction meetings at mutually agreeable times, such meetings to take place no less often than monthly, with respect to Landlord's Construction Work and Tenant Improvements, and (following commencement of the Tenant Improvements) bi-weekly with respect to the Tenant Improvements. The parties shall keep each other reasonably informed with respect to their respective work, and Landlord and Tenant agree to provide each other with such information as may be reasonably requested by the other party with respect to the Landlord's Construction Work and Tenant Improvements, as applicable.

5.3. Landlord Project Developer Fee. Tenant shall be required to pay Landlord a (a) project developer fee in the amount of three (3%) percent of the hard and soft costs of construction of the Landlord's Construction Work (other than the LCW by Tenant, for which such percentage shall be two (2%) percent), and (b) an oversight fee in the amount of one (1%) percent of the hard and soft costs of construction of the Tenant Improvements (other than the TI by Landlord, for which such percentage shall be two (2%) percent) (collectively, the "**Developer Fee**").

5.4. Changes to Shell and Core Plans. Any changes to the Approved Shell and Core Plans (each, a "**Shell and Core Change**") requested by Landlord or Tenant (other than Shell and Core Permitted Changes by Landlord, which do not require any approval) shall be requested and instituted in accordance with the provisions of this Section 5.4 and shall be subject to the written approval of the other party in accordance with this Work Letter.

(a) Shell and Core Changes Requested by Tenant.

(i) Shell and Core Tenant Change Order Request. Following the Effective Date (but in no event later than the date that is one month following the date that the final Landlord's Shell and Core Plans are submitted by Landlord to Tenant for approval), Tenant may request Shell and Core Changes to the Approved Shell and Core Plans to accommodate the design of the Tenant Improvements by notifying Landlord thereof in writing in a change order form provided by Landlord that is substantially the same form as the AIA standard change order form (a "**Shell and Core Tenant Change Order Request**"), which Shell and Core Tenant Change Order Request shall detail the nature and extent of any requested Shell and Core Changes, including, without limitation, (A) the Shell and Core Change and (B) any modification of the Approved Shell and Core Plans, as applicable. In the event Landlord approves any Shell and Core Change, Landlord shall: (1) notify Tenant if it reasonably believes such Shell and Core Change could cause a delay in the Estimated Delivery Condition Date or the Estimated Substantial Completion Date; and (2) provide Landlord's reasonable estimate of any additional costs and expenses associated with such Shell and Core Change. Shell and Core Tenant Change Order Requests shall be signed by Tenant's Authorized Representative.

(ii) Landlord's Approval of Shell and Core Changes. All Tenant-requested Shell and Core Changes shall be subject to Landlord's prior written approval, which shall not be unreasonably withheld, conditioned or delayed so long as such Shell and Core Change, as reasonably determined by Landlord, (A) could not reasonably be expected to (1) adversely impact (a) the exterior appearance of the Building, (b) the structural aspects of the Building, or (c) any building system, including, without limitation, the HVAC, mechanical, electrical, plumbing or life safety systems installed in connection with the Landlord's Construction Work; (2) create a foreseeable risk of violating any, or actually violate any, Applicable Law or the Permits and Approvals (or require a modification of the same), or any other permit requirement, (3) materially increase insurance premiums; (4) in Landlord's reasonable judgment, materially reduce the quality or value of the Building or the Property, (5) result in a Fundamental Change, or (6) delay the occurrence of Delivery Condition or Substantial Completion of the Landlord's Construction Work by more than 30 days when combined with all other then-existing Tenant Delays (each, a "**Design Problem**"), and (B) will not cause the hard costs of the Landlord's Construction Work to increase by more than one (1%) percent in the aggregate (based on the Landlord's Budget) unless Tenant makes provisions to pay for the same that are acceptable to Landlord and its construction lender. Landlord shall have ten (10) days after receipt of a Shell and Core Tenant Change Order Request to notify Tenant in writing of Landlord's decision either to approve or disapprove Tenant-requested Shell and Core Change. If Landlord fails to respond within such ten (10) day period, Tenant may provide a written reminder notice to Landlord. Landlord's failure to respond to such reminder notice within three (3) days after delivery of such notice shall be deemed approval by Landlord of the Shell and Core Tenant Change Order Request. Any dispute regarding the Landlord's disapproval of a Shell and Core Tenant Change Order Request shall be resolved in accordance with Section 13, below.

(b) Shell and Core Changes Requested by Landlord.

(i) Shell and Core Landlord Change Order Request. Landlord may request Shell and Core Changes to the Landlord's Construction Work by notifying Tenant thereof in writing in a change order form provided by Landlord that is substantially the same form as the AIA standard change order form (a "**Shell and Core Landlord Change Order Request**"), which Shell and Core Landlord Change Order Request shall detail the nature and extent of any requested Shell and Core Changes, including, without limitation, (A) the Shell and Core Change, (B) any modification of the Design Development Plans or the Approved Shell and Core Plans, as applicable, and (C) any changes to the Estimated Delivery Condition Date or Estimated Substantial Completion Date resulting from the Shell and Core Change. Notwithstanding the foregoing or anything herein to the contrary, Landlord shall have no obligation to request the approval of Shell and Core Permitted Changes.

(ii) Tenant's Approval of Shell and Core Change. Tenant shall have ten (10) days after receipt of a Shell and Core Landlord Change Order Request to notify Landlord in writing of Tenant's approval or rejection of the Landlord-requested Shell and Core Change, which approval shall not be unreasonably withheld, conditioned or delayed. If Tenant fails to respond within such ten (10) day period, then Landlord may provide Tenant with a second written notice stating that "Tenant's failure to respond within three (3) days after Landlord's second notice shall be deemed Tenant's approval to such Shell and Core Landlord Change Order Request," and if Tenant does not respond with such three (3) day period, then Tenant shall be deemed to have approved such Shell and Core Landlord Change Order Request. Any dispute regarding the Tenant's disapproval of a Shell and Core Tenant Change Order Request shall be resolved in accordance with Section 13, below.

(c) Shell and Core Permitted Changes. For purposes of this Work Letter, a "**Shell and Core Permitted Change**" shall mean: (i) minor field changes; (ii) changes required by governmental authority or to comply with Permits and Approvals or Applicable Laws; (iii) any other changes that both: (A) could not reasonably be expected to (1) adversely impact (a) the structural aspects of the Building, (b) the exterior appearance of the Building (other than de minimis changes that do not result from a change in exterior material specifications, such as locations of items behind screening on the roof, final adjustments in the positioning of exterior doors or loading bays, and the like), (c) Tenant's ability to construct the Tenant Improvements as shown on the Approved TI Plans, or (d) any building system, including, without limitation, the HVAC, mechanical, electrical, plumbing or life safety systems installed in connection with the Landlord's Construction Work; (2) create a foreseeable risk of violating any, or actually violate any, Applicable Law or the Permits and Approvals (or require a modification of the same), or any other permit requirement, (3) materially increase insurance premiums; or (4) delay the Substantial Completion of the Landlord's Construction Work by more than 30 days, and (B) do not materially change the size, cost, configuration, or overall appearance of the Building, Bridge or Parking Structure, materially and adversely affect Landlord's ability to perform the Landlord's Construction Work or materially and adversely affect Tenant's ability to operate its business in the Building, and (iv) changes required for the ordinary development of the Approved Shell and Core Plans in a manner not inconsistent with the Approved Shell and Core Plans. Shell and Core Permitted Changes may be made by Landlord in its reasonable discretion. Shell and Core Permitted Changes to the LCW by Tenant may be requested by Tenant in its reasonable discretion and shall be implemented by Landlord, but, with respect to changes described in clauses (ii) and (iii) of this subparagraph (c), only in consultation with Landlord and with the Landlord's reasonable approval.

6. Tenant Improvements. Following delivery of the Premises to Tenant on the Delivery Date, the Tenant Improvements shall be performed by Tenant (or, with respect to the TI by Landlord, by Landlord) at Tenant's sole cost and expense (subject to the TI Allowance) substantially in accordance with the Approved TI Plans (subject only to changes made in accordance with Section 6.3), the provisions of the Lease governing Alterations (to the extent not inconsistent with this Work Letter), and this Work Letter. The schedule for the construction of the Tenant Improvements (other than the TI by Landlord) shall be in accordance with a schedule to be prepared by Tenant's general contractor (the "**TI Schedule**"). Tenant shall prepare the TI Schedule so that it is a reasonable schedule for the completion of the Tenant Improvements (other than the TI by Landlord), taking into account the work necessary for Landlord to achieve Substantial Completion by the date set forth in the GMP Contract. The TI Schedule shall clearly identify estimated dates and time periods when Tenant's contractor will require access to areas that are under construction by Landlord. As soon as the TI Schedule is completed, Tenant shall deliver the same to Landlord for Landlord's approval, which approval shall not be unreasonably withheld, conditioned or delayed. Such TI Schedule shall be approved or disapproved by Landlord, following consultation with Landlord's General Contractor, within ten (10) business days after delivery to Landlord. Landlord's failure to respond within such ten (10) business day period shall be deemed approval by Landlord. If Landlord disapproves the TI Schedule, then Landlord shall notify Tenant in writing of its objections to such TI Schedule, with reasonable detail, and the parties shall confer and negotiate in good faith to reach agreement on the TI Schedule.

6.1. TI Plans. Tenant shall retain an architect reasonably approved by Landlord (the "**TI Architect**") to design the tenant improvements necessary for Tenant's particular use and occupancy of the Premises in accordance with the program attached as Schedule 5 and items identified as "by Tenant" on the allocation of responsibility attached as Schedule 2, including the TI by Landlord. Landlord acknowledges that it has approved the use of DGA as the TI Architect. Tenant shall cause the TI Architect to prepare, and Landlord shall approve, schematic plans, design development plans, and 100% construction document plans (the "**TI Plans**"), in each case fully coordinated with the Approved Core and Shell Plans, all in accordance with the milestone dates set forth on Schedule 4, subject to Force Majeure and Landlord Delays (as defined below). The TI Plans shall provide for a minimum investment equal to the TI Allowance across the entire Premises in accordance with the Approved Budget (as defined below). All material and equipment furnished by Tenant or its contractors as the Tenant Improvements shall be new or "like new;" and the quality of the Tenant Improvements shall be of a nature and character not less than a first-class standard for life sciences facilities. Any engineers used by Tenant or Tenant's TI Architect in the design of the Tenant Improvements shall be subject to Landlord's reasonable consent, Landlord acknowledging that the engineers referenced in Section 4.2 above, are deemed approved. Even if any such architect or engineers may have been otherwise engaged by Landlord or Landlord's affiliates in connection with the Landlord's Construction Work or any other property, Tenant shall be solely responsible for the liabilities and expenses of all architectural and engineering services relating to the Tenant Improvements (subject to reimbursement from the TI Allowance as provided below) and for the adequacy and completeness of the TI Plans submitted to Landlord.

Landlord and Tenant acknowledge that the TI Plans shall provide for the division of the Tenant Improvements into two phases, as shown and further described on Schedule 5, attached, the first phase of which is referred to herein as the "Day 1 Space" and the second phase of which is referred to herein as the "Day 2 Space" (each such phase, as applicable, being referred to herein as a "phase". The LCW by Tenant shall in all events be included within the first phase, regardless of whether it is located in the Day 1 Space or the Day 2 Space.

"**Landlord Delays**" means any actual delay in the design of the Tenant Improvements for a phase to the extent resulting from the acts or omissions of Landlord or any Landlord Party, including, without limitation, any Landlord-requested TI Change. Except for Landlord Delays due to any Landlord requested TI Change for which Tenant provided to Landlord the estimated amount of any associated Landlord Delay (for which no notice will be required, and no obligation of Tenant to grant such request other than as expressly provided herein), if there is an event that Tenant contends is a Landlord Delay, then Tenant shall give Landlord written notice of such Tenant Delay as soon as is practicable following Tenant's knowledge of such delay ("**TI Delay Notice**") (provided, however, that no Landlord Delay shall be deemed to accrue under this Work Letter with respect to the Landlord Delay referenced in a TI Delay Notice until Tenant provides Landlord with such TI Delay Notice).

Any Landlord Delay of less than a full day shall be deemed to be equal to a delay of one (1) full day. Landlord and Tenant have agreed to determine the length of any Landlord Delay as follows: (i) any delays resulting from the failure of Landlord to act within a time period specified in this Work Letter with respect to the approval of the TI Plans shall be equal to one (1) day for each day that the applicable Landlord Delay continues beyond the applicable time period required for such action under the Lease, (ii) in the event of any agreed Landlord Delay, as the parties may agree in writing from time to time, the length of such Landlord Delay shall be as agreed upon in writing by the parties at the time such Landlord Delay arises, and (iii) with respect to any other Landlord Delay, Tenant shall notify Landlord in writing of the claimed estimated length of such Landlord Delay within ten (10) business days after its occurrence and Landlord may elect by written notice delivered to the other within ten (10) business days thereafter to dispute the claimed estimated Landlord Delay in accordance with Section 13 of this Work Letter. Unless such estimate is disputed by written notice delivered within such ten (10) business day period, the length of such Landlord Delay shall be no less than the claimed estimated Landlord Delay.

6.2. Approved TI Plans. Tenant shall prepare TI Plans for each phase of the Tenant Improvements (inclusive of the TI by Landlord) that: (a) are consistent with and are logical evolutions of the previously approved iteration of the TI Plans, (b) incorporate any TI Permitted Changes, and (c) incorporate any other Landlord-requested (and Tenant approved) TI Changes. As soon as an applicable phase (i.e. schematic development, design development, and construction drawings) of TI Plans are completed, Tenant shall deliver the same to Landlord for Landlord's approval, which approval shall not be unreasonably withheld, conditioned, or delayed so long as such TI Plans are consistent with the previously approved TI Plans and do not cause Design Problems. Such TI Plans shall be approved or disapproved by Landlord within ten (10) business days after delivery to Landlord. If Landlord fails to notify Tenant of disapproval within such ten (10) business day period, then Tenant may provide Landlord with a second written notice stating that "Landlord's failure to respond within five (5) business days after Tenant's second notice shall be deemed Landlord's approval to such TI Plans," and if Landlord does not respond within such five (5) business day period, then Landlord shall be deemed to have approved such TI Plans. If the TI Plans are disapproved by Landlord, Landlord shall notify Tenant in writing of its objections to such TI Plans. Any dispute regarding Landlord's disapproval of TI Plans shall be resolved in accordance with Section 13, below. After the 100% final construction document phase of TI Plans for a phase are approved by Landlord and Tenant, Tenant shall promptly submit such TI Plans to each appropriate governmental authority for approval. The TI Plans so approved, and all change orders and other changes thereto specifically permitted by this Work Letter, are referred to herein as the "**Approved TI Plans**".

6.3. Changes to Tenant Improvements. Any changes to the TI Plans or the Approved TI Plans (each, a "**TI Change**") requested by Landlord or Tenant (other than TI Permitted Changes by Landlord which do not require any approval) shall be requested and instituted in accordance with the provisions of this Section 6.3 and shall be subject to the written approval of the other party in accordance with this Work Letter.

(a) TI Changes Requested by Tenant.

(i) TI Tenant Change Order Request. Tenant may request TI Changes after Landlord approves the approved design development phase of the TI Plans or the Approved TI Plans, on a phase-by-phase basis, by notifying Landlord thereof in writing in a change order form provided by Landlord that is substantially the same form as the AIA standard change order form (a "**TI Tenant Change Order Request**"**),** which TI Tenant Change Order Request shall detail the nature and extent of any requested TI Changes, including, without limitation, (A) the TI Change and (B) any modification of the TI Plans or Approved TI Plans, as applicable.

(ii) Landlord's Approval of TI Changes. All Tenant-requested TI Changes shall be subject to Landlord's prior written approval, which shall not be unreasonably withheld, conditioned or delayed, provided that (a) such changes are not Fundamental Changes, (b) such changes do not require any modification of the Permits and Approvals for the Landlord's Construction Work, (c) such changes do not require any modification of the Landlord's Construction Work, (d) the requested work is compatible with the design, quality, equipment or systems of the Landlord's Construction Work, or (e) such changes otherwise comply with the provisions of the Lease. Landlord shall have ten (10) business days after receipt of a TI Tenant Change Order Request to notify Tenant in writing of Landlord's decision either to approve or disapprove the Tenant- requested TI Change. If Landlord does not approve in writing a Tenant requested TI Change within ten (10) business days after receipt of a TI Tenant Change Order Request, Tenant may provide a written reminder notice to Landlord. Landlord's failure to respond to such reminder notice within five (5) business days after delivery of such notice shall be deemed a rejection of such request by Landlord, and the Tenant Improvements shall not be altered as contemplated by such TI Tenant Change Order Request. Any dispute regarding the Landlord's disapproval of a TI Tenant Change Order Request shall be resolved in accordance with Section 13, below.

(b) TI Changes Requested by Landlord.

(i) TI Landlord Change Order Request. Landlord may request TI Changes by notifying Tenant thereof in writing in a change order form provided by Landlord that is substantially the same form as the AIA standard change order form (a "**TI Landlord Change Order Request**"), which TI Landlord Change Order Request shall detail the nature and extent of any requested TI Changes, including, without limitation, (A) the TI Change, and (B) any modification of the TI Plans or the Approved TI Plans, as applicable. Notwithstanding the foregoing to the contrary, Tenant's approval is not required for TI Permitted Changes, as defined below.

(ii) Tenant's Approval of TI Change. Tenant shall have ten (10) days after receipt of a TI Landlord Change Order Request to notify Landlord in writing of Tenant's approval or rejection of the Landlord-requested TI Change, which approval shall not be unreasonably withheld, conditioned or delayed, so long as such TI Landlord Change Order Request, as reasonably determined by Tenant, (A) could not reasonably be expected to (1) adversely impact the functionality or, in more than a de minimis manner, the appearance of the Tenant Improvements; (2) create a foreseeable risk of violating any, or actually violate any, Applicable Law or the Permits and Approvals (or require a modification of the same), or any other permit requirement, (3) materially increase insurance premiums; (4) result in a Fundamental Change, or (5) delay the completion of the Tenant Improvements in more than a de minimis manner (each, a "**TI Design Problem**"), and (B) following the final approval of the Approved TI Plans, will not cause the hard costs of the Tenant Improvements to increase by more than one (1%) percent in the aggregate (unless Landlord agrees to pay the same, in which case such amount shall be included in Construction Costs as a soft cost). If Tenant fails to respond within such ten (10) days period, then Landlord may provide Tenant with a second written notice stating "that Tenant's failure to respond within three (3) days after Landlord's second notice shall be deemed Tenant's approval to such Landlord-requested TI Change," and if Tenant does not respond within such three (3) day period, then Tenant shall be deemed to have approved such Landlord-requested TI Change.

(c) TI Permitted Changes. For purposes of this Work Letter, a "**TI Permitted Change**" shall mean (i) minor field changes; (ii) changes required by governmental authority or to comply with Applicable Laws; and (iii) changes that, when viewed in the aggregate, constitute Minor Alterations, as defined in the Lease. TI Permitted Changes may be made by Tenant in its sole but reasonable discretion. Tenant shall provide Landlord with reasonable prior notice of any TI Permitted Changes (other than minor field changes, of which Tenant shall provide notice as soon as reasonably practicable).

6.4. Construction of the Tenant Improvements and LCW by Tenant; Coordination.

(a) Tenant shall retain the Landlord's General Contractor to construct the Tenant Improvements and the LCW by Tenant and shall obtain Landlord's prior written approval of the construction contract for the Tenant Improvements and the LCW by Tenant, which approval shall not be unreasonably withheld, conditioned, or delayed. Following approval of the Approved TI Plans, Tenant shall obtain all governmental approvals, authorizations, licenses, and permits (collectively, the "**Approvals**") necessary for the construction of the Tenant Improvements (other than the TI by Landlord) and the LCW by Tenant and provide copies of the same to Landlord. Tenant shall provide Landlord with a copy of the application for any material Approvals prior to submitting the same. The Approvals shall not contain material conditions that survive the termination of the Lease without the prior written consent of Landlord, such consent not to be unreasonably withheld, conditioned or delayed. Landlord shall cooperate with Tenant to obtain the Approvals, at no out of pocket cost or liability to Landlord. Following receipt of the Approvals, Tenant shall promptly commence and diligently prosecute to completion the Tenant Improvements and the LCW by Tenant in accordance with, and subject to, the provisions of this Work Letter and Section 3.4 of the Lease.

All Tenant Improvements and the LCW by Tenant shall be performed and constructed by Tenant in accordance with the Approved TI Plans and, with respect to the LCW by Tenant, the Approved Shell and Core Plans, and in compliance with Applicable Laws and the Approvals. No Tenant Improvements and the LCW by Tenant shall be performed except in accordance with the Approved TI Plans or the Approved Shell and Core Plans, as applicable, as they may be modified in accordance with this Work Letter. Prior to the commencement of the Tenant Improvements and the LCW by Tenant, Tenant shall deliver to Landlord a copy of any contract with Tenant's contractors (including the architect), and certificates of insurance from the architect and any contractor performing any part of the Tenant Improvements and, as applicable, the LCW by Tenant evidencing insurance in compliance with the terms of the Lease. Tenant shall endeavor to have Landlord named as a third-party beneficiary (on a non-exclusive basis) of any contract entered into by Tenant with the Tenant's architect, any consultant providing design or engineering services for the Tenant Improvements, any contractor or any subcontractor, and of any warranty or indemnity made by any contractor or any subcontractor. Landlord shall not exercise its rights with respect to its third party beneficiary status under the immediately preceding sentence unless (i) Tenant is in default under the Lease beyond applicable notice and cure periods, (ii) the Lease has otherwise terminated or otherwise is no longer in effect, or (iii) otherwise where Landlord has a bona fide, good faith claim against such architect, consultant, contractor, or subcontractor, in which case Landlord and Tenant will cooperate to pursue such claim. All Tenant Improvements and the LCW by Tenant shall be constructed in a good and workmanlike manner, in compliance with Applicable Laws. All Tenant contracts related to the Tenant Improvements and the LCW by Tenant shall provide that Tenant may assign such contracts and any warranties with respect to the Tenant Improvements and the LCW by Tenant to Landlord, upon Landlord's request, effective at the end of the Term or in the event of a Default by Tenant under the Lease. Tenant shall take, and shall require its contractors to take, commercially reasonable steps to protect the Premises from damage as a result of the performance of any Tenant Improvements and the LCW by Tenant, including covering or temporarily removing any window coverings so as to guard against dust, debris or damage. Tenant shall conduct the Tenant Improvements and the LCW by Tenant in a manner that reasonably minimizes interference with other construction activities at the Premises, in a manner consistent with first-class life sciences buildings.

Tenant shall diligently prosecute and substantially complete the Tenant Improvements and the LCW by Tenant on or before the first anniversary of the Commencement Date with respect to the Day 1 Space and on or before the first day of the 18th month following the Commencement Date with respect to the Tenant Improvements for the Day 2 Space, subject to extension due to Landlord Delay or Force Majeure. For purposes of this paragraph, "substantially complete" and "substantial completion" shall mean that the Tenant Improvements and the LCW by Tenant have been completed, other than minor punchlist-type items the completion of which will not unreasonably delay or interfere use of the affected areas of the Premises for the regular conduct of business. Promptly following substantial completion of each phase and the LCW by Tenant, Tenant shall provide Landlord with a certificate of substantial completion by Tenant's architect on a form reasonably approved by Landlord. Notwithstanding anything to the contrary herein, the determination of substantial completion with respect to the TI by Landlord shall be made by Landlord's architect.

If Tenant fails to complete the LCW by Tenant or Tenant Improvements for the second phase by the applicable date set forth in the immediately preceding paragraph, Landlord shall provide Tenant with thirty (30) days written notice of its intent to undertake the work necessary to complete the same ("**Self-Help**"). If Tenant fails to complete the LCW by Tenant or the Tenant Improvements for the second phase, as applicable, within such thirty (30) day period, then Landlord shall have the right to exercise Self-Help and, with respect to the Tenant Improvements, apply the balance of the TI Allowance against the Construction Costs reasonably and actually incurred by Landlord in connection with the same. Tenant shall reimburse Landlord for any such reasonable costs actually incurred by Landlord (in excess of the TI Allowance, with respect to the Tenant Improvements) within 30 days following invoice together with reasonable evidence by Landlord, together with interest at the rate payable with respect to late payments of rent by Tenant, and if Tenant fails to timely pay such amounts then Landlord shall have the right, but not the obligation, to draw on the Letter of Credit as further provided in Section 2.5 of the Lease. If Tenant has not yet prepared and finalized Approved TI Plans for such phase of Tenant Improvements in accordance with this Work Letter, then, in connection with the exercise of its rights under this paragraph, Landlord may complete the same in a manner reasonably consistent with the then-existing TI Plans for such phase as previously submitted to Landlord and otherwise in a manner consistent with first class office and lab space and meeting the Fundamental Requirements. The provisions of this paragraph shall survive the termination or earlier expiration of the Lease. In no event shall Landlord have any obligation to apply unused TI Allowance amounts towards the cost of the LCW by Tenant in the exercise of its rights pursuant to this paragraph.

(b) Landlord and Tenant shall reasonably cooperate and proceed in good faith so as to coordinate the management, administration, and schedule of the Landlord's Construction Work and the Tenant Improvements following the Delivery Date in a manner that will permit Landlord to achieve its obligations to lenders and Tenant, and permit Landlord to achieve Substantial Completion by the Estimated Substantial Completion Date, and permit Tenant to complete the Tenant Improvements in a reasonably expeditious manner and in a manner consistent with Tenant's schedule for the Tenant Improvements. Such cooperation shall include coordinating the schedules of the General Contractor with respect to the TI by Landlord with Tenant's general contractor's schedule for the Tenant Improvements.

(c) Landlord shall reimburse Tenant for the Construction Costs of the LCW by Tenant in the same manner applicable to Tenant Improvements funded by the TI Allowance, except as otherwise expressly provided in this Work Letter. The LCW by Tenant shall be performed under a lump sum or cost plus fee subject to a guaranteed maximum price change order to the construction contract for the Tenant Improvements and Tenant shall cause its general contractor to segregate the accounting of the same. Notwithstanding anything to the contrary herein, in no event shall Landlord's obligation to fund the LCW by Tenant exceed the amount for such work shown on Schedule 9, attached. Following the completion of the LCW by Tenant, Tenant shall provide Landlord with such information as is reasonably required for the final reconciliation of such costs such that the entire amount of the Construction Costs incurred by Landlord on account of the LCW by Tenant is included within the calculation of Base Rent (subject, however, to the limitation set forth above in this paragraph).

7. Force Majeure. Any prevention, delay or stoppage due to strikes, lockouts, labor disputes, acts of God, acts of war, terrorist acts, inability to obtain, or delays in obtaining, services, labor, or materials or reasonable substitutes therefor (including without limitation supply chain delays), governmental actions, civil commotions, casualty, actual or threatened public health emergency (including, without limitation, epidemic, pandemic, famine, disease, plague, quarantine, and other significant public health risk, such as the epidemic known as COVID-19 and its variants), governmental edicts, actions, declarations or quarantines by a governmental entity or health organization (including, without limitation, any shelter-in-place orders, stay at home orders or any restrictions on travel related thereto that preclude Tenant, its agents, contractors or its employees from accessing the Project for the activities related to construction of the Improvements, national or regional emergency), breaches in cybersecurity, and other causes beyond the reasonable control of the party obligated to perform, regardless of whether such other causes are (i) foreseeable or unforeseeable or (ii) related to the specifically enumerated events in this paragraph (collectively, a "**Force Majeure**"), shall excuse the performance of such party for a period equal to any such prevention, delay or stoppage and, therefore, if this Work Letter specifies a time period for performance of an obligation of either party, that time period shall be extended by the period of any delay in such party's performance caused by a Force Majeure. For purposes of this Section 5, the following shall be included as causes beyond the reasonable control of the party obligated to perform: epidemic; pandemic; disease; illness; national, regional or local emergency; quarantine; and governmental order. Notwithstanding anything to the contrary in this Work Letter, neither the inability to obtain financing or investment, lack of funding, nor any micro- or macro-economic or other adverse financial events impacting a party's business judgment, decisions, or priorities (e.g., by resulting in budgetary choices that cause delays) shall excuse a party's performance of its obligations hereunder. Nothing in the prior sentence shall be deemed to obligate either party to incur unusual or excessive costs to avoid the occurrence of Force Majeure.

8. Insurance.

8.1. Property Insurance. At all times during the period beginning with commencement of construction of the Landlord's Construction Work (excluding the LCW by Tenant) and ending when the Landlord's Construction Work is Complete pursuant to Section 11 of this Work Letter, Landlord shall maintain or cause to be maintained (in addition to the insurance required pursuant to the Lease) property insurance insuring Landlord and its affiliates, agents and employees, as their interests may appear. Such policy shall, on a completed values basis for the full insurable value at all times, insure against loss or damage by fire, vandalism and malicious mischief and other such risks as are customarily covered by the so-called "broad form extended coverage endorsement" upon all Landlord's Construction Work (other than the LCW by Tenant) and the TI by Landlord and the General Contractor's and any subcontractors' machinery, tools and equipment, all while each forms a part of, or is contained in, the Landlord's Construction Work and TI by Landlord or any temporary structures on the Premises, or is adjacent thereto; provided that, for the avoidance of doubt, insurance coverage with respect to the General Contractor's and any subcontractors' machinery, tools and equipment shall be carried on a primary basis by such General Contractor or subcontractor. Landlord agrees to pay any deductible, which deductible amount shall be considered a Construction Cost. Said property insurance shall contain an express waiver of any right of subrogation by the insurer against Tenant and its affiliates, agents and employees.

8.2. Workers' Compensation Insurance. At all times during the period of construction of the Landlord's Construction Work (other than the LCW by Tenant) and TI by Landlord, Landlord shall, and shall cause its contractors or subcontractors to, maintain statutory workers' compensation insurance as required by Applicable Laws.

8.3 Tenant's Insurance. At all times during the period of construction of the Tenant Improvements (other than the TI by Landlord) and the LCW by Tenant, Tenant shall, and shall its contractors and subcontractors to, maintain insurance as required pursuant to the Tenant Construction Manual referenced in the Lease.

9. Requests for Consent. Except as otherwise provided in this Work Letter, Tenant shall respond to all requests for consents, approvals, information, or directions made by Landlord pursuant to this Work Letter within five (5) days following Tenant's receipt of such request. If Tenant fails to respond within such five (5) days period, then Landlord may provide Tenant with a second written notice stating, in bold and prominent print, that "Tenant's failure to respond within two (2) days after Landlord's second notice shall be deemed approval by Tenant," and if Tenant does not respond within such two (2) day period, then Tenant shall be deemed to have approved such item.

Except as otherwise provided in this Work Letter, Landlord shall respond to all requests for consents, approvals, information, or directions made by Tenant with respect to the LCW by Tenant pursuant to this Work Letter within five (5) days following Landlord's receipt of such request. If Landlord fails to respond within such five (5) days period, then Tenant may provide Landlord with a second written notice stating, in bold and prominent print, that "Landlord's failure to respond within two (2) days after Tenant's second notice shall be deemed approval by Landlord," and if Landlord does not respond within such two (2) day period, then Landlord shall be deemed to have approved such item.

10. Budget and Tenant Improvement Allowance.

10.1. Budget. A preliminary budget for all hard and soft costs pertaining to the Landlord's Construction Work is attached hereto as Schedule 6 to the Work Letter (as the same may be modified or otherwise updated in accordance with this Work Letter, the "**Budget"**). The Budget includes a line item for contingency. Landlord may reallocate line items within the Budget and use the contingency in its sole discretion at any time. Landlord will use commercially reasonable efforts to provide Tenant with updates to the Budget and shall revise the Budget to reflect the final GMP; *provided* at a minimum, following the final approval of the Approved Core and Shell Plans Landlord shall provide Tenant with a monthly updated Budget and a reconciliation of actual costs incurred through the prior month. In addition, Landlord will (or will request that the General Contractor) copy Ionis Chief Accounting Officer, Darren Gonzales (e-mail address: [***]) on all draw packages submitted to Landlord by the General Contractor related to the Landlord's Construction Work. The Budget is for informational purposes only and is not binding on Landlord in any respect, and shall not create any limit on Aggregate Disbursements. The parties acknowledge that the LCW by Tenant is included within the Budget attached but shall not be included in subsequent updates to the Budget, as such work is being performed by Tenant.

10.2. Tenant Improvement Allowance; Funding of TI by Landlord. (a) Provided no monetary or material non-monetary Event of Default exists, Landlord shall provide Tenant with a Tenant Improvement allowance ("**TI Allowance**") of $41,208,250.00, which TI Allowance shall automatically be reduced by the amount of $15 per gross square foot (based on the agreed-upon 164,757 gross square feet set forth in the Lease) for every whole 1% reduction in the ratio of lab to office below 40% as finally determined in the Approved TI Plans for the entire Tenant Improvements (inclusive of the Day 2 Space) by the Architect (or as affected by any subsequent TI Change), nothing in this sentence being deemed to modify the Fundamental Requirements, which require the lab-to-office ratio to be no less than 35% to 65%, taking into account all of the Tenant Improvements (inclusive of the Day 2 Space). The TI Allowance can be applied by Tenant to offset the cost to permit, design and construct the Tenant Improvements, inclusive of the TI by Landlord (provided that in no event shall the TI Allowance be applied towards design and other so-called "soft costs", including without limitation consultant fees and the costs to acquire and install furniture, fixtures, and equipment) in an amount that exceeds 10% of the TI Allowance. Except as set forth in the immediately preceding sentence, in no event shall any of the TI Allowance be used for the acquisition of Tenant's furniture, fixtures, or equipment or other items of personal property, such as cabling and wiring, or for the LCW by Tenant. In no event may the TI Allowance be used for payments to any affiliates of Tenant. Landlord shall have no obligation to make any disbursements of TI Allowance not properly requisitioned by Tenant by the date that is one year following the Commencement Date and Tenant shall have no further right to any undisbursed TI Allowance thereafter; provided that the portion of the TI Allowance not requisitioned by Tenant with respect to the Day 1 Space may be requisitioned by Tenant by the date that is 18 months following the Commencement Date, and, thereafter, Tenant shall have no further right to any undisbursed TI Allowance.

(i) The TI Allowance will be available for monthly disbursements for permitted soft costs from and after the Effective Date of the Lease and for permitted hard costs following the commencement of the Tenant Improvements subject to the requirements set forth in this Work Letter. Landlord shall pay Landlord's Proportion (as defined below) of invoices made by Tenant on a form provided by Landlord within forty-five (45) days of receipt of a complete submission from Tenant (as set forth below), if Tenant requests and Landlord has received a satisfactory confirmation of non-responsibility on a form provided by Landlord, directly to the applicable vendor as requested by Tenant or to Tenant (to the extent Tenant has paid such requisitioned costs) on a progress payment basis. As a condition to Landlord's disbursement of any portion of the TI Allowance, Tenant shall provide Landlord with (A) appropriate paid or unpaid receipts or invoices for the amount requested to be paid from the TI Allowance, (B) partial, conditional lien waivers for such work from all persons or entities that could file mechanics' or materialmen's liens against the Building or the Project with respect to all work performed or services or materials provided through the date of each such invoice (subject only to receipt of the requisitioned amount) and, as a condition to the final release of retainage, final unconditional lien waivers for final payments, as applicable, for any contracts greater than Twenty Five Thousand Dollars ($25,000.00), which lien waivers shall comply with the appropriate provisions of California Civil Code, as reasonably determined by Landlord, (C) written authorization from Tenant to disburse the portion of the TI Allowance being requisitioned on a reasonable form provided by Landlord, (D) an application for payment from the Tenant's general contractors as approved and executed by Tenant and Tenant's architect, (E) evidence that amounts previously requisitioned by Tenant from the TI Allowance have been paid in full to the applicable third parties, and (F) such other documentation as may be reasonably requested by Landlord or its lender**.** Tenant may not make a requisition for application of the TI Allowance more frequently than once a month. The final disbursement of the TI Allowance shall be conditioned upon the recording of a Notice of Completion in a form reasonably approved by Landlord in the applicable county office.

"**Landlord's Proportion**" shall be determined separately for each phase of the Tenant Improvements by a fraction, the numerator of which is the TI Allowance (attributed 55.77% to the Day 1 Space and 44.23% to the Day 2 Space) and the denominator of which is the sum of (1) the total contract price for the design and engineering of the applicable phase of the Tenant Improvements and (2) the total contract price for the construction of the Tenant Improvements for the applicable phase of the Tenant Improvements (in each case, as evidenced by reasonably detailed documentation delivered to Landlord upon Landlord's request). Notwithstanding anything to the contrary set forth elsewhere in this Work Letter, Landlord shall not have any obligation to expend any portion of the TI Allowance until Landlord has approved in writing the budget for the Tenant Improvements, including the TI by Landlord (the "**Approved Budget**"), such approval not to be unreasonably withheld, conditioned, or delayed. The proposed Approved Budget shall be approved or disapproved by Landlord within ten (10) business days after delivery to Landlord. If Landlord fails to notify Tenant of disapproval within such ten (10) business day period, then Tenant may provide Landlord with a second written notice stating that "Landlord's failure to respond within five (5) business days after Tenant's second notice shall be deemed Landlord's approval to such Approved Budget," and if Landlord does not respond within such five (5) business day period, then Landlord shall be deemed to have approved Tenant's proposed Approved Budget. Prior to Landlord's approval of the Approved Budget, Tenant shall pay all of the costs and expenses incurred in connection with the Tenant Improvements as they become due, subject to reimbursement from the TI Allowance following Landlord's approval of the Approved Budget. The Approved Budget shall provide for approximately proportionate spending across the entire Premises on a per square foot basis (subject to customary and/or reasonable variations on a floor-by-floor basis for the applicable use mix on such floor, such as between office and laboratory space). Landlord shall not be obligated to reimburse Tenant for costs or expenses relating to the Tenant Improvements that exceed the amount of the TI Allowance. Landlord and Tenant shall cooperate to develop the budget for the TI by Landlord as part of Tenant's budgeting process, the parties acknowledging that such work will be performed by the General Contractor.

(ii) In the event Landlord fails to fund any portion of the TI Allowance when properly due hereunder within the aforementioned forty-five (45) day period, Tenant shall deliver written notice to Landlord and its lender stating that "Failure to fund the amount set forth in this request within 30 days may result in Tenant offset rights". If Landlord fails to remit such payment within an additional thirty (30) days following Landlord's receipt of Tenant's notice, Tenant shall have the right to offset such amounts against the next installments of Monthly Rent that become due and owing, which unpaid amounts shall bear interest at the Interest Rate accruing from the date the same were due and payable through the date paid in. Notwithstanding the foregoing, no such offset shall arise or accrue if Landlord disputes the Tenant's claim to an offset within ten (10) business days following Tenant's notice of the same. Any such disputes shall be resolved in accordance with Section 13, below.

(b) To the extent the cost of any TI by Landlord exceeds the TI Allowance, Tenant shall pay the same as Additional Rent within 30 days after invoice by Landlord as such work progresses, together with reasonable backup evidencing the same. Following the completion of the TI by Landlord, Landlord shall provide Tenant with such information as is reasonably required for the final reconciliation of such costs such that the entire amount of the Construction Costs incurred by Landlord on account of the TI by Landlord is included within the calculation of Base Rent (subject, however, to the limitations set forth in this Work Letter with respect to the TI Allowance).Notwithstanding anything to the contrary herein, in no event shall Tenant's obligation to fund the TI by Landlord pursuant this subparagraph (b) apply to the extent that such costs exceed the amount for such work shown on Schedule 9 unless and except to the extent such excess costs result from a TI Tenant Change Order Request or Tenant-requested Shell and Core Change.

11. Completion of Improvements. The Landlord's Construction Work shall be deemed "**Complete**" at such time as (a) Substantial Completion has occurred, (b) Landlord shall have provided Tenant with evidence that (i) the Landlord's Construction Work has been completed and paid for in full (which shall be evidenced by the Architect's certificate of completion), other than as provided in clause (ii), below, and (ii) the Punchlist Items (including any deficiencies noted in a third-party commissioning report for the Landlord's Construction Work, to the extent the same is included within the scope of the GMP Contract) have been completed and paid for in full, other than seasonal work such as landscaping. Following Completion, Landlord shall provide Tenant with electronic CADD files of the Landlord's Construction Work. Notwithstanding anything to the contrary in this Work Letter or the Lease, neither the LCW by Tenant nor the TI by Landlord is included for purposes of the determination of when the Landlord's Construction Work is Complete. Following the completion of the Landlord's Construction Work required for the Delivery Date to occur, Landlord shall continue to diligently prosecute the TI by Landlord in coordination with the completion of the Tenant Improvements by Tenant. If Landlord fails to substantially complete the TI by Landlord by the date (the "**TI Completion Date**") that Tenant substantially completes all of its Tenant Improvements and occupies the Premises for the conduct of its business, subject to extension for Tenant Delay and Force Majeure, then Tenant shall be entitled to a day-for-day abatement of Base Rent in the affected areas of the Premises from and after the TI Completion Date until the date that the TI by Landlord is substantially complete.

12. Tenant Delays.

(a) "**Tenant Delay**" means any actual delay in the Landlord's Construction Work or the TI by Landlord to the extent resulting from the acts or omissions of Tenant or any Tenant Party (rather than from Force Majeure or other delays that may have occurred due to Landlord's General Contractor, including delays caused by the Landlord's General Contractor's prosecution of the TI by Landlord, for example), including, without limitation, due to any accommodation of a Tenant initiated request (e.g., a Tenant requested change to the Schedule), any Tenant requested Shell and Core Change, the scope and design of the TI by Landlord (or any changes by Tenant to the same) as it impacts the permitting and Schedule for the Landlord's Construction Work or the TI by Landlord, interference with the Substantial Completion of the Landlord's Work (including without limitation on account of Tenant's early access pursuant to Section 3.4, above) or the substantial completion of the TI by Landlord, or failure of Tenant to provide its specifications for the Building Management System by the date required on Schedule 3. Except for Tenant Delays due to accommodation of a Tenant initiated request or any Tenant requested Shell and Core Change or change to the TI by Landlord for which Landlord provided to Tenant the estimated amount of any associated Tenant Delay (for which no notice will be required, and no obligation of Landlord to grant such request other than as expressly provided herein) or delays resulting from Tenant's failure to respond to act within the periods set forth in this Work Letter, if there is an event that Landlord contends is a Tenant Delay, then Landlord shall give Tenant written notice of such Tenant Delay as soon as is practicable following Landlord's knowledge of such delay ("**LW Delay Notice**") (provided, however, that no Tenant Delay shall be deemed to accrue under this Work Letter with respect to the Tenant Delay referenced in a LW Delay Notice until Landlord provides Tenant with such LW Delay Notice).

(b) Any Tenant Delay of less than a full day shall be deemed to be equal to a delay of one (1) full day. Landlord and Tenant have agreed to determine the length of any Tenant Delay as follows: (i) any delays resulting from the failure of Tenant to act within a time period specified in this Work Letter shall be equal to one (1) day for each day that the applicable Tenant Delay continues beyond the applicable time period required for such action under the Lease, (ii) in the event of any agreed Tenant Delay, as the parties may agree in writing from time to time, the length of such Tenant Delay shall be as agreed upon in writing by the parties at the time such Tenant Delay arises, and (iii) with respect to any other Tenant Delay, Landlord shall notify Tenant in writing of the claimed estimated length of such Tenant Delay within ten (10) business days after its occurrence and Tenant may elect by written notice delivered to the other within ten (10) business days thereafter to dispute the claimed estimated Tenant Delay in accordance with Section 13 of this Work Letter. Unless such estimate is disputed by written notice delivered within such ten (10) business day period, the length of such Tenant Delay shall be no less than the claimed estimated Tenant Delay.

(c) If the Landlord's Construction Work is delayed by Tenant Delay, then the date on which the Landlord's Construction Work would have achieved Delivery Condition or been Substantially Complete but for such Tenant Delay (i.e., without regard for Force Majeure or other delays that may have occurred but do not constitute Tenant Delays), as evidenced by written notice from Landlord to Tenant, shall be deemed to be the Delivery Date or the date of Substantially Completion, as applicable, unless such notice disputed in a written notice by Tenant to Landlord within five (5) business days after delivery of such determination, in which case such dispute will be determined by arbitration pursuant to 13, below.

13. **Dispute Resolution Process.**

13.1. All disputes between Landlord and Tenant regarding Tenant Delays and other matters expressly referencing this Section 13 shall be resolved in accordance with this Section 13. Any arbitration decision under this Section 13 shall be enforceable in accordance with Applicable Laws in any court of proper jurisdiction.

(a) Any arbitration conducted pursuant to this Section 13 shall be conducted in as expeditious manner as possible to avoid delays in the construction of Landlord's Construction Work and Tenant Improvements.

(b) Any and all claims or disputes to be resolved pursuant to this Section 13 shall be resolved as follows: Landlord and Tenant shall promptly meet and confer to attempt in good faith to resolve such dispute and, if such dispute is not fully resolved within fifteen (15) days after delivery of written notice of such dispute, the parties agree that the claims or disputes shall be settled by arbitration administered by the American Arbitration Association ("**AAA**") under its Construction Industry Arbitration Rules (or any successor organization), and judgment on the award rendered by the arbitrator may be entered in any court having jurisdiction thereof. Further, Landlord and Tenant agree to direct the San Diego Regional Office of the AAA to appoint a single arbitrator who (i) shall have a minimum of fifteen (15) years of experience in construction disputes involving first class office and laboratory buildings in the appliable market, (ii) has not worked for either party for the prior five (5) years, (iii) is not be affiliated with either Landlord or Tenant, and (iv) has not worked for either party or its affiliates at any time during the prior five (5) years (a "**Qualified Construction Arbitrator**").

13. 2 Both Landlord and Tenant shall have the opportunity to present evidence and outside consultants to the appointed arbitrator. The arbitrator shall decide the dispute by written decision. The arbitration shall be conducted in accordance with the expedited procedures of the AAA's Construction Industry Arbitration Rules insofar as such rules are not inconsistent with the provisions of the Lease (in which case the provisions of the Lease shall govern) and shall be concluded, with a decision issued, no later than ten (10) business days after the date that such dispute is submitted to the appointed arbitrator. The decision of the arbitrator shall be final and binding on the parties. The parties shall comply with any orders of the arbitrator establishing deadlines for any such proceeding. The fee of the arbitrator shall be paid equally by the parties, and each party shall pay all other costs incurred by it in connection with the arbitration.

14. Miscellaneous.

14.1. Number; Headings. Where applicable in this Work Letter, the singular includes the plural and the masculine or neuter includes the masculine, feminine and neuter. The section headings of this Work Letter are not a part of this Work Letter and shall have no effect upon the construction or interpretation of any part hereof.

SCHEDULE 1 (to Exhibit B)

PERMITS AND APPROVALS

Entitlements:

Architectural Committee Review under the CCRs
CEQA determination that the project is exempt from CEQA
Site Development Plan

Ministerial Approvals:

Grading Permit
Lot Line Adjustment between Lots 21 & 22
Building Permit for Landlord’s Construction Work
Shoring Permit
Landscaping Permit
Traffic Control Permit for Pedestrian Bridge

SCHEDULE 2 (to Exhibit B)

CONCEPT PLAN AND ALLOCATION OF RESPONSIBILITY

Site Development Permit Package SDP 2021-0029 Prepared by DGA and last revised 8/31/22

Site Development Permit Package SDP 2021-0029 – Landscape Plans - Prepared by DGA and last revised 8/31/22

Site Development Permit Package SDP 2021-0029 – Civil Plans - Prepared by DGA and last revised 8/31/22

Copies of the foregoing plans are on file with Landlord.

[***]

SCHEDULE 3 (to Exhibit B)

DEVELOPMENT SCHEDULE

[***]

SCHEDULE 4 (to Exhibit B)

TENANT IMPROVEMENT DESIGN MILESTONES

Phase I (includes Schematic Design through Design Development for Phase I and Phase II)
100% Schematic Design April 28,2023
100% Design Development July 17, 2023
85% Construction Documents (Permit Submittal) November 3, 2023
100% Construction Documents March 15, 2024

Phase II
Schematic Design Submitted in Phase I
Updated Design Development September 15, 2025
85% Construction Documents (Permit Submittal) January 9, 2026
100% Construction Documents April 21, 2026

SCHEDULE 5 (to Exhibit B)

TENANT IMPROVEMENT PROGRAM

The program for the Tenant Improvements shall be compatible in all respects with the Fundamental Requirements, provide for the improvements necessary for full occupancy of the Premises, and otherwise be consistent with first-class office and laboratory use, with ancillary uses as permitted pursuant to the Permitted Use. The Tenant program shall provide for fit and finishes consistent with, or of a better quality than, Tenant's existing office and laboratory premises located at 2855 Gazelle Ct., Carlsbad, California. The fit plan attached is representative of the scope and nature of the Tenant Improvements.

[***]

SCHEDULE 6 (to Exhibit B)

PRELIMINARY BUDGET

Cost Item	Ref	Estimate	$PSF
Land Acquisition		33,000,000	200
Closing Costs Allocation		495,000	3
Soft Costs		12,955,502	79
Hard Costs		87,782,086	533
Landlord Tenant Improvement Allowance		41,208,250	250
Development Fee		3,434,210	21
Operating Shortfall		2,352,572	14
Financing Costs		17,812,408	108
Total Budget	**(A)**	**199,040,029**	**1,208**

SCHEDULE 7 (to Exhibit B)

DELIVERY CONDITION

1. The Building becomes “dried in” meaning that it is a “water tight shell”, whether by permanent or temporary measures, in a manner that Landlord reasonably determines in good faith, based on the input of General Contractor, will not interfere with the progress of the Tenant Improvements in any material way due to the condition of the Building exterior.
2. As part of Tenant’s schematic document submission to Landlord for the Tenant Improvements, Tenant shall identify any locations (not to exceed a reasonable number) where Tenant desires to place deck inserts on each floor of the Premises to accommodate Tenant’s internal staircases or similar, customary items consistent with comparable first-class buildings used for life sciences purposes. Landlord shall cooperate and collaborate with Tenant to allow for the installation of such approved deck inserts, if any, prior to the occurrence of Delivery Condition, subject to agreeing with Tenant on the minimum amount of Tenant Delay resulting from the same and the other terms and conditions of the Work Letter.
3. Tenant shall have safe and reasonably efficient access to the work site.
4. Installation of floors should be sufficiently complete to allow layout to begin of floor surfaces, column lines, control lines or (to the extent applicable) Trimble reference points. Any stored material for Landlord’s Construction Work (including turnover attic stock) must be located outside of the building (on site), or in an area or areas on each applicable floor designated by the General Contractor that permit the orderly progress of Tenant Improvements.
5. Site access is available, as reasonably designated by the General Contractor, for efficient material delivery and Building loading.
6. Site access is available for the Tenant Improvement contractor and subcontractor’s construction trailer (if applicable) and laydown space in a location reasonably designated by the General Contractor.
7. Temporary electrical infrastructure is available to the Premises and Building, with sufficient capacity to power small tools, temporary lighting, and equipment to provide temporary ventilation/heating to perform the Tenant Improvements using normal means of power use. Electrical rooms within the Premises to be constructed as part of the Landlord’s Construction Work are accessible for performance of the Tenant Improvements, should Tenant Improvements be required in those areas.
8. Tenant’s Contractor has ability to terminate electrical wires in electrical switchgear and distribution boards installed as part of the Landlord’s Construction Work.
9. All base Building shafts within the Premises are framed.
10. Tenant’s contractor is able to use fire stairs to travel to and from the street level and between each Tenant floor. Use of stairs subject to coordination with Landlord’s completion of finishes and inspections of the stairs. Completion of and ability to connect Landlord-provided wet stacks (vent, sanitary, storm) to the extent included within Landlord’s Construction Work, subject to any required government approvals.
11. Fire Life Safety systems (fire sprinkler, fire alarm) are able to be tied into by the Tenant Improvement contractor (for purposes of clarity, the fire standpipes shall be installed, the fire alarm backbone will be installed but not yet operational).

Schedule 8 (to Exhibit B)

Minimum Vertical MEP Infrastructure Standards

Must include the following:

Tenant will size the following spaces to accommodate equipment for a 50/50 lab office ratio given the "Typical San Diego Life Science Tenant MEP Performance Table" set forth below for the following areas: service yard for generator; sizing for main electrical room; floor level electrical room sizing and risers; plumbing site connections for sanitary, storm, domestic water and natural gas (if code allows); plumbing room sizing; service yard sizing for cooling towers; mechanical room sizing for chillers, boilers and air handling units; roof area allocated for MEP equipment; mechanical shaft sizes/locations – supply air, lab exhaust air, restroom exhaust and office return air.

Tenant agrees to meet the typical 50/50 lab office ratio minimum for cooling tonnage listed in the "Typical San Diego Life Science Tenant MEP Performance Table" (1163 tons), which includes sizing of the chillers, cooling tower/s, chiller pumps, chill water piping (upstream of the air handling units), insulation and associated electrical services to the equipment listed above.

Tenant agrees to meet the typical 50/50 lab office ratio minimum for heating loads listed in the "Typical San Diego Life Science Tenant MEP Performance Table" (5830 MBH), which includes sizing of heating hot water boilers, heating hot water pumps, heating hot water piping (upstream of the air handling units), insultation and associated electrical services to the equipment listed above.

May include the following ("Tenant Optional MEP Infrastructure"):

Tenant may, but shall not be required to, meet the minimum supply and exhaust CFM/SF per the "Typical San Diego Life Science Tenant MEP Performance Table". All ductwork and its insulation, air handling units, and exhaust fans will be sized to meet the TI Plans.

Typical San Diego Life Science Tenant MEP Performance Table

	CFM/SF (Supply)	CFM/SF (Exhaust)	Heating Loads (MBH)	Cooling Tons
Typical 40/60 Lab Office Ratio	1.52	0.93	5357	1040
Typical 50/50 Lab Office Ratio	1.6	1.15	5830	1163

To the extent that the Approved Core and Shall Plans do not contain any of the Tenant Optional MEP Infrastructure, then Landlord shall have the option to either (1) on or before the first to occur of (x) the date that is 90 days following the Tenant's final approval of the Approved Core and Shell Plans or (y) the date that is fifteen (15) days following Tenant's delivery of the schematic design phase of the TI Plans to Landlord, notify Tenant in writing of Landlord's election pursuant to this clause (1) and thereafter cause the Architect to modify the Approved Core and Shell Plans to include such Tenant Optional MEP Infrastructure as Landlord may elect and the General Contractor to construct the same as part of the Landlord's Construction Work (but such costs shall not be included within the Construction Costs) (any such changes being deemed to be Shell and Core Permitted Changes), or (2) notwithstanding anything in the Lease to the contrary, in the event that the Lease terminates prior to the scheduled expiration date, draw on the Letter of Credit in whole or in part, as Landlord elects, from time to time and use the funds so drawn to design and construct all or any part of the Tenant Optional MEP Infrastructure not included within the Approved Core and Shell Plans. The provisions of this paragraph shall survive the termination or earlier expiration of the Lease.

Schedule 9 (to Exhibit B)

LCW by Tenant and TI by Landlord

IONIS - BTS

SCHEDULE 9 - EXECUTIVE SUMMARY
PUBLISH DATE 9/22/2023

		ANTICIPATED CONTRACT AMOUNT FOR GENERAL CONTRACTOR ($)	LANDLORD HELD CONTINGENCY ($) 5%	BUILDER'S RISK INSURANCE COSTS ($)	TOTAL ($)
CORE & SHELL	TI BY LANDLORD	$ 2,220,477	$ 111,024	$ 396,231	$ 2,727,732
WARMUP	LCW BY TENANT	$ 9,934,548	$ 496,727	$ -	$ 10,431,276

TI BY LANDLORD			
ITEM NUMBER	DESCRIPTION	COSTS ($)	REMARKS
1	Underground package to Building - site electrical	$ 207,990	Tenant requested change for second electrical service
2	Building passenger elevator (1 cab) upgraded from 3,500# capacity to 5,000#	$ 133,202	Tenant requested change
3	TI underground piping in C&S permitting package (not included WU underground sanitary)	$ 535,377	Tenant requested change
4	Emergency Electrical service for 50/50 (office/lab) split above 5W/SF on lab SF	$ 444,716	Tenant requested change
5	Fire suppression deduct to remove upturned heads and mains	$ -	Included in Landlord scope
6	Structural dunnage above roof of AHUs (concrete pads at roof)	$ 31,178	Tenant requested change
7	Exterior changes to curtain wall	$ 140,000	Includes BNB indirect costs
8	Depressed slabs (Lobby / Restrooms)	$ 2,857	Tenant requested change
9	Delta A - 1/2 cost of Delta A Roof top Pump Room	$ 170,514	Tenant requested change
10	Delta C - Structural Changes	$ 288,386	Tenant requested change
11	Control area fire rating changes	$ 215,240	Tenant requested change
12	East Electrical Room - Walls/DFH/FSD	$ 49,058	Tenant requested change for second electrical room
13	L3 Slab Extension	$ 1,959	Tenant requested change
14	Exterior skin modifications to accommodate CO2 + LN refill requirements	$ -	Door / opening move only, no cost impact, caught early during design coordination
15	Delta A - 1/2 cost of thickened slab edge	$ 127,699	Tenant requested change
SUBTOTAL BNB COSTS		$ 2,220,477	
16	Builders Risk Insurance	$ 396,231	Based on 51% (Landlord) / 49% (Tenant) split
TOTAL COST		$ 2,616,708	

IONIS - BTS

SCHEDULE 9 - LCW BY TENANT (WARMUP)
PUBLISH DATE 9/22/2023

LCW BY TENANT			
ITEM NUMBER	ITEM DESCRIPTION	COSTS ($)	REMARKS
1	BNB Warmup Budget (publish date 8/31/23)	$ 12,001,004	Ref. Item # 2 onward for more detail. Includes all indirect costs. Adjusted for credit for utility sets
2	Tonnage increase - 1163 on to 1350 ton	$ (451,506)	Tenant requested change to increase capacity from Schedule B. Includes all indirect costs.
3	Heating hot water from 5,800 MBH to 9,500 MBH	$ (392,156)	Tenant requested change to increase capacity from Schedule B. Includes all indirect costs.
4	Office & Lab Exhaust	$ (582,445)	Tenant requested change to increase capacity from Schedule B. Includes all indirect costs.
5	Credit for utility sets	$ (314,314)	Approved value engineering option. Includes all indirect costs. $464K total credit for utility sets. Tenant allocation of credit ~$150K.
6	Equipment Premium	$ (326,035)	Tenant requested equipment selection premium costs for Daikin ILO York (Chillers); Parker ILO Cleaver Brooks (Condensing Boilers); BAC ILO Morely (Cooling Towers). Includes all indirect costs.
TOTAL COSTS		$ 9,934,548	

EXHIBIT C

FORM OF TENANT ESTOPPEL CERTIFICATE

The undersigned as Tenant under that certain Lease Agreement (the "**Lease**") made and entered into as of _____,with LOTS 21 & 22 OWNER (DE) LLC, a Delaware limited liability company, as Landlord, for the Building, land, and parking facilities located at 2850, 2855 & 2859 Gazelle Court, Carlsbad, California (the "**Premises**"), certifies as follows:

1. Attached hereto as Exhibit A is a true and correct copy of the Lease and all amendments and modifications thereto. The documents contained in Exhibit A represent the entire agreement between the parties as to the leasing of the Premises. Capitalized terms used but not defined herein have the meanings ascribed to them in the Lease.

2. The undersigned has commenced occupancy of the Premises described in the Lease, currently occupies the Premises, and the Term commenced on _____, 20___.

3. The Lease is in full force and effect and has not been modified, supplemented or amended in any way except as provided in Exhibit A. Tenant is not entitled to receive any concession or benefit (rental or otherwise) or other similar compensation in connection with leasing the Premises other than as set forth in the Lease.

4. Tenant has not transferred, assigned, or sublet any portion of the Premises nor entered into any license or concession agreements with respect thereto except as follows _____.

5. Rent became payable on _____, 20___.

6. The current Term expires on _____, 20___.

7. The Lease is enforceable and neither Tenant nor, to Tenant's actual knowledge, Landlord is in default thereunder except as follows: _____. Without limiting the foregoing, (i) all construction and installation of tenant improvements required to be performed by or paid by Landlord under the Lease have been completed and paid and (ii) there are no unpaid allowances or rental concessions payable or creditable to Tenant which have not been paid or credited in full, except as follows: _____.

8. No rental has been paid in advance.

9. As of the date hereof, Tenant has no presently exercisable defenses or offsets which preclude enforcement of the Lease by Landlord except as follows: _____.

10. All monthly installments of Base Rent, Additional Rent, and Taxes have been paid when due through _____. The current monthly installment of Base Rent is $_____.

11. Except for the Right of First Negotiation granted to Tenant pursuant to Article 11, Tenant does not have any option to purchase or right of first refusal or first offer to purchase the Premises, or any portion thereof, or any interest therein and the only interest of Tenant in such property is as the Tenant under the Lease.

12. The amount of the Security Deposit held by Landlord, to secure Tenant's performance under the Lease is _____ Dollars ($_____). No portion of the Security Deposit has been utilized or applied by Landlord.

13. Tenant is not the subject of any bankruptcy, insolvency, debtor's relief, reorganization, receivership or other similar proceeding.

The undersigned acknowledges that this Estoppel Certificate may be delivered to Landlord's prospective mortgagee, trust deed holder or a prospective purchaser or investor, and acknowledges that it recognizes that if same is done, in addition to Landlord, said mortgagee, prospective mortgagee, trust deed holder or prospective purchaser or investor will be relying upon the statements contained herein in making the loan or acquiring the Premises, and in accepting an assignment of the Lease as collateral security, and that receipt by it of this Estoppel Certificate is a condition of making the loan or acquisition of the Premises.

If Tenant is a corporation, limited liability company or partnership, each individual executing this Estoppel Certificate on behalf of Tenant hereby represents and warrants that Tenant is a duly formed and existing entity qualified to do business in the State of California, if required by law, and that Tenant has full right and authority to execute and deliver this Estoppel Certificate and that each person signing on behalf of Tenant is authorized to do so.

Tenant, by providing this Estoppel Certificate, does not waive (i) any of its claims, defenses, offsets, or rights against Landlord discovered after the date hereof, or (ii) any of Tenant's rights first arising after the date hereof provided by any federal, state or local laws, ordinances, rules and regulations, court orders, governmental directives and governmental orders and all interpretations of the foregoing.

Nothing in this Estoppel Certificate shall be deemed to amend, modify or alter the Lease and in the event of any conflict between the Lease and this Estoppel Certificate, the Lease shall prevail. This Estoppel Certificate is delivered in good faith and shall not subject Tenant or the individual signatory to any liability (other than estoppel effect) for any purpose, including, without limitation, damages for inaccuracies, errors or omissions, except to the extent resulting from fraud or an intentional and material misstatement of fact.

[Remainder of page intentionally left blank]

Executed at_____ on the_____day of_____, 20_____.

"Tenant"

IONIS PHARMACEUTICALS, INC., a
Delaware corporation

By: _____
Name: _____
Title: _____
Date Signed: _____

EXHIBIT D

FORM OF MEMORANDUM OF LEASE

This Memorandum of Lease (this "**Memorandum of Lease**") is made as of this [ ]day ____ of [_____] , 20__, by and between LOTS 21 & 22 OWNER (DE) LLC, a Delaware limited liability company with its principal mailing address of [___] ("**Landlord**"), and IONIS PHARMACEUTICALS, INC., a Delaware corporation, with its principal mailing address of [_____] ("**Tenant**"). All capitalized terms not otherwise defined herein shall have the meaning ascribed to such term in the Lease (as defined below).

1. Premises. Landlord owns and leases, demises and grants to Tenant, and Tenant leases from Landlord, that certain real property located at 2850, 2855 & 2859 Gazelle Court, Carlsbad, California, 92010, as more particularly described on Schedule A attached hereto and made a part hereof (the "**Leased Premises**") pursuant to the terms, covenants and conditions of that certain Lease Agreement dated as of _____, 20__ (the "**Lease**"). Capitalized terms used herein shall have the same meaning as set forth in the Lease, except to the extent such terms are specifically defined in this Memorandum of Lease.

2. Term. The initial Term of the Lease shall be for a period of fifteen (15) years commencing on [_____], [20___] and expiring on the last day of the one hundred eightieth (180th) full calendar month next following such date.

3. Option to Extend. Landlord grants to Tenant the option to extend the term of the Lease at the expiration of the Initial Term for two (2) successive periods of five (5) years each, aggregating ten (10) years. Each such renewal option must be exercised no later than twelve (12) months prior to the expiration of the initial Term or the then-current Renewal Term.

4. Successors and Assigns. The conditions and provisions hereof shall inure to the benefit of and shall be binding upon Landlord, Tenant, and their respective successors and assigns, and shall run with the land.

5. Memorandum. The rentals to be paid by Tenant and all of the obligations and rights of Landlord and Tenant are set forth in the Lease. This Memorandum of Lease is merely a memorandum of the Lease and is subject to all of its terms, conditions and provisions. In the event of any inconsistency between the terms of the Lease and this Memorandum of Lease, the terms, covenants and conditions of the Lease shall prevail.

6. Counterparts. This Memorandum of Lease may be executed in any number of counterparts, each of which shall be an original, but all of which shall together constitute one and the same document.

[No further text on this page. Signature page to follow.]

IN WITNESS WHEREOF, Landlord has caused its duly authorized officer to execute this Memorandum of Lease as of the date first noted above.

LANDLORD:
LOTS 21 & 22 OWNER (DE) LLC, a
Delaware limited liability company

By: _____
Name: _____
Title: _____

STATE/COMMONWEALTH OF _____)
CITY/COUNTY OF _____)

On the ____ day of _____ in the year 20__, before me, the undersigned, a Notary Public in and for said state, personally appeared _____, personally known to me or proved to me on the basis of satisfactory evidence to be the individual whose name is subscribed to the within instrument, and acknowledged to me that he executed the same in his capacity, and that by his signature on the instrument, the individual, or the person upon behalf of which the individual acted, executed this instrument.

_____
Notary Public

My Commission Expires:_____

IN WITNESS WHEREOF, Tenant has caused its duly authorized officer to execute this Memorandum of Lease as of the date first noted above.

TENANT:

IONIS PHARMACEUTICALS, INC., a
Delaware corporation

By: _____
Name: _____
Title: _____

A notary public or other officer completing this certificate verifies only the identity of the individual who signed the document to which this certificate is attached, and not the truthfulness, accuracy, or validity of that document.

STATE OF CALIFORNIA)
) §
County of _____)

On _____, before me,_____ a Notary Public, personally appeared _____who proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within instrument and acknowledged to me that he/she/they executed the same in his/her/their authorized capacity(ies), and that by his/her/their signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the foregoing paragraph is true and correct

WITNESS my hand and official seal.

_____
Signature of Notary

(Affix seal here)

Schedule A to

Memorandum of Lease

[to be attached]

EXHIBIT E

FORM OF SNDA

WHEN RECORDED MAIL TO
_____
_____
_____
Attention: _____

SPACE ABOVE THIS LINE FOR RECORDER'S USE

SUBORDINATION, NON-DISTURBANCE AND ATTORNMENT AGREEMENT

This SUBORDINATION, NON-DISTURBANCE AND ATTORNMENT AGREEMENT (hereafter referred to as "Agreement") made as of _____, 2022, by and between _____, having an address at _____, as administrative agent (with its successors or assigns, "Agent") for itself and certain lenders now or hereafter party to the Loan Agreement (as hereinafter defined) (the "Lenders"), _____, a _____, having an address of _____ ("Tenant") and _____, a _____, having an address at _____ ("Landlord").

The Lenders have made a loan to Landlord in the maximum principal amount of $_____ in accordance with the terms of that certain [Loan Agreement] dated as of _____, 2022 (the "Loan"), by and among Landlord, Agent and Lenders (as the same may hereafter be amended, reinstated, extended, supplemented or otherwise modified from time to time, the "Loan Agreement"),

Pursuant to the Loan Agreement, the Agent, for the benefit of the Lenders, is the holder of a certain [Deed of Trust, Security Agreement, Assignment of Leases and Rents, and Fixture Filing] (as the same may be amended, extended, supplemented or otherwise modified or restated from time to time, the "Security Instrument") granted by Landlord to Agent, for the benefit of the Lenders, and recorded in the official records of San Diego County, California, which constitutes a first lien against the real property described on Schedule A attached hereto and the improvements thereon or to be constructed thereon (the "Property").

Tenant has entered into a lease with Landlord dated as of _____, 2022 (the "Lease") covering all of the Property (the "Premises"). All capitalized terms used but not defined in this Agreement shall have the meanings set forth in the Lease.

For mutual consideration, including relying on the mutual covenants and agreements contained in this Agreement, the receipt and sufficiency of which are hereby acknowledged, Agent, Landlord and Tenant agree as follows:

1. **Subordination of Lease**. Subject to the terms of this Agreement, the Lease and all of Tenant's right, title, and interest in and to the Property thereunder (including, but not limited to, any option to purchase, right of first refusal to purchase, or right of first offer to purchase the Property or any portion thereof) is and shall be subject and subordinate to the Security Instrument and to all present and future advances under the obligations secured thereby and all renewals, amendments, modifications, consolidations, replacements and extensions thereof, to the full extent of the principal amount and other sums secured thereby and interest thereon, so that at all times the Security Instrument shall be and remain a lien on the Property prior to and superior to the Lease for all purposes, subject to the provisions set forth in this Agreement. Such subordination shall have the same force and effect as if the Security Instrument and such renewals, modifications, consolidations, replacements and extensions of the Security Instrument had been executed, acknowledged, delivered and recorded prior to the Lease, all amendments or modifications of the Lease, and any notice of the Lease.

2. **Attornment**. Tenant will attorn to and recognize: (i) Agent (including for this purpose any transferee or nominee of Agent), whether as mortgagee in possession or otherwise; or (ii) any purchaser at a foreclosure sale under the Security Instrument; or (iii) any transferee that acquires possession of or title to the Property (whether by acceptance of a deed in lieu of foreclosure or otherwise); or (iv) any successors and assigns of such purchasers and/or transferees (each of the foregoing persons or entities described in clauses (i) through (iv) above, a "Successor"), as its landlord for the unexpired balance (and any extensions, if exercised) of the term of the Lease upon the terms and conditions set forth in the Lease (as affected by this Agreement), and Tenant shall pay and perform in favor of Successor all of the obligations of Tenant under the Lease as if Successor were the original lessor under the Lease. Such attornment shall be effective and self-operative without the execution of any further instruments by any party hereto; provided, however, that Tenant will, upon request by Agent or any Successor, execute a reasonable written agreement attorning to Agent or such Successor, which agreement shall, in any event, be subject to the terms and provisions of this Agreement.

3. **Non-Disturbance**. So long as the Lease is in effect and Tenant complies with Tenant's obligations under this Agreement and is not in default (beyond the expiration of any applicable cure period) under the Lease, Agent and any Successor (i) will recognize the Lease and Tenant's rights and options under the Lease as the tenant of the Premises for the remainder of the term of the Lease (as affected by this Agreement), including any extension options, if exercised, and (ii) will not disturb Tenant's use, possession and quiet enjoyment of the Premises, nor will Tenant's rights under this Lease be impaired (except as provided in this Agreement), and (iii) shall not name or join Tenant as a defendant in any foreclosure action, sale under a power of sale or transfer in lieu of the foregoing (collectively, a "Foreclosure") unless a joinder is required by law to perfect a Foreclosure or other remedy, but then only for such purpose and not for the purpose of terminating the Lease.

4. **Assignment of Leases**. Tenant acknowledges that it has been advised that Landlord has assigned the Lease and the rents thereunder to Agent, for the benefit of the Lenders, pursuant to the Security Instrument. Tenant acknowledges that the interest of the Landlord under the Lease is to be assigned to Agent solely as security for the purposes specified in the Security Instrument, and, on account of the Security Instrument, Agent shall have no duty, liability or obligation whatsoever under the Lease or any extension or renewal thereof, either by virtue of the Security Instrument or by any subsequent receipt or collection of rents thereunder, unless Agent shall specifically undertake such liability in writing. The foregoing agreement by Tenant shall not adversely affect any rights of Tenant under the Lease with respect to the Landlord in the event of nonperformance by Landlord, subject to the terms of this Agreement. Tenant agrees that if Agent, pursuant to the Security Instrument, and whether or not it becomes a mortgagee in possession, shall give written notice to Tenant that Agent has elected to require Tenant to pay to Agent the rent and other charges payable by Tenant under the Lease, Tenant shall (without any duty to inquire as to the enforceability or validity of Agent's notice) until Agent shall have canceled such election in writing, thereafter pay to Agent all rent and other sums payable under the Lease and such payments to Agent shall be treated as payments made under the Lease. Any such payment shall be made notwithstanding any right of setoff, defense or counterclaim which Tenant may have against Landlord, or any right to terminate the Lease. Landlord authorizes and directs Tenant to immediately and continuously make all such payments at the direction of Agent, releases Tenant of any and all liability to Landlord for any and all payments so made, and agrees that payments actually made by Tenant to Agent shall be credited towards the amounts due under the Lease.

5. **Limitation of Liability**. In the event that Agent (including for this purpose any transferee or nominee of Agent) or any other Successor succeeds to the interest of Landlord under the Lease, or title to the Property, then none of Agent, any Lender or any Successor shall be: (i) liable in any way to Tenant for any act or omission, neglect or default on the part of any prior landlord under the Lease; provided, that, nothing in this clause being deemed to relieve Agent or any Successor of an ongoing default on the part of Landlord with respect to repair and maintenance of the Premises that first arose prior to such succession, provided that Tenant notified Agent of such default in accordance with Section 7 of this Agreement and Agent failed to cure same and Agent or any Successor shall have the obligation to cure such ongoing repair and maintenance defaults on the part of Landlord that continue from and after Successor succeeds to the rights of Landlord under the Lease, regardless of when such default or obligation from arose, provided that Tenant notified Agent of such default in accordance with Section 7 of this Agreement and Agent failed to cure same; (ii) responsible for any monies (including security deposits) owing by or on deposit with (or any letter of credit on deposit with) Landlord to the credit of Tenant (except to the extent any such deposit or letter of credit is actually received by Agent or such Successor, as applicable); (iii) subject to any defense, counterclaim or setoff which theretofore accrued to Tenant against any prior landlord; provided, however, that the foregoing shall not limit Tenant's right to exercise against Agent or such Successor any offset right otherwise available to Tenant because of events occurring after the date of succession and attornment; (iv) bound by any termination, amendment or modification, or assignment/subletting of the Lease after the date hereof (unless Agent expressly approved in writing such termination, amendment or modification, or assignment or subletting or the same does not require the Agent's approval pursuant to the terms of the Loan Agreement) of the Lease (provided that, (A) as it relates to any assignments/subletting of Lease undertaken in connection with the terms and provisions set forth in the Lease, Agent shall have the same approval rights as the Landlord has with respect to same and (B) no such approval shall be required with respect to amendments solely evidencing the exercise of Tenant's option to extend the Lease and assignments or sublets that do not require the consent of the Landlord pursuant to the terms of the Lease); (v) bound by any previous prepayment of rent for more than one (1) month of the date due, which was not approved in writing by Agent ;(vi) required after a fire, casualty or condemnation of the Property or Premises to repair or rebuild the same to the extent that such repair or rebuilding requires funds in excess of the insurance or condemnation proceeds specifically allocable to the Premises and arising out of such fire, casualty or condemnation which have actually been received by Agent, and then only to the extent required by the terms of the Lease (Agent acknowledging that the exercise by Tenant of its remedies pursuant to Article 9 of the Lease are unaffected by the provisions of this clause (vi)), (vii) be liable for or incur any obligation with respect to any representations or warranties made by Landlord under the Lease; (viii) liable beyond Agent's, such Lender's, or such Successor's, as applicable, interest in the Property and in the rents, proceeds and profits therefrom; or (ix) except as expressly provided below, responsible for any obligation of Landlord to undertake or complete any work or fund any allowance for tenant improvements.

Furthermore, notwithstanding anything to the contrary contained in this Agreement (except as set forth in the immediately following paragraph) or the Lease, no Agent, Lender or Successor shall have any obligation to undertake or complete any of the Landlord's Construction Work (as defined in the Lease) or advance the TI Allowance (as defined in the Lease) after it succeeds to the interest of Landlord under the Lease or title to the Property (collectively, the "Landlord Work Obligations").

[Only applicable prior to the occurrence of Substantial Completion under the Lease:] Notwithstanding the foregoing, if the Landlord Work Obligations have not been fulfilled in accordance with the terms and provisions of the Lease, then Agent or Successor (as applicable) shall have thirty (30) days from the earlier of the date on which either of the following occur (the "Succession Date"): (i) Agent or any Successor (as applicable) provides written notice to the Tenant that Agent or Successor (as applicable) has succeeded to the interest of Landlord under the Lease, or (ii) Agent or Successor (as applicable) has taken title to the Property, to send written notice (the "Intention Notice") to Tenant stating whether or not Agent or such Successor intends to fulfill the remaining Landlord Work Obligations under the Lease (which may include fulfillment of the obligation to complete the Landlord's Construction Work without fulfilling the obligation to fund the TI Allowance or vice versa). If and to the extent in such Intention Notice Agent or such Successor (as applicable) states that Agent or such Successor intends to be so bound, then such provisions of the Lease shall be binding on the Agent or such Successor (as applicable). If in such Intention Notice Agent or Successor (as applicable) states in writing that it does not intend to be so bound with respect to the Landlord's Construction Work or fails to timely provide such Intention Notice to Tenant within such thirty (30) day period, then Tenant shall have the right, by giving a notice to the Agent or such Successor (as applicable) (the "Succession Election Notice") within sixty (60) days following the Intention Notice, or if no Intention Notice has been delivered, within sixty (60) days of the Succession Date, to, subject to compliance with the Tenant Completion Conditions (as defined below), complete the Landlord's Construction Work at its expense in accordance with the terms and conditions of the Lease (in which case Base Rent shall be determined based on amounts previously expended by Landlord for Construction Costs plus any TI Allowance funded by Agent or such Successor, and otherwise in accordance with the Lease), and if Agent or Successor (as applicable) agreed to complete the Landlord's Construction Work but declined to fund any remaining TI Allowance, exercise its right pursuant to the Lease to deduct the remaining amount of TI Allowance when due from Base Rent in accordance therewith to the extent the same has been included in the calculation of Base Rent under the Lease, until the full amount of TI Allowance included within the Base Rent is recouped by Tenant (but without the necessity of giving any additional notices to Landlord); and further provided, however, that the Agent or Successor (as applicable) can render any Succession Election Notice null and void and of no force and effect if, within thirty (30) days after the giving of such Succession Election Notice, the Agent or Successor (as applicable) agrees to be bound by the applicable provisions of the Lease. Tenant's failure to give a Succession Election Notice in the time period required above shall be deemed to be an election pursuant to the [clause (X)][1] of the immediately preceding sentence. To the extent the Tenant delivers the Succession Election Notice, Tenant hereby acknowledges and agrees that the Agent or Successor (as applicable) is released (except to the extent set forth in the Intention Notice and as otherwise expressly set forth in this paragraph) from any and all obligations under the Lease with respect to the Landlord's Construction Work and the payment of the TI Allowance.

As used herein, the "Tenant Completion Conditions" shall mean, provided that the Lender or Successor (as applicable) has not rendered any Succession Election Notice null and void and of no force and effect, compliance with the following conditions:

(a) Within thirty (30) days following the delivery of the Succession Election Notice, if Landlord has not completed all of the Landlord Work Obligations, then Tenant shall provide reasonable evidence to Lender that Tenant has sufficient cash and other liquid assets to fulfill the Landlord Work Obligations ("Tenant Funds");

(b) Tenant shall have entered into a contract with a person or entity ("Replacement Manager"), which Replacement Manager shall be acceptable to the Lender or Successor (as applicable) as determined in Lender's or Successor's (as applicable) reasonable discretion, that is qualified and experienced in the development of properties and construction of improvements which are of similar type and nature to the improvements contemplated to have been constructed by Landlord pursuant to the Approved Shell and Core Plans (as defined in the Lease);

(c) Tenant shall provide Lender or Successor (as applicable) each month through the completion of the Landlord Work Obligations, with the following: (i) the opportunity for Lender to hold an inspection by Lender's or Successor's (as applicable) construction consultant, confirming the work as to which each contractor seeks payment is in compliance with the Approved Shell and Core Plans, (ii) a copy of contractor's application for payment to Tenant and signed by Tenant's architect on AIA Forms G702 and G703/G703A or other forms acceptable to Lender or Successor (as applicable) and confirmed by Lender's or Successor's (as applicable) inspector, (iii) if requested by Lender or Successor (as applicable), paid invoices or receipts and unconditional statutory lien waivers for all construction work and costs included in the previous request for advance, (iv) if requested by Lender or Successor (as applicable), evidence that any inspection required by any governmental authority has been completed with results satisfactory to that governmental authority, (v) such certifications of job progress by Tenant's architect, in form satisfactory to Lender or Successor (as applicable), as Lender or Successor (as applicable) may request, and (vi) such other conditions as are contained within the Loan Agreement and customary in the administration of a construction loan of a size and type as the one evidenced by the Loan Agreement;

(d) Tenant shall complete Landlord Work Obligations by **[NTD: will be the completion date established under the core/shell contract:]** _____, subject to extensions for Force Majeure;

If Tenant fails to comply with any Tenant Completion Condition, Lender or Successor (as applicable) shall provide Tenant with written notice of Tenant's failure to comply therewith and if Tenant fails to cure such non-compliance within thirty (30) days of receipt of written notice thereof (or such reasonable additional time if the cure cannot reasonably be completed within such 30-day period and Tenant has commenced to cure such non-compliance within such 30-day period and thereafter diligently pursues such cure), the Lender shall be entitled to either (i) terminate the Lease, without any liability to the Tenant whatsoever, including, without limitation, under the Lease or under this Agreement, or (ii) fulfill the Landlord Work Obligations.

Tenant agrees that any person or entity which at any time hereafter becomes the landlord under the Lease, including without limitation, Agent or any Successor (as applicable), shall be liable only for the performance of the obligations of the landlord under the Lease that arise during the period of Agent's or such Successor's ownership of the Premises. Tenant further agrees that any liability of Agent or any Successor under the Lease shall be limited to the interest of Agent or such Successor in the Property and in the rents, proceeds and profits therefrom.

6. Purchase Rights. Each of the parties hereto acknowledges that pursuant to the Lease, Tenant holds a right of first offer to purchase the property pursuant to Article 11 of the Lease (the "Purchase Rights"). The parties hereto agree that the Purchase Rights shall remain valid and in full force and effect, but subject and subordinate to the lien(s) of the Security Instrument. In the event that Agent or a Successor succeeds to the interest of Landlord under the Lease, such Purchase Rights shall not be extinguished by a Foreclosure; provided, however, that Agent or Successor shall not be bound to the Purchase Rights, and such Purchase Rights shall not apply, with respect to (i) a Foreclosure, including, without limitation, the granting of, foreclosure under, or giving of a deed-in-lieu of foreclosure under, a mortgage or the granting or exercise of any pledge of ownership interests, or (ii) the first subsequent sale of the Property following Agent's or Successor's acquisition of title to the Property, but thereafter any successor landlord to Agent or such Successor shall be bound by such Purchase Rights in accordance with the terms of the Lease.

7. **Right to Cure Defaults**. Tenant agrees to give to Agent, either by certified U.S. mail (return receipt requested) or overnight courier service (i.e., FedEx), a duplicate of each notice of any default by Landlord under the Lease at the time Tenant gives such notice to Landlord, specifying the nature of such default, and thereupon Agent shall have the right (but not the obligation) to cure such default, and Tenant shall not exercise its remedies under the Lease unless the Tenant first gives such notice to Agent and provides Agent with notice of such default, and an opportunity to cure the same within a period of time that shall be not less than the period of thirty (30) days beyond any period afforded to the Landlord to cure the default under the provisions of the Lease, and a reasonable period of time in addition thereto (i) if the circumstances are such that said default cannot reasonably be cured within such period and Agent has commenced and is diligently pursuing such cure, plus (ii**)** a reasonable period (not to exceed 270 days unless the cure cannot be effected without Agent taking possession of the Property) during any litigation or enforcement action or proceeding, including a foreclosure, bankruptcy, reorganization, possessory action or a combination thereof provided that Agent or any Successor provides Tenant with written notice of its intent to cure such default and then proceeds diligently to cure Landlord's default upon acquiring possession of the Premises. It is specifically agreed that Tenant shall not exercise its remedies under the Lease against Agent or any Successor for failure to cure any bankruptcy, insolvency or reorganization default on the part of Landlord, any breach by Landlord of any representation or warranty, or any other breach or default under the Lease that is personal to Landlord or otherwise not reasonably susceptible of cure by Agent or such Successor. Tenant shall accept performance by Agent of any term, covenant, condition or agreement to be performed by Landlord under the Lease with the same force and effect as though performed by Landlord. Without limitation on the foregoing, if the Lease is terminated for any reason other than (a) a termination which is effected unilaterally by Tenant in accordance with the express terms of the Lease, (b) the expiration of the term of the Lease, or (c) a termination that occurs in compliance with this Agreement, then upon Agent's written request given within thirty (30) days after Agent receives written notice of such termination, Tenant shall, within fifteen (15) days after such request, execute and deliver to Agent a new lease of the Premises for the remainder of the term of the Lease, such new lease to be upon all of the same terms, covenants and conditions of the Lease applicable to the remainder of the term of the Lease (as affected by this Agreement).

8. **Tenant's Agreements**. Tenant hereby represents, warrants, covenants and agrees that: (i) Tenant shall not pay any rent under the Lease more than one month in advance of the date due except as expressly required in the Lease with respect to security deposits, operating expenses, taxes and the like; (ii) Tenant shall have no right to appear in any Foreclosure action under the Security Instrument (unless named by Agent in such action, Agent agreeing however not to name Tenant unless required pursuant to applicable laws, and then only for such purposes); (iii) Tenant shall not amend or modify, or assign or sublet, the Lease and Tenant shall have no right to cancel or terminate the Lease, without Agent's prior written consent (provided that, (x) as it relates to any assignments/subletting of Lease undertaken in connection with the terms and provisions set forth in the Lease, Agent shall have the same approval rights as the Landlord has with respect to same and (y) no such approval shall be required with respect to amendments solely evidencing the exercise of Tenant's option to extend the Lease and assignments or sublets that do not require the consent of the Landlord pursuant to the terms of the Lease), and any attempted amendment or modification, assignment or subletting, cancellation or termination of the Lease in violation of the foregoing shall be of no force or effect as to Agent; (iv) Tenant shall not subordinate the Lease to any lien or encumbrance (other than the Security Instrument) without Agent's prior written consent; (v) except as expressly set forth in Section 6, above, Tenant has no right or option of any nature whatsoever, whether pursuant to the Lease or otherwise, to purchase the Property, or any portion thereof or any interest therein, and to the extent that Tenant hereafter acquires any such additional rights or options, the same is hereby acknowledged to be subject and subordinate to the Security Instrument and is hereby waived and released as against Agent and any Successor, (vi) Tenant shall promptly, to the same extent and within the same time period required by the Lease, deliver to Agent, from time to time, a written estoppel statement in the form, and with the certifications, required by the Lease; (vii) this Agreement supersedes and satisfies any requirement in the Lease relating to the granting of a non-disturbance agreement or providing for subordination of the Lease; (viii) Tenant is the sole owner of the leasehold estate created by the Lease; (ix) the interest of Landlord under the Lease is assigned to Agent solely as security for the obligations secured by the Security Instrument, and neither Agent nor the Lenders shall have any duty, liability or obligation under the Lease or any extension or renewal thereof, unless Agent either (a) specifically undertakes such liability in writing, or (b) subject to the express terms of this Agreement, Agent becomes a Successor; (x) if this Agreement conflicts with the Lease, then this Agreement shall govern as between the parties and any Successor, including upon any attornment pursuant to this Agreement; and (xi) upon Agent's transfer or assignment of Agent's interests in the Loan, the Lease (or any new lease executed pursuant to this Agreement), or the Property, Agent shall be deemed released and relieved of any obligations under this Agreement, the Lease (or any new lease executed pursuant to this Agreement), and with respect to the Property.

9. **Authority**. Each of Landlord, Agent, and Tenant warrants and represents to the other parties hereto that it has duly executed and delivered this Agreement and that the execution, delivery and performance by it of this Agreement (i) are within its powers, (ii) have been duly authorized by all requisite action, and (iii) do not violate any provision of law or any order of any court or agency of government, or any agreement or other instrument to which it is a party or by which it or any of its property is bound.

10. **Miscellaneous**.

Section 10.1 The provisions hereof shall be binding upon and inure to the benefit of Tenant and Agent and their respective successors and assigns, the term "Agent" as used herein includes any successor or assign of the named Agent herein, and the terms "Tenant" and "Landlord" as used herein include any successor and assign of the named Tenant and Landlord herein, respectively; provided, however, that such reference to Tenant's or Landlord's successors and assigns shall not be construed as Agent's consent to any assignment or other transfer by Landlord in any instance where Agent's consent to such assignment or transfer is required hereunder, under the Security Instrument or under any other document executed in connection therewith.

Section 10.2 Any notices, demands or requests to be given under this Agreement shall be in writing and shall be deemed sufficiently given if served personally or upon the first to occur of receipt or the refusal of delivery if mailed by United States certified mail, return receipt requested, postage prepaid, or if sent by prepaid Federal Express or other similar overnight delivery service which provides a receipt, addressed to the Primary Address of Landlord, Tenant, or Agent set forth below, along with copies to the applicable Supplemental Addresses set forth below, or such other address as such party may specify in writing from time to time;

If to Tenant:

Primary Address:

_____

_____

Supplement Addresses:

_____

_____

_____

If to Landlord:

Primary Address:

_____

Supplement Addresses:

If to Agent:

Primary Address:

Supplement Addresses:

Section 10.3 This Agreement may not be changed, terminated, amended, supplemented, waived or modified orally or in any manner other than by an instrument in writing signed by the party against which enforcement of the change, termination, amendment, supplement, waiver or modification is sought.

Section 10.4 The captions or headings at the beginning of each paragraph hereof are for the convenience of the parties and are not part of this Agreement;

Section 10.5 This Agreement shall be governed by and construed under the laws of the State of New York (excluding the choice of law rules thereof);

Section 10.6 This Agreement represents the final agreement between the parties hereto with respect to the subject matter hereof and may not be contradicted by evidence of prior, contemporaneous or subsequent oral agreements of the parties. There are no unwritten oral agreements between the parties with respect to the subject matter hereof.

Section 10.7 If any provision of this Agreement is held to be invalid or unenforceable by a court of competent jurisdiction, such provision shall be deemed modified to the extent necessary to be enforceable, or if such modification is not practicable, such provision shall be deemed deleted from this Agreement, and the other provisions of this Agreement shall remain in full force and effect.

Section 10.8 This Agreement may be executed in one or more counterparts, each of which when so executed and delivered shall be deemed an original, but all of which taken together shall constitute but one and the same instrument.

[Signature Page Follows]

IN WITNESS WHEREOF, the parties hereto have signed and sealed this instrument as of the day and year first above written.

TENANT

By: _____

Name (Print) _____,

Title:

[Acknowledgment to be added]

AGENT:

_____

By: _____
Name (Print) _____,
Title: _____

[Acknowledgment to be added]

LANDLORD

By: _____
Name (Print) _____,
Title: _____

[Acknowledgment to be added]

Schedule A (to Exhibit E)

PROPERTY DESCRIPTION

EXHIBIT F

FORM OF NON-DISCLOSURE AND CONFIDENTIALITY AGREEMENT

NON-DISCLOSURE AND CONFIDENTIALITY AGREEMENT

This Non-Disclosure and Confidentiality Agreement (this "***Agreement***") is entered into_____, 20__ (the "***Effective Date***"), by and between [_____], a [_____], whose address is [_____] ("***Prospective Purchaser***"), and **Ionis Gazelle, LLC**, a Delaware limited liability company, whose address is [_____] ("***Ionis***"). Prospective Purchaser and Ionis are sometimes referred to individually as a "***Party***" and collectively as the "***Parties***".

RECITALS

WHEREAS, Ionis currently leases and occupies that certain real property located on Lots 21 & 22, Whiptail Loop W in Carlsbad, 92010 California (the "***Property***") pursuant to that certain Lease Agreement dated as of [_____], 2022 (the "***Lease***"), by and between Ionis and LOTS 21 & 22 OWNER (DE) LLC, a Delaware limited liability company ("***Landlord***");

WHEREAS, Prospective Purchaser has a bona fide interest in purchasing the Property from Landlord, and may thereby become Ionis' landlord under the Lease;

WHEREAS, in connection with (i) Prospective Purchaser's evaluation of a purchase of the Property, and (ii) Prospective Purchaser's actions as landlord under the Lease, if Ionis shall continue to lease and occupy the Property and in the event Prospective Purchaser purchases the Property (collectively, the "***Purpose***"), Prospective Purchaser may enter the Property and may gain access to materials and information and observe processes which are non-public, confidential or proprietary in nature; and

WHEREAS, the Parties recognize the critical importance of preserving the non-public, confidential or proprietary nature of any disclosed, observed or exchanged materials and information provided in the course of discussions regarding the Purpose and the Property, and Prospective Purchaser potentially becoming Ionis' landlord under the Lease.

NOW THEREFORE, the Parties agree, each with the other, as follows:

1. Confidential Information. Except as set forth in Section 2 below, "***Confidential Information***" means all non-public, confidential or proprietary information (i) disclosed by or on behalf of Ionis, its Affiliates, or their respective agents, or employees (collectively, the "***Ionis Parties***") to Prospective Purchaser, its Affiliates and subcontractors, or their respective agents, employees, or advisors, or any other person or entity providing the services by and through Prospective Purchaser (collectively, the "***PTP Parties***"), whether disclosed orally or in written, electronic or other form or media, and whether or not marked, designated or otherwise identified as "confidential," (ii) observed by any of the PTP Parties in entering on to the Property and (iii) as may be observed or obtained by Prospective Purchaser in the course of acting as landlord under the Lease (should Prospective Purchaser purchase the Property and Ionis shall continue to lease and occupy the Property pursuant to the Lease), including, without limitation, Trade Secret Information, any information that would reasonably be considered non-public, confidential or proprietary given the nature of the information and the Ionis Parties' businesses and all notes, analyses and other materials prepared by or for the Purpose that contain any of the foregoing. As used in this Agreement, "***Trade Secret Information***" means all information that is unique to Ionis' business and that is not commonly known by or available to the public or otherwise known through Prospective Purchaser's business and that: (i) derives or creates economic value for Ionis' business, actual or potential, from not being generally known to, and not being readily ascertainable by proper means by, other persons who can obtain economic value from its disclosure or use; and (ii) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy. The Ionis Parties' Trade Secret Information may include, but is not limited to, all confidential information relating to Ionis' business and operations and in the form of the Ionis Parties' research and development plans and activities; design plans; compilations of data; product plans; inventions; engineering processes and activity; manufacturing plans, processes and activity; proprietary computer software and programs (including object code and source code); and proprietary computer and database technologies, systems, structures, and architectures.

2. Exclusions from Confidential Information. the term "Confidential Information" as used in this Agreement shall not include information that:

(a) at the time of disclosure is, or thereafter becomes, generally available to and known by the public other than as a result of any breach of this Agreement by Prospective Purchaser;

(b) at the time of disclosure is, or thereafter becomes, available to Prospective Purchaser on a non-confidential basis from a third-party source, provided that such third-party is not and was not, to Prospective Purchaser's knowledge, prohibited from disclosing the information to Prospective Purchaser by any legal, fiduciary or contractual obligation;

(c) was known by or in the possession of Prospective Purchaser prior to being disclosed by or on behalf of the Ionis Parties pursuant to this Agreement;

(d) was independently developed by Prospective Purchaser without reference to or use of, in whole or in part, any Confidential Information; or

(e) Ionis has agreed in writing is free of such obligations.

3. Confidential Information and Other Property of the Ionis Parties. All Confidential Information shall be deemed the property of the Ionis Parties. All information, documents, and electronic media (including, but not limited to Confidential Information) furnished by or on behalf of the Ionis Parties to the Prospective Purchaser shall be the property of the Ionis Parties.

4. Prospective Purchaser Obligations. Prospective Purchaser shall:

(a) protect the Confidential Information from unauthorized disclosure and use, with at least the same degree of care as the Prospective Purchaser would use in protecting its own confidential information, but no less than a commercially reasonable degree of care;

(b) not use the Confidential Information, or permit it to be accessed or used, for any purpose other than the Purpose;

(c) not disclose the Confidential Information to any person or entity, including, without limitation, to any of the PTP Parties, except to PTP Parties who: (i) need to know the Confidential Information to assist Prospective Purchaser, or act on its behalf, in relation to the Purpose; (ii) are informed by Prospective Purchaser of the confidential nature of the Confidential Information (each an "***Authorized Party***") (Prospective Purchaser acknowledging that a breach of this Agreement by a PTP Party shall be treated as a breach of this Agreement by Prospective Purchaser);

(d) not use any of the Ionis Parties' computers, computer systems, equipment, tools, or other property of the Ionis Parties without Ionis Parties' consent;

(e) not use any Confidential Information to compete or prepare to compete against the Ionis Parties, or for or on behalf of any competitor of the Ionis Parties;

(f) upon Ionis' written request, destroy or deliver promptly to Ionis, or Ionis' designee, all Confidential Information (including all copies thereof, regardless of the medium in which such information may be stored) and all computers, equipment, tools, and other property of the Ionis Parties that happen to be in Prospective Purchaser's possession;

(g) promptly notify Ionis upon discovery of any unauthorized disclosure of Confidential Information caused by Prospective Purchaser and reasonably cooperate with Ionis in any effort undertaken by Ionis to enforce its rights related to any such unauthorized disclosure;

(h) not record in any form, including by hand, video or audio, any Trade Secret Information observed on the Property, without Ionis' written consent;

(i) be responsible if any provisions of this Agreement are violated by any Authorized Party;

(j) at all times while on the Property be accompanied by an authorized representative of Ionis and not attempt to access areas of the Property without being accompanied by such authorized representative unless Ionis provides its express written consent to access without being accompanied; and

(k) at all times while on the Property follow all safety protocols as instructed by an authorized representative of Ionis.

5. Prospective Purchaser Representations and Warranties. Prospective Purchaser represents and warrants that:

(a) the performance of its obligations herein does not and will not violate any other contract or obligation to which Prospective Purchaser is a party, including covenants not to compete and confidentiality agreements; and

(b) unless and until becoming landlord under the Lease (as and to the extent Ionis continues to lease and occupy the Property pursuant to the Lease), it is entering upon the Property for the sole purpose of evaluating a potential purchase of the Property.

6. No Ionis Representations or Warranties; Disclaimer of Liability. The Ionis Parties make no representation or warranty, express or implied, as to the accuracy or completeness of the Confidential Information disclosed to Prospective Purchaser hereunder. The Ionis Parties shall not be liable to Prospective Purchaser for any losses relating to or resulting from the Prospective Purchaser's use of any of the Confidential Information or any errors therein or omissions therefrom.

7. Court Ordered Disclosure. Notwithstanding anything to the contrary herein, Prospective Purchaser may disclose certain Confidential Information, without violating the obligations of this Agreement, to the extent such disclosure is required by law or regulation or by a subpoena or other validly issued administrative or judicial process, provided that, Prospective Purchaser shall (a) provide Ionis with reasonable prompt notice of the disclosure(s) (to the extent legally permissible), (b) limit disclosure to only that portion of the Confidential Information which Prospective Purchaser is legally compelled to disclose and (c) reasonably cooperate in assisting Ionis (at Ionis' expense) in its efforts to ensure confidential treatment will be accorded any Confidential Information so furnished (to the extent legally permissible).

8. Survival of Obligations; Return or Destruction of Confidential Information. Prospective Purchaser's obligations to protect any Confidential Information received from the Ionis Parties shall continue for a period of three (3) years from the date of disclosure, notwithstanding whether or not Prospective Purchaser purchases the Property. At Ionis' written request, so long as the same is no longer reasonably necessary for Prospective Purchaser's use in connection with the Purpose, Prospective Purchaser shall promptly destroy all copies, whether in written, electronic or other form or media, of the Ionis Parties' Confidential Information and certify in writing to Ionis that such Confidential Information has been destroyed; provided that Prospective Purchaser shall not be required to destroy electronic copies of any portions of the Confidential Information created pursuant to standard archival or back-up procedures and not available to end users, and provided that Prospective Purchaser may retain one (1) copy of the Confidential Information for its legal archives for the sole purpose of documenting its receipt thereof.

9. No Proprietary Interest. Prospective Purchaser understands and agrees that Prospective Purchaser shall not obtain any proprietary interest in any Confidential Information. This Agreement shall not operate in a way to grant or confer any right or license in any of the Confidential Information, nor as a consent by the Ionis Parties to Prospective Purchaser for Prospective Purchaser's use of any Confidential Information which may become public knowledge through any breach of this Agreement by or on behalf of Prospective Purchaser.

10. Agreement Confidential. The existence of this Agreement shall be considered to be of a confidential nature and shall be accorded the same protections as the Confidential Information.

11. No Further Agreement. Nothing in this Agreement shall be construed as representing any commitment by either Party to enter into any other agreement, whether relating to the Purpose or otherwise. Neither the execution and delivery of this Agreement nor the delivery of any Confidential Information hereunder shall be construed as granting to Prospective Purchaser by implication, estoppel or otherwise, any right in or license under any present or future invention, trade secret, trademark, copyright, or patent, now or hereafter owned or controlled by the Ionis Parties.

12. Remedies. Prospective Purchaser acknowledges and agrees that the Confidential Information is a valuable, special and unique asset of the Ionis Parties' business which gives the Ionis Parties an advantage over the Ionis Parties' actual and potential competitors and any unauthorized disclosure or unauthorized use of the Confidential Information may irreparably injure the Ionis Parties. If any action should have to be brought by Ionis against Prospective Purchaser to enforce the provisions of this Agreement, Prospective Purchaser recognizes, acknowledges and agrees that Ionis shall be entitled to seek all of the civil remedies provided by federal, state and local law, including without limitation, preliminary and permanent injunctive relief restraining Prospective Purchaser from any actual or threatened unauthorized use or disclosure of any Confidential Information, in whole or in part. Nothing in this Agreement shall be construed as prohibiting Ionis from pursuing any other legal or equitable remedies available for breach or threatened breach of this Agreement.

13. Notice. Any and all notices or other communications or deliveries required or permitted to be given or made pursuant to any of the provisions of this Agreement shall be in writing and: (i) hand delivered; (ii) sent by a nationally recognized overnight courier, costs prepaid, or (iii) sent by email, provided that the sender promptly delivers a hard copy to the recipient by the method set forth in (i) or (ii), in each case to the applicable addresses set forth below or to such other address as such Party has designated by notice so given to the other Party:

If to Ionis:

Ionis Gazelle, LLC
Attention:
Email:

with a copy to:

Cooley LLP
11951 Freedom Dr.
Suite 1400
Reston, VA 20190
Attn: Michelle Garcia Schulman, Esq.
Email: mschulman@cooley.com

If to Prospective Purchaser:

_____
_____
_____
_____

Such notice sent in accordance with clauses (i) or (ii) shall be deemed to have been given upon the date of actual receipt or delivery (or refusal to accept delivery), as evidenced by the notifying Party's receipt of written or electronic confirmation of such delivery or refusal, and such notice sent electronically in accordance with clause (iii) shall be deemed to have been given upon the date that such electronic notification was sent, provided such notice clearly confirms, without alteration of the email, the date and time the email was sent, in each case if such notice is received by the Party to be notified between the hours of 8:00 A.M. and 5:00 P.M. Pacific time on any business day, with delivery made after such hours to be deemed received the following business day.

14. Rules of Construction.

(a) This Agreement shall be governed and construed in accordance with the statutory and common law of the State of California and applicable federal law, without regard to any conflicts of law principles that. Any actions brought to enforce or interpret this Agreement shall be brought only in a court of competent jurisdiction located in the State of California.

(b) No change, modification or termination of any other terms, provisions, or conditions of this Agreement shall be effective unless made in writing and signed or initialed by both Parties to this Agreement. The waiver by a Party of a breach or a threatened breach of any provision of this Agreement by the other Party shall not be construed as a waiver of any subsequent breach.

(c) Each provision of this Agreement shall be valid and enforced to the fullest extent permitted by law. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision.

(d) This Agreement constitutes the entire Agreement between the Parties pertaining to the subject matter hereof, and it supersedes all negotiations, preliminary agreements, and all prior and contemporaneous discussions and understandings of the Parties in connection with the subject matter hereof. Following the acquisition of the Property by Prospective Purchaser or its Affiliate, if it occurs, this Agreement shall be deemed incorporated into the Lease by reference and shall terminate at such time, if any, as Prospective Purchase or such Affiliate ceases to be the Landlord thereunder.

(e) This Agreement may be executed in any number of counterparts, and by facsimile or electronically transmitted signature and each such counterpart and signature shall be deemed to be an original and all of which shall constitute one agreement that is binding on all parties hereto.

(f) As used herein, "***Affiliates***" means any individual, partnership, corporation, limited liability company, limited liability partnership, trust or other entity that directly, or indirectly through one or more intermediaries, controls, is controlled by or is under common control with a Party. For the purposes of this definition, "control" means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of an individual, partnership, corporation, limited liability company, limited liability partnership, trust or other entity, whether through the ownership of voting securities, by contract or otherwise, and the terms "controlling" and "controlled" have the meanings correlative to the foregoing.

IN WITNESS WHEREOF, the Parties have executed this Agreement effective as of the date first set forth above.

IONIS GAZELLE, LLC	**[PROSPECTIVE PURCHASER]**
By:	By:
Name:	Name:
Title:	Title:

EXHIBIT G

LANDLORD SIGNAGE


OLYMPIA
TILE
100A
OXFORD

EXHIBIT H

COMMENCEMENT AND TERMINATION DATE AGREEMENT

THIS COMMENCEMENT AND TERMINATION DATE AGREEMENT, made as of _____, 20__, is by and between Lots 21 & 22 Owner (DE) LLC, a Delaware limited liability company ("Landlord"), and Ionis Pharmaceuticals, Inc., a Delaware corporation ("Tenant"). Reference is made to that certain Lease Agreement dated _____, 2022, (the "Lease") pursuant to which Landlord leases to Tenant the Premises described therein.

1. Capitalized terms used, but not defined, herein shall have the same meanings given to them in the Lease.

2. The Commencement Date occurred on _____, 20____.

3. The Expiration Date is scheduled to occur on _____, 20____, unless Tenant exercises any option to extend the Term of the Lease or unless the Lease terminates earlier as provided in the Lease.

4. The date of commencement of the first Extension Option shall be _____, 20___, if Tenant effectively exercises its option in respect thereof, and if Tenant does so, the Term of the Lease shall expire on _____, 20___, unless Tenant exercises any option to further extend the Term of the Lease or unless the Lease terminates earlier as provided in the Lease.

5. The date of commencement of the second Extension Option shall be _____, 20___, if Tenant effectively exercises its option in respect thereof, and if Tenant does so, the Term of the Lease shall expire on _____, 20___, unless Tenant exercises any option to further extend the Term of the Lease or unless the Lease terminates earlier as provided in the Lease.

6. The parties agree that this Agreement may be electronically signed pursuant to the terms of the ESIGN Act of 2000 and is legally binding. The parties agree that any electronic signatures appearing on this Agreement are the same as handwritten signatures for the purposes of validity, enforceability and admissibility.

IN WITNESS WHEREOF, the parties hereto have caused this Commencement and Termination Date Agreement to be executed as of the date first above written.

LANDLORD:
Lots 21 & 22 Owner (DE) LLC

By: _____
Name: _____
Title: _____

TENANT:
Ionis Pharmaceuticals, Inc.

By: _____
Name: _____
Title: _____

EXHIBIT I

TENANT CONSTRUCTION MANUAL

[Attached]

Section 1: GENERAL INFORMATION

1.01 Introduction

These Construction Rules and Regulations been prepared to introduce Tenants and Contractors to the Oxford Properties Group Design, Systems and Building Regulations in order to assist in the design and construction of the leased premises. These Rules and Regulations are to be read in conjunction with the building lease document. In the event of any conflict between these Rules and Regulations and the lease, the provisions of the lease or any other specific written agreements between the Landlord and Tenant shall prevail.

Subject to the preceding paragraph, the Landlord reserves the right, from time to time, to add to or amend the information, procedures and regulations contained herein in a reasonable manner consistent with similar single tenant NNN facilities in the Carlsbad, California area and the Lease, upon reasonable prior notice to Tenant. Any such additions or amendments will affect any Construction work undertaken after the addition or amendment has been issued.

1.02 Tenant Coordination

The Landlord will appoint the Property Manager who will act as a point of contact within the Landlord's organization. All questions, comments and submissions are to be addressed to:

Oxford Properties Group
_____
_____

1.03 Tenant Design and Working Drawings

To the extent required by the Lease, please submit for review a detailed scope of work, PDF and CAD ver. 14 or later and three (3) sets of Tenant Design Working Drawings and Specifications of all work proposed within the
Leased premises. The landlord requires that drawing packages are provided in the following stages:

- Preliminary space plan
- Building Permit submission
- Issued for Construction Submission
- As-built drawings as further outlined in the Lease

To the extent Landlord's approvals of such drawings is required by the Lease, once drawings have been reviewed the Landlord will forward an approval letter to the Tenant outlining any comments or changes, if any, that pertain to the drawings. The drawings may be subject to change if requested. Revised drawings are to include all the comments and corrections and a set of prints provided prior to commencing work. Drawings to be resubmitted shall be revised to conform to the requirements and re-submitted for subsequent Landlord review. Any revisions to the Landlord reviewed drawings must be submitted for further review, and work must not proceed until the revised drawings are returned to the contractor. A Copy of the Landlord reviewed drawings must be kept on the job site for viewing throughout the construction period. Landlord shall respond to requests for approval as provided in the Lease.

Additional or expanded information, for purposes of definition or clarification before giving approval may be required. Working drawings should supply the information listed below (depending on the stage).

1.03.01 ***Complete Floor Plans (drawing scale of 1/8" = 1')***

a) Location of all major fixed elements within the leased premises dimensionally related to grid lines and demising partitions.

b) Location and layout of rooms of unusual loading concentrations such as cranes, racking areas and calculations of unusual loadings which may result in floor damage.

c) Location of power, telephone, data and communications outlets. Room names and uses.

d) Floor materials and finishes throughout the premises.

e) Location of exit lights.

1.03.02 ***Complete Reflected Ceiling Plans (scale: 1/8" = 1')***

These should include lighting layout.

1.03.03 ***Complete Construction Details***

These plans should be appropriately scaled and indicate methods of construction.

1.03.04 ***Complete Electrical, Mechanical, Sprinkler, Building Automation, Security, Communications, Data, Life Safety System Drawings (scale: 1/8"=1') complete with Engineer's stamp.***

Details of all alterations and all additions to the **BASE BUILDING**, as well as base building conditions, which remain unchanged.

Details of all metering equipment changes to conform to base building standards. Schedule for any changes to fire, sprinkler and security systems.

1.03.05 ***Complete Structural Drawings***

These drawings must be supplied where special conditions warrant their production i.e. openings in slabs, erection of racking units, the addition of cranes, ramps, etc.

1.03.06 ***Completion***

Upon completion of construction, to the extent required by the Lease the Tenant is responsible to submit “as built” Architectural, Electrical, Mechanical, Security, Communications, Data and Structural Drawings on CAD ver. 14 or later disk to the Landlord for their records.

1.04 Certificates and Approvals

The Tenant is responsible for ensuring that all the following requirements have been complied with before construction begins:

1. **Insurance**. Landlord requires evidence of insurance for contractors and subcontractors as required by the Lease.

2. **Permits** Tenant’s design and construction work must comply with all applicable by-laws. The Tenant must obtain all necessary permits and approvals or construction work in the leased premises from the appropriate government authorities. Permits and approval that are required to commence construction must be obtained before construction begins within the leased premises. A copy of all permits must be delivered to the Landlord. The Tenant must correct immediately any work, which does not meet with the approval of the building inspector, even though the Tenants drawings may have been reviewed previously by the appropriate government authorities and the Landlord.

3. **Applicable Hazardous Materials Law**. All contractors, sub-trades and suppliers shall abide by applicable laws governing use of Hazardous Materials when working in the Building.

4. **Workers Compensation** To the extent applicable, Tenant contractor shall furnish written evidence of good standing with the North Carolina Industrial Commission and that all employees engaged in the work are covered in accordance with the statutory requirements of authorities having jurisdiction.

5. **Occupational Health and Safety** The Tenant acknowledges that it is solely responsible for the health and safety of all its employees and workers, as well as for the continuing safe conditions in the Premises. The Tenant shall comply with and shall require all of its employees and workers to comply with the provisions of all Laws respecting Occupational Health and Safety, the Environment, Worker’s Compensation and the safe condition of the Premises.

   All materials and supplies used by the Tenant’s personnel in the Demised Premises and the Lands shall be used, handled, stored, otherwise dealt with and properly labeled in accordance with the Workplace Hazardous Materials Information System.

1.05 Appointment of Contractors

All Tenant contractors are subject to approval by the Landlord to the extent provided in the Lease.

1.06 Reserved

1.07 Commencement of Construction

For work subject to Landlord consent, the Tenant is required to carry out its construction work in strict accordance with the "Landlord Reviewed Drawings", subject to modifications permitted in accordance with the Lease.

Construction may proceed only after the Tenant has:

a) Submitted acceptable evidence of insurance coverage to the Landlord as set out in these Rules and Regulations.

b) Posted all required permits and safety signage on site, where applicable.

c) For work subject to Landlord's consent, made available on the leased premises one (1) set of prints, of the Tenant Design Working Drawings and Specifications for the duration of the construction period for reference by the Landlord's Tenant Coordinator.

d) For work subject to Landlord's consent, submitted a schedule showing the timetable for the progress and completion of the Tenant's work and a list of all trades requiring access to the premises including the trades address and telephone number.

1.08 Completion of Tenant's Construction

Following completion of the job, and within 30 days, the Tenant must submit to the Landlord a certificate from its architect or designer stating that all work, including that of the mechanical and electrical contractors (if any), has been completed substantially in accordance with the reviewed drawings if such work was subject to Landlord's consent. Upon the request of Landlord or the property manager, Tenant shall provide similar certifications for Minor Alterations previously performed (to the extent not already in the possession of Landlord).

A full set of architectural, mechanical and electrical "as built" CAD drawings ver. 14 or later shall accompany the above noted certificates where required by the Lease.

Further, the Landlord requires copies of all permits and certificates issued by authorities having jurisdiction over all or any part of the Tenant's Alterations. For work requiring Landlord's consent, such copies shall be provided prior to the commencement of work, or within 30 days following the completion of such work to the extent obtained during or following completion. Upon the request of Landlord or the property manager, Tenant shall provide copies of all permits and certificates issued by authorities having jurisdiction over all or any part of Minor Alterations previously performed (to the extent not already in the possession of Landlord).

Section 2: RULES AND REGULATIONS GOVERNING TENANT WORK

While carrying out work in the leased premises, the Tenant and all of its contractors, agents and employees are required to abide by the reasonable rules and regulations defined and communicated by the Landlord in advance. *Failure to comply will result in work stoppage.*

2.01 Inspection of Tenant Work in Progress

As and to the extent provided in the Lease, the Landlord and its agents, architects, engineers and consultants shall have reasonable access to the Tenant's premises for the purpose of inspecting the Tenant work in progress. If Landlord and its architects, engineers or consultants note deficiencies in the Tenant work, Tenant shall correct the same. **Contractor/Tenant must contact the appointed Property Manager to attend final inspection of work that is subject to Landlord's consent under the Lease.**

2.02 Security Control

Tenant is responsible for providing its contractor's access to the Premises.

The Tenant is fully responsible for the physical security of the leased premises and the contents therein throughout the construction period.

2.03 Public Safety

It is the Tenants responsibility to ensure that the Tenant contractor observes and complies with all applicable construction safety regulations.

2.04 Emergency Contact

The Tenant and its contractor are required to post at the site the emergency contact name and telephone number with copies forwarded to Landlord.

2.05 Temporary Services

The Tenant's Contractor is responsible for the distribution of temporary power and telephone service within the leased premises during the construction period. The Tenant and Tenant's Contractor are responsible for providing operable fire extinguishers in the premises throughout the construction period. Landlord shall have no obligation to provide any services to Tenant's Contractor.

2.06 Work Areas

All construction materials, tools, equipment and workbenches must be kept within the leased premises throughout the construction period and not stored in areas outside of the building.

2.07 Waste Removal

Removal of garbage and construction debris generated by the work of a Tenant's contractor will be the total responsibility of the contractor, subject to the waste removal and recycling program of the complex, if any.

All disposals to comply with applicable law.

All cost incurred are responsibility of the Tenant and Contractor.

2.08 Drilling or Cutting

Tenant's contractor is not permitted to drill, cut or chase openings of any description in any part of the building structure without prior approval from the Landlord as and when provided under the Lease. If such work is approved by the Landlord, drilling, etc. shall be carried out by the Tenant's Landlord approved contractor at the Tenant's cost. Any work of this type may require x-ray inspection of the slab prior to drilling, which will also be at the Tenant's expense.

2.09 Welding

If pressurized gas cylinders are used for welding, cutting or other purposes, the Tenant's contractor shall ensure that their use is in accordance with requisite safety provisions and requirements. An operational fire extinguisher shall be available in the immediate vicinity of the work.

No welding or soldering on any part of a floor shall be done without knowledge of the Landlord as these activities may trigger a fire alarm. Work Permits requesting the deactivation of a floor's fire alarm system must be obtained from the Landlord.

2.10 Hot Work Permits

The Contractor is responsible for providing the required "Fire Watch" during and after the Hot Work is completed.

2.11 Wiring and Conduit

All wiring must be a minimum of #12 solid wire for runs under 75 feet and a minimum #10 solid wire for runs greater than 75 feet. Absolutely no BX cable is to be used in the electrical rooms.

All cabling and telephone type wiring used above the ceiling must be installed in conduit in accordance with the Building and Fire Codes. Conduit may not be required when cabling with FT6/IBM type 2 or 4 (fire rated) cable, if approved by the Landlord.

2.12 Smoking

There is no smoking allowed in any Oxford Property managed buildings or loading docks including the Construction areas.

2.13 PENALTIES FOR FALSE ALARMS

Tenant is responsible for all governmental penalties imposed on account of false alarms, except to the extent caused by Landlord or any of its agents or contractors or their respective employees.

Section 3: READY TO START

3.01 Are You Ready to Start Construction?

Prior to a work permit being issued by the Landlord for work requiring Landlord consent, the following items must be completed and submitted to the Landlord's Tenant Coordinator.

- Drawings, Specifications and Scope of Work as outlined within this document.
- Insurance Certificate provided on Landlord's standard form.
- Building Permit or copy of Building Permit application.
- List of Contractors and Trades to be used including contact names and phone numbers.
- Detailed Construction Schedule.
- Emergency Contact Numbers for all contractors and supervisors responsible for project.

3.02 Have You Completed Construction?

It is the tenant's responsibility to ensure the construction has been completed in accordance with this Document. The following documents must be complete and submitted to the Landlord's Tenant Coordinator for work requiring Landlord consent.

- Fire Alarm and Life Safety Verification.
- Architect's Certificate of Completion.
- Final Electrical and Mechanical engineers sign-off stating work is completed substantially in accordance with design drawings and specifications.
- Copies of all permits and certificates related to work.
- As-built Mechanical Drawings with the associated CAD disk ver. 14 or later. Disks are to be labeled as follows:
  - Indicate "As-Builts" – Mechanical
  - Name of Contractor
  - Project Name, Floor and Address
  - Project Date (Month-Year)
  - Name of Company Prepared By
- As and to the extent required by the Lease, As-built Electrical Drawings with the associated CAD disk ver. 14 or later. Disks are to be labeled as follows:
  - Indicate "As-Builts" – Electrical
  - Name of Contractor
  - Project Name, Floor and Address
  - Project Date (Month-Year)
  - Name of Company Prepared By

REQUIRED CONTRACTOR AND SUBCONTRACTOR INSURANCE

Certificates of Insurance

Landlord requires all contractors and subcontractors performing work at the Property to carry insurance. Property Management collects certificates of insurance, which contain information about the vendor's insurance. This insurance must meet certain minimum requirements and name Landlord, Oxford Properties Group, Arcadia Management Group, Inc., and Oxford I Asset Management US as additional insureds.

Service Contractor Certificates

The specific insurance requirements for a particular service contractor are those written into their contract with the building owner/manager or tenant, and to the extent approved by Landlord these may differ from the guidelines listed below. When determining whether or not a certificate shows coverage that meets the actual requirements for a particular service contractor, always refer to the contract wording.

The standard operating procedures require having a certificate of insurance naming Landlord, Oxford Properties Group, Arcadia Management Group, Inc., and Oxford I Asset Management US as additional insured, and having a signed contract/service agreement in place listing the insurance requirements and having an indemnification section.

General Guidelines

The following are insurance guidelines for contractors and subcontractors performing work under $20,000,000; for work in excess of such amount, the limits of liability will be subject to Landlord's reasonable approval. Landlord and Tenant shall reasonably cooperate in good faith to determine such insurance liability limits within thirty (30) days after the Effective Date.

1. **Workers Compensation:** Statutory Coverage in accordance with the laws of your state.

2. **Employers Liability:** Limits of not less than $1,000,000 each accident/occurrence, $1,000,000 each employee/disease, $1,000,000 disease/policy limit.

3. **General Liability:** Please see the chart below for General Liability per Occurrence/ General Aggregate.

   Commercial General Liability, including but not limited to comprehensive form, premises operations, explosion and collapse hazard and underground hazard, products and a minimum of twelve (12) months completed operations hazard, contractual liability on a "blanket" basis designating all written contracts related to the work, broad form property damage (including completed operations), independent contractors' protective, personal injury liability, automobile liability comprehensive form for owned, hired and non-owned vehicles, elevators and escalators hazards, and incidental medical malpractice coverage hazards, and as follows: combined single limits for (i) bodily injury and (ii) property damages, endorsed such that the policy aggregate applies to each property location where work occurs. Bodily injury shall include, without limitation, damages for care and loss of services because of bodily injury, including death at any time resulting therefrom, sustained by any person or persons. Property Damage Liability Insurance shall include, without limitation, losses due to damages to or destruction of tangible property, including loss of use of such property resulting therefrom in compliance with the amounts set forth above; Contractor shall provide X, C and U coverage if Contractor's operations involve any exposure to explosion, collapse or underground damage. Products and Completed Operations to be maintained for 3 years after final payment.

4. **Automobile Liability:** Bodily injury and property damage in an amount not less than $2,000,000 combined single limit covering all owned, non-owned, hired or leased vehicles.

5. **Excess / Umbrella Liability:** $1,000,000 in excess of the above primary Employer's Liability, General Liability, and Automobile Liability.

6. **Property:** Property Insurance will cover the physical loss, including theft, or damage to equipment, machinery, supplies or tools owned, leased, hired or borrowed by contractor, utilized or operated by contractor while performing contracted services. The valuation basis shall be "replacement cost".

7. **Professional Liability (Errors and Omissions):** If the nature of the work involves a professional liability exposure (e.g. design/build), contractor shall maintain professional liability (errors and omissions) coverage at a minimum limit of $2,000,000 or $5,000,000, depending on project size, for each claim.

8. **Contractors Pollution - Asbestos Legal Liability:** If the nature of the services performed involves pollutants or any other materials which would affect soil, water or structures, then the contractor shall maintain contractors pollution – asbestos legal liability coverage for a limit of not less than $1,000,000 each occurrence - $2,000,000 policy aggregate, including errors and omissions. However, see attached requirements for higher limits for asbestos abatement and hazardous material removal contractors.

Certificate Holders, Additional Insured's, and Additionally Insured Endorsement

Service contractors are required to add the Landlord as an additional insured with regard to the General Liability policy. An additional Additionally Insured Endorsement is required based on the required amounts contained in the Certificate of Insurance Limits chart below.

CERTIFICATE OF INSURANCE LIMITS REQUIREMENT

1. For insurance requirements for crane lifts or any special contract work; contact for the property team for specific coverage and language.
2. Commercial General Liability Coverage Required (millions, per occurrence and aggregate) is the sum of the basic coverage + excess umbrella. See Example for Electrical Maintenance below:

- Commercial General Liability Coverage Required = 5MM. This requirement is met by:
- General Liability each Occurrence 3MM + Excess umbrella 2MM = 5MM
- General Liability General Aggregate 3MM + Excess umbrella 2MM = 5MM

Certificate of Insurance Limits

Type of Service	General Liability Each Occurrence / General Aggregate	Employers' Liability Each Accident / Disease – Each Employee / Disease – Policy Limit	Automobile Liability Combined Single Limit	Excess / Umbrella Liability Each Occurrence / Aggregate
Alarm Systems Service and Repair	1MM / 2MM	1MM	1MM	2MM
Appliance Repair & Maintenance	1MM / 1MM	1MM	1MM	1MM
Architectural *	3MM / 3MM	1MM	1MM	2MM
Asbestos Abatement and Hazardous Material Removal ****	5MM / 5MM	1MM	1MM	10MM
Audio-Visual Equipment	1MM / 1MM	1MM	1MM	1MM
Backflow Testing	1MM/1MM	1MM	1MM	1MM
Cabling	1MM / 1MM	1MM	1MM	2MM
Carpet/Floor Finishes	1MM / 2MM	1MM	1MM	2MM
Crane/Rigging	5MM / 5MM	1MM	1MM	10MM
Custom Fabrication & Installation Millwork	1MM / 1MM	1MM	1MM	2MM
Doors & Locks	1MM / 1MM	1MM	1MM	1MM
Electrical Maintenance	3MM / 3MM	1MM	1MM	2MM
Elevator/Escalator Service & Maintenance	5MM / 5MM	1MM	1MM	10MM
Elevator interior installation	2MM / 3MM	1MM	1MM	5MM
Engineering Consulting Service*	3MM / 3MM	1MM	1MM	2MM
Fire Extinguishing in Restaurants	1MM / 1MM	1MM	1MM	2MM
Fitness Equipment Maintenance	1MM / 2MM	1MM	1MM	2MM
Garbage Removal & Disposal, incl. dumpster maintained on premises	1MM / 2MM	1MM	1MM	2MM
General Contractors	3MM / 3MM	1MM	1MM	2MM
Generator Maintenance	1MM / 3MM	1MM	1MM	2MM
Glass Repair & Maintenance	1MM / 2MM	1MM	1MM	2MM
Glass Repair & Maintenance elevated	5MM / 5MM	1MM	1MM	10MM

Type of Service	General Liability Each Occurrence / General Aggregate	Employers' Liability Each Accident / Disease – Each Employee / Disease – Policy Limit	Automobile Liability Combined Single Limit	Excess / Umbrella Liability Each Occurrence / Aggregate
Graffiti Removal	1MM / 3MM	1MM	1MM	2MM
Handyman	1MM / 1MM	1MM	1MM	2MM
Heating, Ventilation & Air Conditioning Service/install	3MM / 3MM	1MM	1MM	2MM
Insulation/Fiberglass	1MM / 3MM	1MM	1MM	2MM
Interior Design Consulting*	1MM / 2MM	1MM	1MM	2MM
Life Safety/Fire Equipment	3MM / 3MM	1MM	1MM	2MM
Life Safety/Monitoring	3MM / 3MM	1MM	1MM	2MM
Lighting re-lamping (interior)	1MM / 2MM	1MM	1MM	2MM
Elevated Lighting Maintenance	5MM /5MM	1MM	1MM	5MM
Moves/Relocations/ reconfiguration	3MM / 3MM	1MM	1MM	2MM
Office Equipment Service	1MM / 2MM	1MM	1MM	2MM
Overhead and Revolving Door	1MM / 2MM	1MM	1MM	2MM
Painting	1MM / 2MM	1MM	1MM	2MM
Parking Surface Maintenance/sweeping	2MM / 2MM	1MM	1MM	2MM
Paving and Striping	2MM / 3MM	1MM	1MM	2MM
Plumbing	3MM / 3MM	1MM	1MM	2MM
Power washing (non-elevated)	1MM / 2MM	1MM	1MM	2MM
Power washing (elevated)	5MM /5MM	1MM	1MM	5MM
Pump Maintenance	3MM / 3MM	1MM	1MM	2MM
Roofing	5MM /5MM	1MM	1MM	10MM
Signage non elevated	2MM / 2MM	1MM	1MM	2MM
Signage Elevated	5MM / 5MM	1MM	1MM	10MM
Sprinkler System Service and Repair	3MM / 3MM	1MM	1MM	2MM
Stonework/Marble/wood/ metal cleaners and refinishers Repair & Maintenance	1MM / 2MM	1MM	1MM	2MM

Type of Service	General Liability Each Occurrence / General Aggregate	Employers' Liability Each Accident / Disease – Each Employee / Disease – Policy Limit	Automobile Liability Combined Single Limit	Excess / Umbrella Liability Each Occurrence / Aggregate
Telecommunications and TV Equip. Master Wiring and Antennas (non-elevated)	3MM / 3MM	1MM	1MM	2MM
Telecommunications and TV Equip. Master Wiring and Antennas (elevated or roof)	5MM / 5MM	1MM	1MM	5MM
UPS/SEP Equipment Maintenance	3MM / 3MM	1MM	1MM	2MM
Walk Off Mat Cleaning	1MM / 1MM	1MM	1MM	2MM
Water Treatment	1MM / 2MM	1MM	1MM	2MM
Window coverings (non- elevated)	1MM / 1MM	1MM	1MM	2MM
Window Washing and Swing Station Equipment Services	5MM / 5MM	1MM	1MM	10MM

***** Design and Engineering vendors must include Professional Errors and Omissions Insurance in the following amounts:

- Architects = 5MM
- Engineers = 5MM
- Interior Design = 2MM (or call Risk Management if limited scope)
- Any deviation from requested amount should be cleared through Oxford Properties Risk Management.
- Errors & Omissions is not based on spend, but rather the scope detail (access liability), such as no structural issues and what amount of damage/cost could be sustained if done incorrectly.

This Exhibit A may be updated from time to time as may be reasonably requested by Landlord at any time after the end of the fifth (5th) Lease Year and no more frequently than once every three (3) Lease Years thereafter, but not in excess of the amounts and types of insurance then being required by landlords of buildings comparable to and in the vicinity of the Building.

EXHIBIT J

TENANT STANDARD OPERATING PROCEDURES

[***]

Exhibit 10.3

Certain portions of this exhibit, marked by [***], have been excluded because they are both not material and are the type that the registrant treats as private or confidential.

RESEARCH, DEVELOPMENT, AND LICENSE AGREEMENT

AMONG

IONIS PHARMACEUTICALS, INC.,

AND

F. HOFFMANN-LA ROCHE LTD

AND

HOFFMANN-LA ROCHE INC.

RESEARCH, DEVELOPMENT, AND LICENSE AGREEMENT

This RESEARCH, DEVELOPMENT, AND LICENSE AGREEMENT (the "***Agreement***") is entered into as of the 26th day of September, 2023 (the "***Effective Date***") by and among **IONIS PHARMACEUTICALS, INC.**, a Delaware corporation, having its principal place of business at 2855 Gazelle Court, Carlsbad, California 92010 ("***Ionis***"), **F. HOFFMANN-LA ROCHE LTD**, a Swiss corporation, having its principal place of business at Grenzacherstrasse 124, 4070 Basel, Switzerland ("***Roche Basel***") and **HOFFMANN-LA ROCHE INC.**, a New Jersey corporation, having its principal place of business at 150 Clove Road, Suite 8, Little Falls, New Jersey 07424 ("***Roche US***"; Roche Basel and Roche US are collectively referred to as "***Roche***"). Roche and Ionis each may be referred to herein individually as a "***Party***" or collectively as the "***Parties***."

RECITALS

WHEREAS, Ionis has expertise in discovering and developing antisense drugs, and is researching compounds to identify and select drugs to treat Huntington's Disease and Alzheimer's Disease;

WHEREAS, Roche has expertise in developing and commercializing drugs, and Roche is interested in researching, developing and commercializing antisense drugs to treat Huntington's Disease and Alzheimer's Disease;

WHEREAS, Roche and Ionis desire to conduct research activities to identify and select at least one antisense drug to treat each of Huntington's Disease and Alzheimer's Disease;

WHEREAS, Roche desires Ionis to develop each drug until delivery of a Handoff Data Package, after which responsibility for further Development, Manufacturing and Commercialization (terms defined further below) of such drug will transition to Roche;

NOW, THEREFORE, in consideration of the respective covenants, representations, warranties and agreements set forth herein, the Parties hereto agree as follows:

ARTICLE 1.
DEFINITIONS

The terms used in this Agreement with initial letters capitalized, whether used in the singular or the plural, will have the meaning set forth in APPENDIX 1, or if not listed in APPENDIX 1, the meaning designated in places throughout the Agreement.

ARTICLE 2.
AGREEMENT OVERVIEW

2.1. The intent of this collaboration is for the Parties to conduct research programs directed to each of the gene targets [***] and [***] (each a "***Target***"). The research programs will be (i) an Ionis [***] program initially centered around the research of Oligonucleotides designed to bind to the RNA that encodes [***] with the goal of designating an Ionis Development Candidate for Huntington's Disease and (ii) an Ionis [***] program centered around the research of Oligonucleotides designed to bind to the RNA that encodes [***] with the goal of designating an Ionis Development Candidate for Alzheimer's Disease, and in each case ((i) and (ii)), Ionis will deliver for each Program a Handoff Data Package to Roche. On a Program-by-Program basis, (a) Ionis will perform and fund the activities allocated to it under the applicable R&D Plan from the Effective Date until the date of Handoff for such Program (the "***Handoff Period***"); (b) after Handoff has taken place, Roche will be responsible for all further development, manufacturing, regulatory and commercial activities related to the Products for such Program (including drafting the IND for such Products), unless agreed otherwise in a written agreement signed by each Party's authorized representative; and (c) the Parties, through a joint manufacturing committee, will discuss and agree upon a manufacturing strategy for each Program through [***] for such Program.

2.2. In addition, the Parties intend to enter into an agreement to conduct [***]. Upon completion of [***]. Any [***], which will incorporate the terms and principles set forth in SCHEDULE 2.2 but in any event will not [***].

2.3. The purpose of this ARTICLE 2 is to provide a high-level overview of the roles, responsibilities, rights and obligations of each Party under this Agreement with regard to the R&D Plans and Products, and therefore this ARTICLE 2 is qualified in its entirety by the more detailed provisions of this Agreement set forth below.

ARTICLE 3.
RESEARCH AND DEVELOPMENT

3.1. **Programs**.

3.1.1. **R&D Plans**. The R&D Plans for each Target are attached hereto as APPENDIX 2. Each such R&D Plan sets forth the research and preclinical Development activities that Ionis (with certain contributions by Roche) will conduct within the given timelines to designate at least one Ionis Development Candidate and deliver one Handoff Data Package.

3.1.2. **Conducting the R&D Plans**. For each Target, during the Handoff Period, Ionis and Roche will use Commercially Reasonable Efforts to conduct the research and Development activities allocated to such Party according to the applicable R&D Plan with the goal of delivering at least one Compound that fulfills the Success Criteria for such Target.

3.1.3. **Ionis Development Candidate Designation; IND-Enabling Toxicology Study Costs**.

(a) Unless otherwise mutually agreed by the Parties, Ionis' Research Management Committee ("***RMC***") [***]. For a given Compound that Ionis' RMC proposes as a potential Ionis Development Candidate, Ionis will provide to Roche the applicable Development Candidate Data Package, which Development Candidate Data Package will identify the proposed Compound and all Related Compounds. Within [***] after Roche's receipt of a Development Candidate Data Package pursuant to this Section 3.1.3(a), Roche will notify Ionis in writing of any omissions or deficiencies that Roche reasonably believes in good faith cause the Development Candidate Data Package to be incomplete with respect to the applicable proposed Ionis Development Candidate or Related Compound(s) described therein (a "***Development Candidate Data Package Deficiency Notice***"). Within [***] after Ionis' receipt of a Development Candidate Data Package Deficiency Notice, Ionis will resubmit a complete Development Candidate Data Package to Roche. Within [***] after Roche's receipt of the applicable complete Development Candidate Data Package, the JSC will convene to discuss and recommend the proposed Compound (or, alternatively, a Related Compound) as an Ionis Development Candidate. Should the JSC recommend the designation of the Compound (or a Related Compound) as an Ionis Development Candidate, then within [***] after such recommendation, Roche shall confirm designation of such Compound as an Ionis Development Candidate.

(b) If the JSC recommends such designation and Roche confirms such designation, then subject to Section 3.1.6 (Roche Performing IND- Enabling Toxicology Studies for First Ionis Development Candidate), Ionis shall be responsible to perform IND-Enabling Toxicology Studies with respect to such Ionis Development Candidate. The cost for such studies, including CMC cost, shall be handled, as follows: (i) if Ionis performs the IND-Enabling Toxicology Studies, then [***] will pay for the cost of such IND-Enabling Toxicology Studies for such Ionis Development Candidate (subject to Section 7.2 ([***])), and [***] will pay [***] for the Costs of the IND-Enabling Toxicology Studies for any subsequent Ionis Development Candidate, if applicable, for the same Target, and (ii) if Roche performs the IND-Enabling Toxicology Studies, then [***] will pay all costs for such studies.

(c) If (i) the JSC does not recommend such designation (and does not, as an alternative, recommend designation of a Related Compound), or (ii) the JSC recommends such designation (or, alternatively, the designation of a Related Compound) but Roche does not confirm the designation of such Compound (or Related Compound, as applicable) as an Ionis Development Candidate within [***], then, unless the Compound is [***] and designated by Ionis as a potential Follow-On Ionis Development Candidate under Section 3.6.2 (Follow-On Development Candidates [***]), Ionis shall have the right to terminate the Agreement for such Program in accordance with Section 3.10 (Failure to Identify or Designate an Ionis Development Candidate).

3.1.4. **Handoff Data Package**. Once available to Ionis, Ionis will promptly deliver to Roche the pharmacology, toxicology, histology and pharmacokinetic data generated from the IND-Enabling Toxicology Studies and any other studies it is responsible for under the R&D Plans and will provide Roche with Ionis' portion of the applicable Handoff Data Package (i.e., the data for which Ionis is responsible). Within [***] after receipt of such information, Roche will notify Ionis of any omissions or deficiencies that Roche believes in good faith cause Ionis' portion of the Handoff Data Package to be incomplete with respect to the applicable Ionis Development Candidate. Within [***] after Ionis' receipt of such notice from Roche, Ionis will resubmit its complete portion of the Handoff Data Package to Roche. Roche will complement the Handoff Data Package with data that Roche is responsible for, and the JSC will then review the Handoff Data Package and assess if the Handoff Data Package Criteria are met, subject to Section 3.1.7 (Failure to Achieve Handoff Data Package Criteria; Disputes over Achievement of Handoff Data Package Criteria). For clarity, [***]. If the Parties mutually agree to [***], then the Parties will memorialize such agreement in a writing signed by each Party's authorized representative.

3.1.5. **Handoff**. On an Ionis Development Candidate-by-Ionis Development Candidate basis, once the Handoff Data Package Criteria for the applicable Ionis Development Candidate is deemed to have been achieved as set forth in Section 3.1.4 (Handoff Data Package) or Section 3.1.6 (Roche Performing IND- Enabling Toxicology Studies for First Ionis Development Candidate), as applicable (the "***Handoff***"), the responsibility for further Development of such Ionis Development Candidate (including drafting the IND for such Ionis Development Candidate) transitions from Ionis to Roche, and Ionis will have no further responsibilities under the applicable R&D Plan.

3.1.6. **Roche Performing IND-Enabling Toxicology Studies for First Ionis Development Candidate**. No later than [***] prior to the JSC's expected designation of an Ionis Development Candidate for a given Target under Section 3.1.3 (Ionis Development Candidate Designation; IND-Enabling Toxicology Study Costs), Roche may, at its discretion, decide to perform IND-Enabling Toxicology Studies for such Ionis Development Candidate and prepare the related data package to be included within the Handoff Data Package instead of Ionis. In such instance, the milestone payment set forth in Section 7.2 ([***]) will not apply and [***] shall be responsible for the costs of such IND-Enabling Toxicology Studies. Once available to Roche, Roche will consolidate the respective pharmacology, toxicology, histology and pharmacokinetic data generated from the IND-Enabling Toxicology Studies together with other data each Party may be responsible for and present the completed Handoff Data Package at the JSC. The JSC will then convene to discuss such data package and confirm whether the Handoff Data Package Criteria have been met. If the JSC does not agree as to whether the Handoff Data Package Criteria have been met, then such matter shall be resolved in accordance with Section 3.1.7 (Failure to Achieve Handoff Data Package Criteria; Disputes over Achievement of Handoff Data Package Criteria). For clarity, [***]. If the Parties mutually agree to [***], then the Parties will memorialize such agreement in a writing signed by each Party's authorized representative.

3.1.7. **Failure to Achieve Handoff Data Package Criteria; Disputes over Achievement of Handoff Data Package Criteria**.

(a) If the Parties agree that the Handoff Data Package Criteria for a given Ionis Development Candidate are not met, then for a period of [***] beginning [***], as applicable, the Parties shall reasonably cooperate to identify suitable Related Compound(s) and Roche may select one of these Related Compounds and present it to the JSC to decide whether to designate such Related Compound as a replacement of the initial Ionis Development Candidate. If the JSC designates such Related Compound as an Ionis Development Candidate, then, at [***] but subject to Section 3.1.7(b), either Roche or Ionis will perform the IND-Enabling Toxicology Studies for such Ionis Development Candidate, and [***] will pay for the costs of such studies.

(b) If the Parties disagree whether the Handoff Data Package Criteria have been met with respect to a given Ionis Development Candidate and Roche wishes to select a Related Compound to replace the initial Ionis Development Candidate, then for a period of [***] beginning [***], Roche may so designate such Related Compound as a replacement Ionis Development Candidate, and Roche will perform the IND-Enabling Toxicology Studies for such Ionis Development Candidate at [***] expense.

3.1.8. Development of Additional Compounds.

(a) **Related Compounds**. On a Target-by Target basis, at any time after [***] under Section 3.1.3(a), *provided that* [***], Roche may initiate a Development program on a Related Compound [***] Roche will promptly provide written notice to Ionis following [***], which notice will identify the Related Compound that is the subject of such Development program. Roche will be solely responsible for all subsequent Development and Commercialization of such Related Compound.

(b) **Compounds that Are Not Related Compounds**. At any time after the Effective Date, *provided that* [***], if Roche wishes to [***] then Roche will notify Ionis in writing of the [***]. Within [***] after such notice, the JSC (or the Parties, if the JSC has been dissolved) will meet to discuss whether [***]. Following such meeting, Roche may [***], unless [***]. Following such meeting [***], Roche will be responsible for all subsequent Development and Commercialization of such Compound.

3.1.9. Performance Milestones During the Handoff Period. For each Target, during the Handoff Period:

(a) Ionis will use Commercially Reasonable Efforts to present to the JSC (i) at least [***] for [***] that Ionis in good faith believes meets the Success Criteria within [***] after the Effective Date and (ii) at least [***] for [***] that Ionis in good faith believes meets the Success Criteria within [***] after the Effective Date;

(b) if Ionis is conducting the IND-Enabling Toxicology Studies for a given Ionis Development Candidate, then Ionis will use Commercially Reasonable Efforts to complete the IND-Enabling Toxicology Studies for such Ionis Development Candidate within [***] after the designation of such Ionis Development Candidate; and

(c) if Roche is conducting the IND-Enabling Toxicology Studies for a given Ionis Development Candidate, then Roche will use Commercially Reasonable Efforts to complete the IND-Enabling Toxicology Studies for such Ionis Development Candidate within [***] after the designation of such Ionis Development Candidate.

3.2. **Disclosure of Results**. Ionis and Roche will provide reports and analyses at each JSC meeting, and more frequently [***], detailing the current status of each R&D Plan.

3.3. **Governance**.

3.3.1. **Joint Steering Committee**.

(a) **Establishment; Composition; Working Groups; Dissolution**. Within [***] after the Effective Date, the Parties will establish a joint steering committee ("***JSC***") to govern the activities under the R&D Plans (i.e. until Handoff). The Parties may utilize either a single JSC or may choose to have a JSC for each Target. The JSC will consist of [***] qualified representatives appointed by Ionis, and [***] qualified representatives appointed by Roche. Each Party will designate one of its representatives to act as the co-chairperson of the JSC. The co- chairpersons will be responsible for overseeing the activities of the JSC. The JSC will determine the JSC operating procedures at its first meeting, which will be codified in the written minutes of the first JSC meeting. The JSC will determine the frequency of meetings, location of meetings, and responsibilities for agendas and minutes. The JSC may hold meetings in person or by audio or video conference as determined by the JSC. Alliance Managers are invited to attend JSC meetings as participating non-members. In addition, upon prior approval of the other Party, each Party may invite its employees or consultants to attend JSC meetings, including any subject matter expert(s) with valuable knowledge of [***], [***], Huntington's Disease, or Alzheimer's Disease. The co-chairpersons will be responsible for ensuring that activities occur as set forth in this Agreement, including ensuring that JSC meetings occur, JSC recommendations are properly reflected in the minutes, and any dispute is given prompt attention and resolved in accordance with Section 3.3.1(c) (Decision-Making), Section 8.2.3 (Inventorship) and Section 13.1 (Dispute Resolution), as applicable. The JSC will form one or more subcommittees and working groups as it determines in order to discuss progress under the R&D Plans, [***], and to carry out its other activities under this Agreement. Any such subcommittees or working groups may act as an informal forum for the exchange of data arising from the performance of the R&D Plans, and will dissolve when the JSC dissolves. Reasonably in advance ([***]) of any meeting of [***], Ionis will share with any such working group [***]. On a Target-by-Target basis, the JSC will dissolve once all Ionis Development Candidates have either [***] or been terminated in accordance with Section 11.2 (Termination).

(b) **Responsibilities**. The JSC will perform the following functions:

(i) Oversee the Parties' activities under the respective R&D Plans;

(ii) Oversee subcommittees of the JSC;

(iii) Approve amendments to the R&D Plans;

(iv) Approve amendments to the Success Criteria;

(v) Determine whether a Development Candidate Data Package is complete;

(vi) Determine whether to recommend designating a Compound or, if applicable, Related Compound as an Ionis Development Candidate following review of the applicable Development Candidate Data Package;

(vii) Determine whether the Handoff Data Package Criteria have been satisfied;

(viii) Approve the Technology Transfer Plan and amendments following Handoff;

(ix) Record recommendations and decisions of the JSC in the JSC's meeting minutes; and

(x) Such other review and advisory responsibilities assigned to the JSC pursuant to this Agreement.

(c) Decision-Making.

(i) Committee Decision-Making. Decisions by the JSC will be made by unanimous consent with each Party's representatives having, collectively, one vote. At any given meeting of the JSC, a quorum will be deemed reached if a voting representative of each Party is present or participating in such meeting. No action taken at any meeting of the JSC will be effective unless there is a quorum at such meeting. Unless otherwise specified in this Agreement, no action will be taken with respect to a matter for which the JSC has not reached unanimous consensus.

(ii) Final Decision-Making Authority.

(1) If the JSC cannot unanimously agree on a matter to be decided by it within [***], then the matter will be referred to the Executives for resolution as set forth in Section 13.1.1 (Escalation), without application of Section 13.1.2 (Binding Arbitration).

(2) Except as set forth otherwise in this Agreement, if the Executives cannot reach agreement on a matter referred by the JSC within [***], then: (A) each Party will have final decision-making authority with respect to the conduct of its activities under each R&D Plan (*provided* that such conduct is in accordance with the applicable R&D Plan); (B) Roche will have final decision- making authority with respect to (1) [***], (2) [***], (3) [***], (x) [***], (y) [***], and (z) [***], (4) [***], (5) [***], and (6) [***].

(3) **Additional Costs Due to [***]**. For a given Program, if [***] or [***], then such increased Costs shall be shared as follows: [***] shall bear such Costs [***]; and [***] shall bear such Costs [***].

(4) Notwithstanding anything to the contrary in this Section 3.3.1(c)(ii) (Final Decision-Making Authority), a Party will not have final decision-making authority with respect to [***] of a Product if the other Party has a reasonable good faith belief that [***].

(5) Except as otherwise expressly stated in this Agreement, the JSC will have no decision-making authority and will act as a forum for sharing information about the activities conducted by the Parties hereunder and as an advisory body, in each case only on the matters described in, and to the extent set forth in, this Agreement.

(iii) **Decision-Making After Handoff**. After Handoff has occurred for a given Ionis Development Candidate, the JSC has no authority to make decisions with respect to such candidate.

3.3.2. Joint Manufacturing Committee.

(a) **Establishment; Composition; Dissolution**. Within [***] after the creation of the JSC, the Parties will establish a joint manufacturing committee ("***JMC***") to govern the manufacturing of API to support the activities under the R&D Plans (i.e. until Handoff). The JMC will be deemed a subcommittee of the JSC, as described above in Section 3.3.1(a) (Establishment; Composition; Working Groups; Dissolution), and will have the responsibilities set forth in Section 3.3.2(b) (JMC Responsibilities). The JMC will consist of [***] qualified representatives appointed by Ionis, and [***] qualified representatives appointed by Roche. Alliance Managers are invited to attend JMC meetings as participating non-members. In addition, upon prior approval of the other Party, each Party may invite its employees or consultants to attend JMC meetings, including any subject matter expert(s) with valuable knowledge of [***], [***], Huntington's Disease, or Alzheimer's Disease. The JMC will dissolve upon the earlier of (i) dissolution of the JSC, (ii) termination of this Agreement, and (iii) the Parties' mutual agreement to dissolve the JMC.

(b) **JMC Responsibilities**. The JMC will perform the following functions:

(i) develop, discuss and approve the manufacturing strategy and plan for manufacturing API and Finished Drug Product for each Program through [***] for such Program, which plan will be part of the R&D Plan for the applicable Program;

(ii) establish and revise the Handoff Data Package Criteria related to CMC matters;

(iii) determine whether the Handoff Data Package Criteria related to CMC matters for each Ionis Development Candidate have been satisfied;

(iv) establish the manufacturing part of the Technology Transfer Plan;

(v) perform such other functions as determined by the JSC.

(c) **JMC Decision-Making**.

(i) **Committee Decision-Making**. Decisions by the JMC will be made by unanimous consent with each Party's representatives having, collectively, one vote. At any given meeting of the JMC, a quorum will be deemed reached if a voting representative of each Party is present or participating in such meeting. No action taken at any meeting of the JMC will be effective unless there is a quorum at such meeting. Unless otherwise specified in this Agreement, no action will be taken with respect to a matter for which the JMC has not reached unanimous consensus.

(ii) **Escalation to JSC**. If the JMC cannot unanimously agree on a matter to be decided by it within [***], then the matter will be referred to the JSC for resolution in accordance with Section 3.3.1(c)(ii) (Final Decision-Making Authority).

3.3.3. **Alliance Managers**. Each Party will appoint a representative to act as its alliance manager (each, an "***Alliance Manager***") for facilitating communication and collaboration between the Parties. Each Alliance Manager will be responsible for (a) facilitating resolution of potential and pending issues and potential disputes to enable the JSC to reach consensus and avert escalation of such issues or potential disputes, (b) supporting the co-chairpersons with organization of JSC meetings, information exchange, meeting minutes, as necessary, and (c) preparing status and progress reports on the above as determined necessary by the JSC.

3.4. **Manufacturing and Supply**. Unless otherwise expressly agreed to by the JMC:

3.4.1. **Supplies for Activities under R&D Plans**.

(a) **Supplies for Activities During Handoff Period**. Subject to Section 3.4.1(c) (Technology Transfer During Handoff Period), on a Program- by-Program basis, during the Handoff Period for such Program, at [***], Ionis will supply cGMP [***] for the [***] Program, and [***] API, or a combination of both [***] API for the [***] Program, in each case for use in IND- Enabling Toxicology Studies for the first Ionis Development Candidate generated under the applicable R&D Plan and, at [***] cost, cGMP material for use in the [***] for such Ionis Development Candidate. Ionis' supply obligation hereunder will be at least [***], but no more than [***] of cGMP API per Ionis Development Candidate.

(b) **Supplies for Activities After Handoff**. After Handoff, Ionis will deliver to Roche, if Roche desires, any inventory of cGMP API, radiolabeled material, cGMP Finished Drug Product, packaged clinical trial material, and cGMP packaged trial material containing the Ionis Development Candidate then in Ionis' possession, and Roche will pay Ionis for such materials at Ionis' Fully Absorbed Cost of Goods, as set forth in SCHEDULE 3.4.1(b).

(c) **Technology Transfer During Handoff Period.** For any Compound (except [***] as an Ionis Development Candidate that is designed to bind to the RNA that encodes [***]), Roche may, at its discretion, no later than [***] before the anticipated designation of an Ionis Development Candidate, request a technology transfer under Section 3.5 (Technology Transfer Implementation) and assume responsibility to manufacture and supply API for the IND-Enabling Toxicology Studies for such Ionis Development Candidate (and for all future Clinical Studies of such Ionis Development Candidate).

3.5. **Technology Transfer Implementation**. After Handoff for a given Ionis Development Candidate (or earlier if agreed between the Parties), the Parties will establish a technology transfer plan ("***Technology Transfer Plan***") under which Ionis will provide reports and information generated by or on behalf of Ionis in performing its activities under the applicable R&D Plan that are necessary for Roche to draft the IND, and the Parties will conduct the transfer activities with respect to the applicable Ionis Development Candidate in accordance with such Technology Transfer Plan.

3.5.1. **Licensed Know-How – Generally**. As part of the activities to be performed under the Technology Transfer Plan, Ionis will deliver to Roche copies of Licensed Know-How with respect to the applicable Ionis Development Candidate (other than the Ionis Manufacturing and Analytical Know-How) in the Field in Ionis' possession not previously provided hereunder, for use solely in accordance with the license granted under Section 5.1.2 (Development and Commercialization License Grant to Roche) to Roche for such Ionis Development Candidate, together with all regulatory documentation (including drafts) related to such Ionis Development Candidate. To assist with the transfer of such Licensed Know-How, Ionis will make its personnel reasonably available to Roche during normal business hours to transfer such Licensed Know-How.

3.5.2. **Ionis Manufacturing and Analytical Know-How**. As part of the activities to be performed under the Technology Transfer Plan, Ionis will deliver, at Roche's election, to one of either (a) [***], or (b) [***] solely to Manufacture API on Roche's behalf, copies of the Ionis Manufacturing and Analytical Know-How relating to the applicable Ionis Development Candidate in Ionis' possession not previously provided hereunder, which is necessary for the exercise by Roche, its Affiliates or a Third Party of the Manufacturing rights granted under Section 5.1.2 (Development and Commercialization License Grant to Roche).

3.5.3. **Technology Transfer Costs**. Ionis will provide up to [***] of technology transfer activities under this Section 3.5 (Technology Transfer Implementation) at [***]. Thereafter, if reasonably requested by Roche, Ionis will provide reasonable transfer support, and [***].

3.6. Follow-On Ionis Development Candidates.

3.6.1. Follow-On Development Candidates [***]. On a Program- by-Program basis, for a period starting from [***] and ending on the date that is [***], if Ionis' RMC designates as a development candidate ready to start IND-Enabling Toxicology Studies one or more [***] discovered by or on behalf of Ionis that are designed to bind to the RNA that encodes the applicable Target for such Program and that satisfy the Success Criteria and that are not Compounds, then Ionis will notify Roche in writing and will provide Roche with the data package presented to Ionis' RMC in connection with the approval by Ionis' RMC of such [***]. Roche will then have [***] from delivery of such data package to provide written notice to Ionis electing to deem such [***] as a Follow-On Ionis Development Candidate and thereafter such Follow-On Ionis Development Candidate and [***] shall be considered Compounds, and Roche shall continue activities under this Agreement with respect to such Follow-On Ionis Development Candidate. If Roche provides such timely written notice, then Roche will be responsible for the conduct and costs of any further research, Development, Manufacturing, and Commercialization activities for such Follow-On Ionis Development Candidate, and all terms of this Agreement will apply to such Follow-On Ionis Development Candidate, including, but not limited to, Section 7.3 (One-time Milestone Payments for Achievement of Milestone Events), Section 7.4 (Royalties), and Section 7.5 (Royalty Payments and Reports). If [***], then [***].

3.6.2. Follow-On Development Candidates [***]. Subject to Section 3.6.3 ([***]), on a Program-by-Program basis, for a period starting from [***] and ending on the date that is [***], if Ionis' RMC designates as a development candidate ready to start IND-Enabling Toxicology Studies one or more [***] discovered by Ionis that are designed to bind to the RNA that encodes the applicable Target for such Program and that satisfy the Success Criteria and that are not Compounds, then Ionis will notify Roche in writing and will provide Roche with the data package presented to Ionis' RMC in connection with the approval by Ionis' RMC of such [***]. Roche will then have [***] from delivery of such data package to provide written notice to Ionis electing to deem such [***] as a Follow-On Ionis Development Candidate and thereafter continue activities under this Agreement with respect to such Follow-On Ionis Development Candidate. If Roche provides such timely written notice, then such Follow-On Ionis Development Candidate and [***] shall be considered Compounds, and Roche will be responsible for the conduct and costs of any further research, Development, Manufacturing, and Commercialization activities for such Follow-On Ionis Development Candidate, and all terms of this Agreement will apply to such Follow-On Ionis Development Candidate, including, but not limited to, Section 7.3 (One-time Milestone Payments for Achievement of Milestone Events), Section 7.4 (Royalties), and Section 7.5 (Royalty Payments and Reports). If [***], then [***].

3.6.3. Roche [***]. On a [***] basis, at any time after [***] until the [***], if [***], then [***]. Upon [***] receipt of [***], [***] will [***] with respect to [***].

3.6.4. **Agreement by the Parties to Discover and Develop Additional Ionis Development Candidates**. At any time after the expiration of the period ending [***] after [***], the Parties may mutually agree to collaborate on the research, discovery and development of an Oligonucleotide designed to bind to a Target that is not a Related Compound or a Follow-On Ionis Development Candidate. Any such future collaboration is subject to the Parties' good faith negotiation and execution of a new agreement or an amendment of this Agreement.

3.7. **Subcontracting**. Each Party may engage Third Party subcontractors to perform certain of its obligations under this Agreement. Any subcontractor engaged to perform a Party's obligations under this Agreement will meet the qualifications typically required by such Party for the performance of work similar in scope and complexity and will execute such Party's standard nondisclosure agreement. Any Party engaging a subcontractor hereunder will remain responsible for such activities.

3.8. **Materials Transfer**. To facilitate the activities under each R&D Plan, either Party may provide certain materials for use by the other Party. All such materials will be used by the receiving Party in accordance with terms of this Agreement solely for purposes of exercising its rights and performing its obligations under this Agreement, and the receiving Party will not transfer such materials to any Third Party except with the written consent of the supplying Party. Except as expressly set forth herein, THE MATERIALS ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

3.9. **Applicable Laws**. Each Party will perform its activities pursuant to this Agreement in compliance with good laboratory and clinical practices and, except where stated otherwise, cGMP, in each case as applicable under the laws and regulations of the country and the state and local government wherein such activities are conducted.

3.10. **Failure to Identify or Designate an Ionis Development Candidate**. On a Program- by-Program basis:

3.10.1. if, despite Ionis' Commercially Reasonable Efforts, Ionis has not proposed any Compound for potential designation as an Ionis Development Candidate within (a) [***] after [***] for the [***] Program, or (b) [***] after [***] for the [***] Program, then, notwithstanding any provision to the contrary in this Agreement, (i) work under the applicable R&D Plan will stop; (ii) the Parties will no longer have an obligation to perform any activities under this ARTICLE 3 with respect to the applicable Program; and (iii) either Party may terminate the applicable Program, as further specified in Section 11.2.6(a); and

3.10.2. if the JSC does not recommend the designation of a proposed Compound (and does not, as an alternative, recommend designation of a Related Compound) within the timeline set forth in Section 3.1.3(a), or Roche, following the JSC's recommendation to designate a Compound (or Related Compound, as applicable) as an Ionis Development Candidate, does not confirm such recommendation [***] in accordance with Section 3.1.3 (Ionis Development Candidate Designation; IND-Enabling Toxicology Study Costs), then, except as set forth in Section 3.1.3(c), and notwithstanding any other provision to the contrary in this Agreement, (a) work under the applicable R&D Plan will stop; (b) the Parties will no longer have an obligation to perform any activities under this ARTICLE 3 with respect to the applicable Program; and (c) Ionis may terminate the applicable Program, as further specified in Section 11.2.6(b).

ARTICLE 4.
EXCLUSIVITY COVENANTS

4.1. Exclusivity.

4.1.1. [***] Exclusivity Covenants Before Handoff. On a Target-by-Target basis, except in the performance of its obligations or exercise of its rights under this Agreement, and except as set forth in Section 4.1.3 (Limitations and Exceptions to Exclusivity Covenants), [***] will work [***] (including the grant of any license to any Third Party) with respect to the [***] that is designed to bind to the RNA that encodes the applicable Target in the Field from the Effective Date until the earlier of (a) the date of Handoff with respect to the first Ionis Development Candidate directed to such Target and (b) termination of this Agreement with respect to such Target.

4.1.2. [***] Exclusivity Covenants After Handoff. On a Target-by-Target basis, except in the performance of its obligations or exercise of its rights under this Agreement, and except as set forth in Section 4.1.3 (Limitations and Exceptions to Exclusivity Covenants), [***] will not work on its own or with any of its Affiliates or any Third Party (including the grant of any license to any Third Party) with respect to the [***] that is designed to bind to the RNA that encodes the applicable Target in the Field from the date of Handoff with respect to the first Ionis Development Candidate directed to such Target until the earlier of (a) the [***] and (b) termination of this Agreement with respect to such Target; *provided, however*, that if (i) [***], then [***] exclusivity obligations hereunder will end on the [***], and (ii) *provided that* [***], then [***] exclusivity obligations hereunder will end on the [***].

4.1.3. Limitations and Exceptions to Exclusivity Covenants. Notwithstanding anything to the contrary in Section 4.1.1 ([***] Exclusivity Covenants Before Handoff) and Section 4.1.2 ([***] Exclusivity Covenants After Handoff), the Parties and their Affiliates may perform the following activities:

(a) all activities permitted or contemplated under this Agreement; and

(b) with regard to Ionis and its Affiliates: (i) any activities pursuant to the Prior Agreements as in effect on the Effective Date; and (ii) the granting of, or performance of obligations or exercise of rights under, Permitted Licenses.

4.2. **Effect of Exclusivity on Indications**. Ionis and Roche are subject to certain exclusivity covenants under Section 4.1.1 ([***] Exclusivity Covenants Before Handoff) and Section 4.1.2 ([***] Exclusivity Covenants After Handoff); *however*, the Parties acknowledge and agree that each Party (on its own or with a Third Party or an Affiliate) may pursue products for the same indication as a Product so long as such product does not breach Section 4.1 (Exclusivity).

ARTICLE 5.
LICENSE GRANTS

5.1. **License Grants; Sublicense Rights**.

5.1.1. **Research License Grant to Roche**. Subject to the terms of this Agreement, Ionis hereby grants to Roche a worldwide, non-exclusive, royalty-free, sublicensable (in accordance with Section 5.1.4 (Sublicense Rights) below) license under the Licensed Technology to perform the Roche R&D Activities during the Handoff Period; *provided* that, (a) for clarity, such license shall not include a license to conduct any clinical Development activities with respect to, or Commercialize, any Compounds or Products, and (b) such license includes a license under the Ionis Manufacturing and Analytical Patents and Ionis Manufacturing and Analytical Know-How to Manufacture API only if Roche elects to assume responsibility for Manufacturing and supplying such API under Section 3.4.1(c) (Technology Transfer During Handoff Period).

5.1.2. **Development and Commercialization License Grant to Roche**. Subject to the terms of this Agreement, Ionis hereby grants to Roche a worldwide, exclusive, royalty-bearing, sublicensable (in accordance with Section 5.1.4 (Sublicense Rights) below) license under the Licensed Technology to research, Develop, Manufacture, have Manufactured (in accordance with Section 5.1.4 (Sublicense Rights) below) and Commercialize Compounds and Products in the Field; *provided that* [***].

5.1.3. **Cross-Licenses under Collaboration Intellectual Property**.

(a) **Enabling License to Roche from Ionis**. Subject to the terms of this Agreement (including [***]), Ionis hereby grants to Roche a worldwide, fully paid-up, royalty-free, non-exclusive, sublicensable license under any Ionis Collaboration Technology to research, develop, manufacture, have manufactured and commercialize products that are not Products in the Field; and

(b) **Enabling License to Ionis from Roche**. Subject to the terms of this Agreement (including [***]), Roche hereby grants to Ionis a worldwide, fully paid-up, royalty-free, non-exclusive, sublicensable license under any Roche Collaboration Technology, to research, develop, manufacture, have manufactured and commercialize products that are not Products in the Field.

5.1.4. **Sublicense Rights**.

(a) Subject to the terms of this Agreement, Roche will have the right to grant sublicenses under any license granted under Section 5.1.1 (Research License Grant to Roche), Section 5.1.2 (Development and Commercialization License Grant to Roche) and Section 5.1.3(a) (Enabling License to Roche from Ionis):

(i) under the Ionis Core Technology Patents, Ionis Product-Specific Patents, Ionis Collaboration Technology and Ionis Know-How to an Affiliate of Roche or a Third Party; and

(ii) under the Ionis Manufacturing and Analytical Patents and Ionis Manufacturing and Analytical Know-How solely to (y) [***] or (z) [***].

(b) **Requests to Grant Sublicenses to CMOs**. If Roche provides Ionis with a written request that Ionis grant a license under the Ionis Manufacturing and Analytical Patents and Ionis Manufacturing and Analytical Know- How to a CMO designated by Roche that is not a Licensed CMO, solely for such CMO to Manufacture Products for Roche, its Affiliate or Sublicensee in a manufacturing facility owned or operated by such CMO, Ionis will [***].

(c) **Enforcing Sublicenses**. Each sublicense by Roche under this Agreement will be subject to, and consistent with, the terms of this Agreement. Roche shall be responsible to ensure compliance by its Sublicensees with the terms and conditions of this Agreement. If Ionis reasonably believes a Roche Sublicensee may be violating the terms of this Agreement, then, within [***] after [***], Roche will provide Ionis a full and complete copy of the sublicense Roche entered with such Sublicensee.

5.1.5. **No Implied Licenses**. All rights in and to Licensed Technology not expressly licensed to Roche under this Agreement are hereby retained by Ionis or its Affiliates. All rights in and to Roche Technology not expressly licensed or assigned to Ionis under this Agreement, are hereby retained by Roche or its Affiliates. Except as expressly provided in this Agreement, no Party will be deemed by estoppel or implication to have granted the other Party any license or other right with respect to any intellectual property.

5.1.6. **License Conditions; Limitations**. Any license granted under Section 5.1.2 (Development and Commercialization License Grant to Roche) and the sublicense rights under Section 5.1.4 (Sublicense Rights) are subject to and limited by (a) the Permitted Licenses, and (b) the Prior Agreements, in each case [***].

5.1.7. **Trademarks for Products**. Roche shall be the owner and solely responsible for all trademarks, trade dress, logos, slogans, designs, copyrights and domain names used on or in connection with Products licensed under Section 5.1.2 (Development and Commercialization License Grant to Roche).

ARTICLE 6.
DEVELOPMENT, MANUFACTURING, COMMERCIALIZATION AND DILIGENCE

6.1. Roche Development, Manufacturing & Commercialization

6.1.1. **Responsibility**. On an Ionis Development Candidate-by-Ionis Development Candidate basis, after Handoff for an Ionis Development Candidate, subject to the terms of this Agreement, Roche is solely responsible for all Development, Manufacturing and Commercialization activities, and for all costs and expenses associated therewith, with respect to the Development, Manufacture and Commercialization of Products containing such Ionis Development Candidate.

6.1.2. **Clinical Development Plan**. After the Handoff for a given Ionis Development Candidate Roche will provide Ionis with a written [***] plan [***] of the [***] of the applicable Product through [***]. Such plan will include key [***] events for the applicable Product [***] for the achievement of such events [***] for such Product. Roche will provide to Ionis [***].

6.1.3. **[***]**. On an Ionis Development Candidate-by-Ionis Development Candidate basis, after Handoff for an Ionis Development Candidate, [***] Roche will provide to Ionis the [***] for such Ionis Development Candidate, and subsequent updated versions of [***], [***]. The sharing of the [***] contemplated hereunder [***], and such [***] shall be Roche's Confidential Information.

6.1.4. **Regulatory Communications and Submissions**. As between the Parties, Roche will be responsible for (a) determining the regulatory plans and strategies for the Products, (b) making all regulatory filings with respect to the Products, and (c) obtaining and maintaining Approvals in the name of Roche or its Affiliates or Sublicensees. Up to and including [***], Roche will provide Ionis with any Key Regulatory Submissions to any Regulatory Authority in each Major Market for such Product before providing such submission to the applicable Regulatory Authority for Ionis to provide any comments on the contents thereof. Ionis will have [***] from the date of receipt of such submission to provide comments with respect thereto. Roche will [***] by Ionis. Following [***], Roche [***] also [***]. For clarification, [***].

6.1.5. **Class Generic Claims**. If Roche intends to make any claims in a Product label or regulatory filing that are class generic to Oligonucleotides or Ionis' chemistry platform(s), then Roche will provide such claims and regulatory filings to Ionis in advance and will [***] any proposals and comments made by Ionis.

6.2. **Diligence**. On a Target-by-Target basis, after Handoff for an Ionis Development Candidate, Roche will use Commercially Reasonable Efforts to further Develop and Commercialize at least one Product with respect to the Target for such Ionis Development Candidate in the Field in the Territory. Without limiting the foregoing, within [***] after [***], Roche will [***]; *provided, however*, [***].

6.3. IND; Global Safety Database.

6.3.1. IND. Roche will be the holder of the IND for each Ionis Development Candidate and will assume responsibility for the global safety database related to such Ionis Development Candidate. After Handoff, Roche will be solely responsible for reporting to Regulatory Authorities in accordance with the Applicable Law for expeditable adverse events and for periodic safety reporting relating to the safety of such Ionis Development Candidate and all subsequent Ionis Development Candidates with respect to the same Target.

6.3.2. Ionis' Antisense Safety Database.

(a) Ionis maintains an internal database that includes information regarding the tolerability of its drug compounds, individually and as a class, including information discovered during pre-clinical and clinical development (the "***Ionis Internal Oligonucleotide Safety Database***"). In an effort to maximize understanding of the safety profile and pharmacokinetics of Ionis compounds, after Handoff, Roche will cooperate in connection with populating the Ionis Internal Oligonucleotide Safety Database. Roche and Ionis will [***].

(b) Ionis utilizes the information in the Ionis Internal Oligonucleotide Safety Database to conduct analyses to keep Ionis and its partners informed regarding class generic properties of Oligonucleotides, including with respect to safety. As such, if and when Ionis identifies safety or other related issues that may be relevant to a Product (including any potential class-related toxicity), Ionis will promptly inform Roche of such issues and, if requested, provide the data supporting Ionis' conclusions.

ARTICLE 7.
FINANCIAL PROVISIONS

7.1. Upfront Fee. Within [***] days following the Effective Date and receipt by Roche of an invoice from Ionis, Roche will pay Ionis an upfront fee equal to sixty million dollars ($60,000,000). All dollar amounts in this Agreement are in U.S. dollars.

7.2. [***] IND-Enabling Toxicology Studies [***]. For the *first* Ionis Development Candidate for a given Target, [***] will decide which Party will conduct IND-Enabling Toxicology Studies in accordance with Section 3.1.6 (Roche Performing IND-Enabling Toxicology Studies for First Ionis Development Candidate), and will either (a) [***], or (b) [***]. In case of (a) above, [***].

7.3. One-time Milestone Payments for Achievement of Milestone Events.

7.3.1. Development Milestones for [***]. Subject to Section 7.3.1(a) ([***]) and Section 7.3.1(b) ([***]), Roche will pay Ionis the milestone payments set forth in TABLE 1 below the first time a milestone event listed in TABLE 1 is first achieved by a Product directed to [***], regardless of how many times thereafter such Milestone Event is achieved by a subsequent Product to such Target.

Table 1: Milestone Events for [***]

Milestone Event	Milestone Payment for [***] Product
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
Total [***] **Milestones**	**$**[***]

(a) **[***]**. The Milestone Event payment for "[***]" in TABLE 1 will be [***], subject to the following [***]:

(i) If achievement of the "[***]" Milestone Event is [***] and [***] achieves the "[***]" Milestone Event, then [***].

(ii) Following achievement of the "[***]" Milestone Event with a Product [***] and payment of the corresponding milestone payment, if [***], then [***].

(b) **[***]**. If (i) following [***] with respect to a Product directed to [***], [***], (ii) [***], (iii) [***], and (iv) [***], then [***]. The [***].

7.3.2. **Development Milestones for [***]**.

(a) Subject to Section 7.3.2(b) ([***]), Roche will pay Ionis the milestone payments set forth in TABLE 2 below the first time a Milestone Event listed in TABLE 2 is first achieved by a Product directed to [***], regardless of how many times thereafter such Milestone Event is achieved by a subsequent Product to such Target.

Table 2: Milestone Events for [***]

Milestone Event	Milestone Payment for [***] Product
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
Total [***] Milestones	**$**[***]

(b) **[***]**. If (i) [***], (ii) [***], (iii) [***], and (iv) [***], then [***].

7.3.3. **Milestone Payments for First Achievement of Sales Milestone Event by [***] Product**. Roche will pay Ionis the applicable one-time milestone payments set forth in TABLE 3 below after the first achievement of the listed events by a first Product directed against [***], regardless of how many times thereafter another Product directed against [***] achieves such event, by or on behalf of Roche or its Affiliates or Sublicensees. For clarity, notwithstanding any provision to the contrary in this Agreement, [***]. Net Sales will be [***], as applicable.

TABLE 3

Sales Milestone	Sales Milestone Payment
≥ $[***] in aggregate worldwide Annual Net Sales of [***] Product	$[***]
≥ $[***] in aggregate worldwide Annual Net Sales of [***] Product	$[***]
≥ $[***] in aggregate worldwide Annual Net Sales of [***] Product	$[***]
Total Sales Milestone Payments	**$[***]**

7.3.4. **Limitations on Milestone Payments; Exceptions; Notice**.

(a) Each milestone payment set forth in TABLE 1 in Section 7.3.1 (Development Milestones for [***]) and in TABLE 2 in Section 7.3.2 (Development Milestones for [***]) and in TABLE 3 in Section 7.3.3 (Milestone Payments for First Achievement of Sales Milestone Event by [***] Product) above will be paid only once upon the first achievement of the Milestone Event regardless of how many times such Milestone Event is achieved by the same or another Product directed to the same Target.

(b) If a particular Development Milestone Event (i.e., [***]) in TABLE 1 in Section 7.3.1 (Development Milestones for [***]) or in TABLE 2 in Section 7.3.2 (Development Milestones for [***]) is not achieved because Development activities transpired such that achievement of such earlier Milestone Event was unnecessary or did not otherwise occur, then upon achievement of a later Milestone Event the Milestone Event payment applicable to such earlier Milestone Event will also be due. For example, if Roche proceeds directly to "[***]" without achieving the "[***]," then upon achieving the "[***]" Milestone Event, both the "[***]" and "[***]" Milestone Event payments are due to Ionis.

(c) Each time a Milestone Event is achieved under this Section 7.3 (One- time Milestone Payments for Achievement of Milestone Events), Roche will send to Ionis a written notice thereof promptly (but no later than [***]) following the date of achievement of such Milestone Event and such payment will be due within [***] of the date such Milestone Event was achieved and receipt of an invoice by Roche from Ionis.

7.4. Royalties.

7.4.1. Royalty Rates. As partial consideration for the rights granted to Roche hereunder, subject to the provisions of this Section 7.4.1 (Royalty Rates) and Section 7.4.3 (Royalty Adjustments), Roche will pay to Ionis royalties on worldwide Annual Net Sales of Products sold by Roche, its Affiliates or Sublicensees, on a country-by-country and Product-by-Product basis during the Royalty Term, in each case in the amounts (on an incremental basis) as follows:

TABLE 4

Royalty Tier	Annual Worldwide Net Sales	Royalty Rate for Product Comprising an Ionis Development Candidate
1	For the portion of Annual worldwide Net Sales < $[***]	[***]%
2	For the portion of Annual worldwide Net Sales ≥ $[***] but < $[***]	[***]%
3	For the portion of Annual worldwide Net Sales ≥ $[***] but < $[***]	[***]%
4	For the portion of Annual worldwide Net Sales ≥ $[***]	[***]%

(a) For purposes of TABLE 4, worldwide Annual Net Sales for a particular Product will be calculated by summing the aggregate Net Sales for that Product for all countries in the world for such Product. For example, if worldwide Net Sales of a Product for a given Calendar Year are $[***], then royalties owed to Ionis on such Net Sales of such Product for that Calendar Year shall equal [***] dollars ($[***]), calculated as follows:

[([***]) + ([***])] = $[***] royalty payment

7.4.2. Royalty Term. Roche's obligation to pay Ionis royalties with respect to a Product will continue on a country-by-country and Product-by-Product basis from the date of First Commercial Sale of such Product in such country until the latest of (a) the date of expiration of the last Valid Claim [***], as applicable ([***]) that are licensed by Ionis to Roche under this Agreement that Covers the Product in the country in which such Product is made, used or sold, (b) the date of [***], and (c) the [***] anniversary after the First Commercial Sale of such Product in such country (the "***Royalty Term***"). Notwithstanding anything herein to the contrary, [***].

7.4.3. **Royalty Adjustments**. For the purpose of calculating royalties owed for a Product, the royalty rates set forth in Section 7.4.1 (Royalty Rates) shall be subject to the following adjustments, as applicable:

(a) **Net Sales Adjustment for [***] Product**.

(i) If Roche or its Affiliates or Sublicensees intend to [***], then the Parties shall meet approximately [***] after [***] to negotiate in good faith and agree to an appropriate adjustment to Net Sales to reflect [***]. If, after such good faith negotiations not to exceed [***], the Parties cannot agree to an appropriate adjustment, the dispute shall be initially referred to the Executives in accordance with Section 13.1.1 (Escalation), without application of Section 13.1.2 (Binding Arbitration).

(ii) If the Executives are unable to agree on the [***] within [***] of such referral (a "[***]"), then such [***] Dispute shall be determined by arbitration pursuant to the terms set forth in SCHEDULE 7.4.3(a)(ii).

(b) **Adjustment of [***] for a [***] Product**. On a [***] Product-by-[***] Product basis, for purposes of determining the [***] for a [***] Product, [***] shall be the [***] of such [***] Product in the relevant country.

(c) **No Valid Claim**. Subject to Section 7.4.3(g) (Maximum Deduction), for a given Product, (i) if in a given country within the Territory there is no Valid Claim [***] that Covers the [***] Product, then the royalty rates listed in TABLE 4 in Section 7.4.1 (Royalty Rates) applicable to such Product will be reduced by [***] %; (ii) if [***], then [***]; and (iii) if both (i) and (ii) of this Section 7.4.3(c) (No Valid Claim) apply, then [***].

(d) **Generic Product**. Subject to Section 7.4.3(g) (Maximum Deduction), on a country-by-country and Product-by-Product basis, if at any time during the Royalty Term a Generic Product is sold in such country and the aggregate Net Sales of such Product in such country in any Calendar Quarter thereafter decline by more than [***]% of the level of the Net Sales of such Product achieved in any of the [***] full Calendar Quarters immediately prior to the Calendar Quarter in which the Generic Product was first sold, then the royalty rates listed in TABLE 4 in Section 7.4.1 (Royalty Rates) applicable to such Product in such country will be [***] reduced by [***] ([***]%).

(e) **[***] Adjustment**. Subject to Section 7.4.3(g) (Maximum Deduction), if at any time during the Royalty Term (i) [***], (ii) [***], and (iii) [***], then the royalty rates listed in TABLE 4 in Section 7.4.1 (Royalty Rates) applicable to such [***] Product will be [***] ([***]%) in the [***] solely for [***]. For any subsequent Calendar Quarter in which the [***].

(f) Third Party Payments.

(i) Additional Ionis Core Intellectual Property.

(1) Roche will promptly provide Ionis written notice of any [***] ("***Additional Ionis Core IP***") that Roche believes it has identified, and Ionis will have the first right, but not the obligation, to negotiate with, and obtain a license from, the Third Party Controlling such Additional Ionis Core IP. For clarity, Additional Ionis Core IP does not include any Patent Rights claiming (or intellectual property related to) [***]. If Ionis obtains such a Third Party license, then Ionis will include such Additional Ionis Core IP in the license granted to Roche under Section 5.1.2 (Development and Commercialization License Grant to Roche), and any financial obligations under such Third Party agreement will be paid [***].

(2) If, however, Ionis elects not to obtain such a license to such Third Party intellectual property, then Ionis will so notify Roche, and Roche may obtain such a Third Party license and, subject to Section 7.4.3(g) (Maximum Deduction), Roche may offset an amount equal to [***]% of any [***] paid by Roche under such Third Party license against any [***] due to Ionis under Section [***] of this Agreement in such country for [***].

(3) If Ionis does not agree with Roche that a license to such [***], then Ionis will send written notice to such effect to Roche, and the Parties will engage a mutually agreed independent Third Party intellectual property lawyer, not regularly engaged or employed by either Party within the [***] prior to such written notice, with expertise in the patenting of Oligonucleotides and appropriate professional credentials in the relevant jurisdiction, to determine the question of whether such Third Party intellectual property is Additional Ionis Core IP. The determination of the Third Party expert engaged under the preceding sentence will be binding on the Parties solely for purposes of determining whether Roche is permitted to apply the offset under Section 7.4.3(f)(i)(2) above. The costs of any Third Party expert engaged under this Section 7.4.3(f)(i)(3) will be paid by the Party against whom the Third Party lawyer makes his or her determination.

(ii) **Other Necessary Third Party Intellectual Property**. Roche shall be responsible for and pay or have paid any consideration owed to any Third Party in relation to any other Third Party intellectual property rights necessary to make, use or sell Products. Subject to Section 7.4.3(g) (Maximum Deduction), Roche shall have the right to deduct [***]% of such consideration actually paid to a Third Party with respect to a Product from royalty payments otherwise due and payable by Roche to Ionis for such Product under Section 7.4 (Royalties). Any such deduction shall be permitted on a Product-by-Product and country-by-country basis.

(g) **Maximum Deduction**. Except as set forth in this Section 7.4.3(g) (Maximum Deduction), in no event shall the aggregate royalty reductions set forth in Section 7.4.3 (Royalty Adjustments) reduce the royalties payable to Ionis for Net Sales of a Product in the applicable country in any given period to an amount that is less than [***]% of the royalty rates listed in TABLE 4 within Section 7.4.1 (Royalty Rates). Notwithstanding the foregoing, [***]. Roche may carry forward any amounts not utilized as a result of the maximum deduction cap in this Section 7.4.3(g) (Maximum Deduction) and offset against future royalties payable to Ionis for the applicable Product any amounts that, but for this Section 7.4.3(g) (Maximum Deduction), Roche would have been entitled to deduct from any royalty payments to Ionis until any amounts not utilized are fully deducted.

7.5. **Royalty Payments and Reports**.

7.5.1. **Commencement**. Beginning with the Calendar Quarter in which the First Commercial Sale, [***] is made and for each Calendar Quarter thereafter, Roche will make royalty payments to Ionis under this Agreement within [***] days following the end of each such Calendar Quarter.

7.5.2. **Royalty Reporting**.

(a) Each royalty payment will be accompanied by a report, summarizing in writing for the relevant Calendar Quarter on a Product-by-Product basis the following information:

(i) Sales in Swiss Francs on a country-by-country basis;

(ii) Net Sales in Swiss Francs on a country-by-country basis;

(iii) Total worldwide Net Sales in Swiss Francs;

(iv) Exchange rate used for the conversion of Net Sales from Swiss Francs to U.S. dollars pursuant to Section 7.6 (Mode of Payment);

(v) Royalty rate pursuant to Section 7.4.1 (Royalty Rates) and/or Section 7.4.3 (Royalty Adjustments), as applicable; and

(vi) Total royalty payable in U.S. dollars.

(b) In addition, Roche will include in each report under this Section 7.5.2 (Royalty Reporting) information regarding any Net Sales of Products sold for named patient, compassionate use or other similar sales and any consideration received from any Compulsory Sublicensees.

(c) On a country-by-country basis, after first Approval, if no royalties or other payments from Product sales are payable in respect of a given Calendar Quarter, Roche will submit a written royalty report to Ionis so indicating together with an explanation as to why no such royalties are payable. In addition, beginning with the Calendar Quarter in which the First Commercial Sale for a Product (or any named patient sale, compassionate use sale or other similar sales of a Product) is made and for each Calendar Quarter thereafter, within [***] following the end of each such Calendar Quarter, Roche will provide Ionis a preliminary non-binding report estimating the total (A) Sales and Net Sales for Products projected for such Calendar Quarter, and (B) if available, the amount of any consideration payable to Roche under sublicenses with Compulsory Sublicensees.

7.6. **Mode of Payment**. All payments under this Agreement will be (i) payable in full in U.S. dollars, regardless of the country(ies) in which sales are made, (ii) made by wire transfer of immediately available funds to an account designated by Ionis in writing, and (iii) irrevocable and non-refundable. Any corrections to calculations of royalty payments previously paid shall be adjusted to the next royalty payment due. When calculating the Sales of a Product that occur in currencies other than U.S. dollars, Roche will convert the amount of such sales into Swiss Francs and then into U.S. dollars using Roche's then current internal foreign currency translation actually used on a consistent basis in preparing its audited financial statements (currently YTD average rate as reported by Reuters).

7.7. **Records Retention**. Commencing with the First Commercial Sale [***] of a Product, Roche will keep complete and accurate records pertaining to the sale of Products for a period of [***] after the year in which such sales occurred, and in sufficient detail to permit Ionis to confirm the accuracy of the Net Sales or royalties paid by Roche hereunder.

7.8. **Audits.** During the Agreement Term and for a period of [***] thereafter, at the request and expense of Ionis, Roche will permit an independent certified public accountant of internationally recognized standing appointed by Ionis, at reasonable times and upon at least [***] written notice, but in no case more than [***] per Calendar Year, to examine such records as may be necessary for the purpose of verifying the accrual of any milestone payments, the calculation and reporting of Net Sales, and the correctness of any milestone or royalty payment made under this Agreement for any full Calendar Quarter within the preceding [***]. No Calendar Year can be audited more than once. Any and all records of Roche examined by such independent certified public accountant will be deemed Roche's Confidential Information. The independent certified public accountant shall share all draft reports with Roche before the draft audit report is shared with Ionis and before the final document is issued. Upon completion of the audit, the accounting firm will provide both Roche and Ionis with a written report disclosing whether the calculation of Sales, Net Sales and royalty payments made by Roche are correct and the specific details concerning any discrepancies ("***Audit Report***"). If any Audit Report shows that Roche's payments under this Agreement were less than the milestone or royalty amount that should have been paid, then Roche will make all payments required to be made by paying Ionis the difference between such amounts to eliminate any discrepancy revealed by said inspection with the next payment due, with interest calculated in accordance with Section 7.10 (Interest). If any Audit Report shows that Roche's payments under this Agreement were greater than the amount that should have been paid, then [***] equal to the difference between the amounts paid by Roche and the amounts that should have been paid. Ionis will pay all fees charged by such accountant pursuant to the audit, *except that*, if the audit determines that any additional amounts payable by Roche for an audited period exceed [***] percent ([***]%) of the amount actually paid for such audited period, then, in addition to paying Ionis any unpaid amounts discovered in such audit, and interest calculated in accordance with Section 7.10 (Interest), Roche will pay the fees and expenses charged by such accountant. Roche shall also [***].

7.9. Taxes.

7.9.1. **Taxes on Income**. Each Party will be solely responsible for the payment of all taxes imposed on its share of income arising directly or indirectly from the activities of the Parties under this Agreement.

7.9.2. **Withholding Tax**. To the extent the paying Party is required to deduct and withhold taxes on any payment, the paying Party will pay the amounts of such taxes to the proper governmental authority for the account of the receiving Party and remit the net amount to the receiving Party in a timely manner. The paying Party will promptly furnish the receiving Party with proof of payment of such taxes. If documentation is necessary in order to secure an exemption from, or a reduction in, any withholding taxes, the Parties will provide such documentation to the extent they are able to do so. In accordance with the procedures set forth in Section 10.3 (Procedure), the receiving Party will also indemnify the paying Party for any tax, interest or penalties imposed on the paying Party if the paying Party improperly reduces or eliminates withholding tax based upon representations made by the receiving Party.

7.9.3. **Tax Cooperation**. At least [***] prior to the date a given payment is due under this Agreement, the non-paying Party will provide the paying Party with any and all tax forms that may be reasonably necessary in order for the paying Party to lawfully not withhold tax or to withhold tax at a reduced rate with respect to such payment under an applicable bilateral income tax treaty. Following the paying Party's timely receipt of such tax forms from the non- paying Party, the paying Party will not withhold tax or will withhold tax at a reduced rate under an applicable bilateral income tax treaty, if appropriate under the Applicable Laws. The non-paying Party will provide any such tax forms to the paying Party upon request and in advance of the due date. Each Party will provide the other with reasonable assistance to enable the recovery, as permitted by Applicable Law, of withholding taxes resulting from payments made under this Agreement, such recovery to be for the benefit of the Party who would have been entitled to receive the money but for the application of withholding tax under this Section 7.9 (Taxes). The provisions of this Section 7.9 (Taxes) are to be read in conjunction with the provisions of Section 13.4 (Assignment and Successors) below.

7.10. **Interest**. Any undisputed payments to be made hereunder that are not paid on or before the date such payments are due under this Agreement will bear interest at a rate per annum equal to the lesser of (i) [***]% above the six-month CME Term Secured Overnight Financing Rate (USD SOFR) from the date on which such payment would have been first due until the date of payment, or (ii) the maximum rate permissible under Applicable Law.

ARTICLE 8.
INTELLECTUAL PROPERTY

8.1. **Ownership**.

8.1.1. **Ionis Technology and Roche Technology**. As between the Parties, Ionis will own and retain all of its rights, title and interest in and to the Licensed Know- How and Licensed Patents and Roche will own and retain all of its rights, title and interest in and to the Roche Know-How and Roche Patents, subject to any assignments, rights or licenses expressly granted by one Party to the other Party under this Agreement.

8.1.2. **Agreement Technology**. Each Party will promptly disclose to the other Party in writing, and will cause its Affiliates to so disclose, the discovery, development, or creation of any invention made solely or jointly by such Party in connection with the performance of obligations under this Agreement. Except as expressly provided in this Agreement, neither Party will have any obligation to account to the other for profits with respect to, or to obtain any consent of the other Party to license or exploit, Joint Collaboration Technology by reason of joint ownership thereof, and each Party hereby waives any right it may have under the laws of any jurisdiction to require any such consent or accounting.

8.2. **Joint Patent Committee**.

8.2.1. **Establishment**. The Parties will establish a "***Joint Patent Committee***" or "***JPC***." The JPC will serve as the primary contact and forum for discussion between the Parties with respect to intellectual property matters arising under this Agreement and will cooperate with respect to the activities set forth in this ARTICLE 8. The JPC determines the invention classification for each invention arising under this Agreement. The classifications are (i) Ionis Product-Specific Patents, (ii) Roche Collaboration Patents, (iii) Ionis Collaboration Patents, and (iv) Joint Collaboration Patents (collectively, the "***Program Patents***"). The JPC will endeavor to separate the claims within such Patent Rights into separate and distinct patent applications corresponding with the categories described in this Section 8.2.1 (Establishment) to the extent possible without diminishing the patentability of the inventions.

8.2.2. **Scope**. The JPC will discuss strategies with regard to (a) prosecution and maintenance, defense and enforcement of Program Patents licensed to Roche under Section 5.1.2 (Development and Commercialization License Grant to Roche) in connection with a Product; (b) defense against allegations of infringement of Third Party Patent Rights; and (c) licenses to Third Party Patent Rights or Know-How (including whether to obtain any licenses under any such Third-Party Patent Rights or Know-How, and whether there are any known Third Party Obligations applicable to a particular Product), in each case ((a)- (c)) to the extent such matter would be reasonably likely to have a material impact on the Agreement or the licenses granted hereunder, which strategies will be considered in good faith by the Party entitled to prosecute, enforce and defend such Patent Rights hereunder, but will not be binding on such Party.

8.2.3. **Inventorship**. The JPC will be responsible for the determination of inventorship. The determination of inventorship will be in accordance with United States patent laws and therefore will determine if the invention is solely or jointly owned by the relevant Party or Parties. In case of a dispute in the JPC (or otherwise between Ionis and Roche) over inventorship or classification, if the JPC cannot resolve such dispute, even after seeking the JSC's input, such dispute will be resolved by an independent patent counsel not engaged or regularly employed in the past two years by either Party and reasonably acceptable to both Parties. The decision of such independent patent counsel will be binding on the Parties. Expenses of such patent counsel will be shared equally by the Parties.

8.2.4. **Composition**. The JPC will comprise an equal number of members from each Party. The JPC will meet as often as agreed by them (and at least semi- Annually), to discuss matters arising out of the activities set forth in this ARTICLE 8. The JPC will determine by unanimous consent the JPC operating procedures at its first meeting. To the extent reasonably requested by either Party, the JPC will solicit the involvement of more senior members of their respective legal departments with respect to critical issues. Each Party's representatives on the JPC will consider comments and suggestions made by the other in good faith. If either Party deems it reasonably advisable, the Parties will enter into a mutually agreeable common interest agreement covering the matters contemplated by this Agreement.

8.3. **Prosecution and Maintenance of Patents**.

8.3.1. **Patent Filings**. The Party responsible for Prosecution and Maintenance of any Patent Rights as set forth in Section 8.3.2 (Ionis Patents and Roche Patents) and Section 8.3.3 (Joint Collaboration Patents) will endeavor to obtain patent protection for a Product as it Prosecutes and Maintains its other patents Covering products in development, using counsel of its own choice but reasonably acceptable to the other Party, in such countries as the responsible Party sees fit.

8.3.2. **Ionis Patents and Roche Patents**.

(a) **Ionis Patents**.

(i) **Ionis Core Technology Patents, Ionis Collaboration Patents, and Ionis Manufacturing and Analytical Patents**. Ionis will at all times control and be responsible for all aspects of Prosecution and Maintenance of (A) the Ionis Core Technology Patents, (B) the Ionis Collaboration Patents, and (C) the Ionis Manufacturing and Analytical Patents.

(ii) **Ionis Product-Specific Patents**. On an Ionis Development Candidate-by-Ionis Development Candidate basis, before Handoff with respect to such Ionis Development Candidate, Ionis will control and be responsible for all aspects of the Prosecution and Maintenance of all Ionis Product-Specific Patents and will use commercially reasonable efforts to Prosecute and Maintain such Patent Rights. After Handoff and subject to Section 8.3.4 (Other Matters Pertaining to Prosecution and Maintenance of Patents), at Roche's expense, Roche will control and be responsible for all aspects of the Prosecution and Maintenance of all Ionis Product-Specific Patents and will either (i) use commercially reasonable efforts to Prosecute and Maintain such Patent Rights or (ii) offer to assign Roche's entire right, title and interest in such Patent Rights to Ionis, in which case following any such assignment all licenses granted in this Agreement by Ionis to Roche under such Patent Rights shall become non-exclusive and the exclusivity covenants under Section 4.1 (Exclusivity) will no longer apply to such Patent Rights. Such Ionis Product-Specific Patents will continue to be royalty-bearing under Section 7.4 (Royalties).

(b) **Roche Patents**. Roche will at all times control and be responsible for all aspects of the Prosecution and Maintenance of all Roche Patents.

8.3.3. **Joint Collaboration Patents**. Roche will control and be responsible for all aspects of the Prosecution and Maintenance of Joint Collaboration Patents and will (i) use commercially reasonable efforts to Prosecute and Maintain such Patent Rights, or (ii) offer to assign Roche's entire right, title and interest in such Joint Collaboration Patents to Ionis, in which case following any such assignment all licenses granted in this Agreement by Ionis to Roche under such Patent Rights shall become non-exclusive and the exclusivity covenants under Section 4.1 (Exclusivity) will no longer apply to such Patent Rights.

8.3.4. **Other Matters Pertaining to Prosecution and Maintenance of Patents.**

(a) Each Party will keep the other Party informed through the JPC as to material developments with respect to the Prosecution and Maintenance of the Program Patents for which such Party has responsibility for Prosecution and Maintenance pursuant to Section 8.3.2 (Ionis Patents and Roche Patents), Section 8.3.3 (Joint Collaboration Patents) or this Section 8.3.4 (Other Matters Pertaining to Prosecution and Maintenance of Patents), including by providing copies of material data as it arises, any office actions or office action responses or other correspondence that such Party provides to or receives from any patent office, including notice of all interferences, reissues, re-examinations, oppositions or requests for patent term extensions, and all patent-related filings, and by providing the other Party the timely opportunity to have reasonable input into the strategic aspects of such Prosecution and Maintenance.

(b) If Roche elects (i) not to file and prosecute patent applications for the Program Patents for which Roche has responsibility for Prosecution and Maintenance pursuant to Section 8.3.2 (Ionis Patents and Roche Patents) ("***Roche-Prosecuted Patents***") in a particular country, (ii) not to continue the prosecution (including any interferences, oppositions, reissue proceedings, re-examinations, and patent term extensions, adjustments, and restorations) or maintenance of any Roche-Prosecuted Patent in a particular country, or (iii) not to file and prosecute patent applications for the Roche-Prosecuted Patent in a particular country following a written request from Ionis to file and prosecute in such country, then Roche will so notify Ionis promptly in writing of its intention in good time to enable Ionis to meet any deadlines by which an action must be taken to establish or preserve any such Patent Right in such country; and Ionis will have the right, but not the obligation, to file, prosecute, maintain, enforce, or otherwise pursue such Roche- Prosecuted Patent in the applicable country at its own expense with counsel of its own choice. In such case, Roche will cooperate with Ionis to file for, or continue to Prosecute and Maintain or enforce, or otherwise pursue such Roche-Prosecuted Patent in such country in Ionis' own name and Roche will keep a non-exclusive license under such Roche-Prosecuted Patents, and the exclusivity covenants under Section 4.1 (Exclusivity) will no longer apply to such Patent Rights. Notwithstanding anything to the contrary in this Agreement, if Ionis assumes responsibility for the Prosecution and Maintenance of any such Roche-Prosecuted Patent under this Section 8.3.4(b), then Ionis will have no obligation to notify Roche if Ionis intends to abandon such Roche-Prosecuted Patent. The analogous situation shall apply *mutatis mutandis* with regard to Patent Rights (excluding Ionis Core Technology Patents and Ionis Manufacturing and Analytical Patents) for which Ionis has responsibility for Prosecution and Maintenance pursuant to Section 8.3.2 (Ionis Patents and Roche Patents).

(c) The Parties, through the JPC, will cooperate in good faith to determine if and when any divisional or continuation applications will be filed with respect to any Program Patents, and where a divisional or continuation patent application filing would be practical and reasonable, then such a divisional or continuation filing will be made.

(d) If the Party responsible for Prosecution and Maintenance pursuant to Section 8.3.3 (Joint Collaboration Patents) intends to abandon such Joint Collaboration Patent, without first filing a continuation or substitution, then such Party will notify the other Party of such intention at least [***] days before such Joint Collaboration Patent will become abandoned, and such other Party will have the right, but not the obligation, to assume responsibility for the Prosecution and Maintenance thereof at its own expense (subject to Section 8.3.1 (Patent Filings)) with counsel of its own choice, in which case the abandoning Party will, and will cause its Affiliates to, assign to the other Party (or, if such assignment is not possible, grant a fully-paid exclusive license in) all of their rights, title and interest in and to such Joint Collaboration Patents. If a Party assumes responsibility for the Prosecution and Maintenance of any such Joint Collaboration Patents under this Section 8.3.4(d), then such Party will have no obligation to notify the other Party of any intention of such Party to abandon such Joint Collaboration Patents.

(e) In addition, the Parties will consult, through the JPC, and take into consideration the comments of the other Party for all matters relating to interferences, reissues, re-examinations and oppositions with respect to those Patent Rights in which such other Party (i) has an ownership interest, (ii) has received a license thereunder in accordance with this Agreement, or (iii) may in the future, in accordance with this Agreement, obtain a license or sublicense thereunder.

8.4. Patent Costs.

8.4.1. Joint Collaboration Patents. Unless the Parties agree otherwise, Ionis and Roche will share equally the Patent Costs associated with the Prosecution and Maintenance of Joint Collaboration Patents according to Section 8.3.3 (Joint Collaboration Patents); *provided that*, either Party may decline to pay its share of costs for filing, prosecuting and maintaining any Joint Collaboration Patents in a particular country or particular countries, in which case the declining Party will, and will cause its Affiliates to, assign to the other Party (or, if such assignment is not possible, grant a fully-paid exclusive license in) all of their rights, titles and interests in and to such Joint Collaboration Patents.

8.4.2. Ionis Patents and Roche Patents. Except as set forth in and Section 8.3.4 (Other Matters Pertaining to Prosecution and Maintenance of Patents), each Party will be responsible for all Patent Costs incurred by such Party prior to and after the Effective Date in all countries in the Prosecution and Maintenance of Patent Rights for which such Party is responsible under Section 8.3.2 (Ionis Patents and Roche Patents); *provided, however*, that on an Ionis Development Candidate-by-Ionis Development Candidate basis after Handoff, Roche will be solely responsible for Patent Costs arising from the Prosecution and Maintenance of the Ionis Product-Specific Patents Covering such Ionis Development Candidate; *provided that*, Roche may decline to pay for filing, prosecuting and maintaining any Ionis Product-Specific Patents in a particular country or particular countries, in which case all licenses granted in this Agreement by Ionis to Roche under such Patent Rights shall become non- exclusive and the exclusivity covenants under Section 4.1 (Exclusivity) will no longer apply to such Patent Rights.

8.5. Defense of Claims Brought by Third Parties.

8.5.1. Third-Party Claims Regarding Products. If a Third Party initiates a Proceeding claiming a Patent Right owned by or licensed to such Third Party is infringed by the Development, Manufacture or Commercialization of a Product, **(a)** Ionis will have the first right, but not the obligation, to defend against any such Proceeding initiated prior to Handoff at its sole cost and expense and (b) Roche will have the first right, but not the obligation, to defend against any such Proceeding initiated after Handoff at its sole cost and expense. If the Party having the first right to defend against such Proceeding (the "***Lead Party***") elects to defend against such Proceeding, then the Lead Party will have the sole right to direct the defense and to elect whether to settle such claim (but only with the prior written consent of the other Party, not to be unreasonably withheld, conditioned or delayed). The other Party will reasonably assist the Lead Party in defending such Proceeding and cooperate in any such litigation at the request and expense of the Lead Party. The Lead Party will provide the other Party with prompt written notice of the commencement of any such Proceeding that is of the type described in this Section 8.5 (Defense of Claims Brought by Third Parties), and the Lead Party will keep the other Party apprised of the progress of such Proceeding. If the Lead Party elects not to defend against a Proceeding, then the Lead Party will so notify the other Party in writing within [***] after the Lead Party first receives written notice of the initiation of such Proceeding, and the other Party (the "***Step-In Party***") will have the right, but not the obligation, to defend against such Proceeding at its sole cost and expense and thereafter the Step-In Party will have the sole right to direct the defense thereof, including the right to settle such claim. In any event, the Party not defending such Proceeding will reasonably assist the other Party and cooperate in any such litigation at the request and expense of the Party defending such Proceeding. Each Party may at its own expense and with its own counsel join any defense initiated or directed by the other Party under this Section 8.5 (Defense of Claims Brought by Third Parties). Each Party will provide the other Party with prompt written notice of the commencement of any such Proceeding under this Section 8.5 (Defense of Claims Brought by Third Parties), and such Party will promptly furnish the other Party with a copy of each communication relating to the alleged infringement that is received by such Party.

8.5.2. Third Party Claims Regarding Discontinued Products. If a Third Party initiates a Proceeding claiming that any Patent Right or Know-How owned by or licensed to such Third Party is infringed by the Development, Manufacture or Commercialization of a Discontinued Product, Ionis will have the first right, but not the obligation, to defend against and settle such Proceeding at its sole cost and expense. Roche will reasonably assist Ionis in defending such Proceeding and cooperate in any such litigation at the request and expense of Ionis. Each Party may at its own expense and with its own counsel join any defense directed by the other Party. Ionis will provide Roche with prompt written notice of the commencement of any such Proceeding, or of any allegation of infringement of which Ionis becomes aware and that is of the type described in this Section 8.5.2 (Third Party Claims Regarding Discontinued Products), and Ionis will promptly furnish Roche with a copy of each communication relating to the alleged infringement received by Ionis.

8.5.3. Interplay Between Enforcement of IP and Defense of Third Party Claims. Notwithstanding the provisions of Section 8.5.1 (Third Party Claims Regarding Products) and Section 8.5.2 (Third Party Claims Regarding Discontinued Products), to the extent that a Party's defense against a Third Party claim of infringement under this Section 8.5 (Defense of Claims Brought by Third Parties) involves (a) the enforcement of the other Party's Know-How or Patent Rights, or (b) the defense of an invalidity claim with respect to such other Party's Know-How or Patent Rights, then, in each case, the general concepts of Section 8.6 (Enforcement of Patents Against Competitive Infringement) will apply to the enforcement of such other Party's Know-How or Patent Rights or the defense of such invalidity claim (i.e., each Party has the right to enforce its own intellectual property, except that the relevant Commercializing Party will have the initial right, to the extent provided in Section 8.6 (Enforcement of Patents Against Competitive Infringement), to enforce such Know-How or Patent Rights or defend such invalidity claim, and the other Party will have a step-in right, to the extent provided in Section 8.6 (Enforcement of Patents Against Competitive Infringement), to enforce such Know-How or Patent Rights or defend such invalidity claim).

8.6. Enforcement of Patents Against Competitive Infringement.

8.6.1. **Duty to Notify of Competitive Infringement**. If either Party learns of an infringement, unauthorized use, misappropriation or threatened infringement by a Third Party to which such Party does not owe any obligation of confidentiality with respect to any Ionis Product-Specific Patents by reason of the development, manufacture, use or commercialization of a product directed against the RNA that encodes a Target in the Field ("***Competitive Infringement***"), such Party will promptly notify the other Party in writing and will provide such other Party with available evidence of such Competitive Infringement; *provided, however*, that for cases of Competitive Infringement under Section 8.6.6 (35 USC § 271(e)(2) Infringement) below, the notifying Party will provide such written notice within ten (10) Business Days.

8.6.2. **Enforcement**. For any Competitive Infringement with respect to a Product that Roche is Developing or Commercializing, Roche will have the first right, but not the obligation, to institute, prosecute, and control a Proceeding with respect thereto by counsel of its own choice at its own expense, and Ionis will have the right, at its own expense, to be represented in that action by counsel of its own choice. If Roche fails to initiate a Proceeding within a period of [***] after receipt of written notice of such Competitive Infringement (subject to a [***] extension to conclude negotiations, if Roche has commenced good faith negotiations with an alleged infringer for elimination of such Competitive Infringement within such [***] period), then Ionis will have the right to initiate and control a Proceeding with respect to such Competitive Infringement by counsel of its own choice, and Roche will have the right to be represented in any such action by counsel of its own choice at its own expense. Notwithstanding the foregoing, Ionis will at all times have the sole right to institute, prosecute, and control any Proceeding under this Section 8.6.2 (Enforcement) to the extent involving any Ionis Core Technology Patents, Ionis Manufacturing and Analytical Patents, or Ionis Collaboration Patents.

8.6.3. **Joinder**.

(a) If a Party initiates a Proceeding in accordance with this Section 8.6 (Enforcement of Patents Against Competitive Infringement), the other Party agrees to be joined as a party plaintiff where necessary and to give the first Party reasonable assistance and authority to file and prosecute the Proceeding. Subject to Section 8.6.4 (Share of Recoveries), the costs and expenses of each Party incurred pursuant to this Section 8.6.3(a) will be borne by the Party initiating such Proceeding.

(b) If one Party initiates a Proceeding in accordance with this Section 8.6 (Enforcement of Patents Against Competitive Infringement), the other Party may join such Proceeding as a party plaintiff where necessary for such other Party to seek lost profits with respect to such infringement.

8.6.4. **Share of Recoveries**. Any damages or other monetary awards recovered with respect to a Proceeding brought pursuant to this Section 8.6 (Enforcement of Patents Against Competitive Infringement) will be shared as follows:

(a) the amount of such recovery will first be applied to the Parties' reasonable out-of-pocket costs incurred in connection with such Proceeding (which amounts will be allocated *pro rata* if insufficient to cover the totality of such expenses); then

(b) any remaining proceeds constituting direct or actual damages for acts of infringement occurring prior to Handoff will be (i) [***]; or (ii) [***]; then

(c) any remaining proceeds constituting direct or actual damages for acts of infringement occurring after Handoff will be [***], and [***]; then

(d) any remaining proceeds constituting punitive or treble damages will be allocated between the Parties as follows: the Party initiating the Proceeding will receive and retain [***] of such proceeds and the other Party will receive and retain [***] of such proceeds.

8.6.5. **Settlement**. Notwithstanding anything to the contrary under this ARTICLE 8, neither Party may enter a settlement, consent judgment or other voluntary final disposition of a suit under this ARTICLE 8 that disclaims, limits the scope of, admits the invalidity or unenforceability of, or grants a license, covenant not to sue or similar immunity under a Patent Right Controlled by the other Party without first obtaining the written consent of the Party that Controls the relevant Patent Right.

8.6.6. **35 USC § 271(e)(2) Infringement**. Notwithstanding anything to the contrary in this Section 8.6 (Enforcement of Patents Against Competitive Infringement), solely with respect to Licensed Patents, for a Competitive Infringement under 35 USC § 271(e)(2), the time period set forth in Section 8.6.2 (Enforcement) during which a Party will have the initial right to bring a Proceeding will be shortened to a total of twenty-five (25) days, so that, to the extent the other Party has the right, pursuant to such Section to initiate a Proceeding if the first Party does not initiate a Proceeding, such other Party will have such right if the first Party does not initiate a Proceeding within twenty-five (25) days after such first Party's receipt of written notice of such Competitive Infringement.

8.7. **Other Infringement**.

8.7.1. **Joint Collaboration Patents**. With respect to the infringement of a Joint Collaboration Patent that is not a Competitive Infringement, the Parties will cooperate in good faith to bring suit together against such infringing party or the Parties may decide to permit one Party to solely bring suit. Any damages or other monetary awards recovered with respect to a Proceeding brought pursuant to this Section 8.7.1 (Joint Collaboration Patents) will be shared as follows: (a) the amount of such recovery will first be applied to the Parties' reasonable out-of-pocket costs incurred in connection with such Proceeding (which amounts will be allocated *pro rata* if insufficient to cover the totality of such expenses); (b) any remaining proceeds constituting direct damages will be [***]; and (c) any remaining proceeds constituting punitive or treble damages will be allocated as follows: (i) if the Parties jointly initiate a Proceeding pursuant to this Section 8.7.1 (Joint Collaboration Patents), [***]; and (ii) if only one Party initiates the Proceeding pursuant to this Section 8.7.1 (Joint Collaboration Patents), such Party will receive [***] of such proceeds and the other Party will receive [***] of such proceeds.

8.7.2. **Patents Solely Owned by Ionis**. Ionis will retain all rights to pursue an infringement of any Patent Right solely owned by Ionis which is other than a Competitive Infringement and Ionis will retain all recoveries with respect thereto.

8.7.3. **Patents Solely Owned by Roche**. Roche will retain all rights to pursue an infringement of any Patent Right solely owned by Roche which is other than a Competitive Infringement and Roche will retain all recoveries with respect thereto.

8.8. **Patent Listing**.

8.8.1. **Roche's Obligations**. Roche will promptly, accurately and completely list, with the applicable Regulatory Authorities during the Agreement Term, all applicable Patent Rights that Cover a Product. Prior to such listings, the Parties will meet, through the JPC, to evaluate and identify all applicable Patent Rights, and Roche will have the right to review, where reasonable, original records relating to any invention for which Patent Rights are being considered by the JPC for any such listing. Notwithstanding the preceding sentence, Roche will retain final decision-making authority as to the listing of all applicable Patent Rights for a Product that are not Ionis Core Technology Patents, Ionis Collaboration Patents, or Ionis Manufacturing and Analytical Patents, regardless of which Party owns such Patent Rights.

8.8.2. **Ionis' Obligations**. Ionis will promptly, accurately and completely list, with the applicable Regulatory Authorities during the Agreement Term, all applicable Patent Rights that Cover a Discontinued Product. Prior to such listings, the Parties will meet, through the JPC, to evaluate and identify all applicable Patent Rights, and Ionis will have the right to review, where reasonable, original records relating to any invention for which Patent Rights are being considered by the JPC for any such listing. Notwithstanding the preceding sentence, Ionis will retain final decision-making authority as to the listing of all applicable Patent Rights for such Discontinued Products, as applicable, regardless of which Party owns such Patent Rights.

8.9. **Joint Research Agreement under the Leahy-Smith America Invents Act**. If a Party intends to invoke its rights under 35 U.S.C. § 102(e) of the Leahy-Smith America Invents Act, it will notify the other Party and neither Party will make an election under such provision when exercising its rights under this ARTICLE 8 without the prior written consent of the other Party (such consent not to be unreasonably withheld, conditioned or delayed), and the Parties will use reasonable efforts to cooperate and coordinate their activities with respect to any submissions, filings or other activities in support thereof. The Parties acknowledge and agree that this Agreement is a "*joint research agreement*" as defined in 35 U.S.C. § 100(h).

8.10. **Obligations to Third Parties**. Notwithstanding any of the foregoing, each Party's rights and obligations with respect to Licensed Technology under this ARTICLE 8 will be subject to the Third Party rights and obligations (i) for which Roche is responsible under Section 7.4.3(f) (Third Party Payments) and (ii) under Prior Agreements; *provided, however*, that, to the extent that Ionis has a non-transferable right to prosecute, maintain or enforce any Patent Rights licensed to Roche hereunder, and this Agreement purports to grant any such rights to Roche, Ionis will act in such regard with respect to such Patent Rights at Roche's direction.

8.11. **Additional Right and Exceptions**. Notwithstanding any provision of this ARTICLE 8, but subject to Section 8.5.3 (Interplay Between Enforcement of IP and Defense of Third Party Claims), Ionis retains the sole right to Prosecute and Maintain Ionis Core Technology Patents, Ionis Collaboration Patents, and Ionis Manufacturing and Analytical Patents during the Agreement Term and to control any enforcement of Ionis Core Technology Patents, Ionis Collaboration Patents, and Ionis Manufacturing and Analytical Patents, and will take the lead on such enforcement solely to the extent that the scope or validity of any Patent Rights Controlled by Ionis and Covering the Ionis Core Technology Patents, Ionis Collaboration Patents, or Ionis Manufacturing and Analytical Patents is at risk. If Ionis determines, in Ionis' sole discretion, to not enforce any Ionis Core Technology Patents, Ionis Collaboration Patents, or Ionis Manufacturing and Analytical Patents and does not permit Roche to so enforce such Patent Rights, then the Parties will mutually agree on an appropriate adjustment (if any) of the future consideration payable by Roche under this Agreement to reflect any adverse impact Ionis' failure to enforce such Patent Rights has on Products.

8.12. **Patent Term Extension**. The Parties will cooperate with each other in gaining patent term extension wherever applicable to a Product, including European supplementary protection certificates and pediatric exclusivity. After Handoff, Roche will determine which patents will be extended and what extensions will be sought.

ARTICLE 9.
REPRESENTATIONS AND WARRANTIES

9.1. **Representations and Warranties of Both Parties**. Each Party hereby represents and warrants and, where indicated, covenants, to the other Party, as of the Effective Date, that:

9.1.1. such Party is duly organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;

9.1.2. such Party has taken all necessary action on its part to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder;

9.1.3. this Agreement has been duly executed and delivered on behalf of such Party, and constitutes a legal, valid and binding obligation, enforceable against it in accordance with the terms hereof;

9.1.4. the execution, delivery and performance of this Agreement by such Party will not constitute a default under or conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it is bound, or to the best of its knowledge and belief violate any law or regulation of any court, governmental body or administrative or other agency having jurisdiction over such Party;

9.1.5. to the best of its knowledge and belief, no government authorization, consent, approval, license, exemption of or filing or registration with any court or governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign, under any applicable laws, rules or regulations currently in effect, is or will be necessary for, or in connection with, the transaction contemplated by this Agreement or any other agreement or instrument executed in connection herewith, or for the performance by it of its obligations under this Agreement and such other agreements; and

9.1.6. it has not employed (and, to the best of its knowledge and belief, has not used a contractor or consultant that has employed) and in the future will not employ (or, to the best of its knowledge, use any contractor or consultant that employs, *provided* that such Party may reasonably rely on a representation made by such contractor or consultant) any Person debarred by the FDA (or subject to a similar sanction of EMA or foreign equivalent), or any Person which is the subject of an FDA debarment investigation or proceeding (or similar proceeding of EMA or foreign equivalent), in the conduct of the Pre-Clinical Studies or Clinical Studies of a Product and its activities under the R&D Plans.

9.2. **Representations and Warranties of Ionis**. Ionis hereby represents and warrants to Roche, as of the Effective Date, and solely with respect to the Oligonucleotide within an Ionis Development Candidate that:

9.2.1. To the best of its knowledge and belief, there are no additional licenses (beyond those that would be granted to Roche under Section 5.1.2 (Development and Commercialization License Grant to Roche) upon the Handoff for a Product arising under the R&D Plans) under any intellectual property owned or Controlled by Ionis or its Affiliates as of the Effective Date that would be required in order for Roche to further Develop and Commercialize a Product arising under the R&D Plan existing on the Effective Date.

9.2.2. The Licensed Technology existing as of the Effective Date constitutes all of the Patent Rights and Know-How Controlled by Ionis as of the Effective Date that are necessary to Develop, Manufacture or Commercialize Compounds contemplated under the R&D Plan existing on the Effective Date in the Field. Ionis has not previously assigned, transferred, conveyed or otherwise encumbered its right, title and interest in the Licensed Technology in a manner that conflicts with any rights granted to Roche hereunder.

9.2.3. There are no claims, judgments or settlements against or owed by Ionis or its Affiliates or pending against Ionis or, to the best of Ionis' knowledge, threatened against Ionis, in each case relating to the Licensed Technology that could impact activities under this Agreement. To the best of Ionis' knowledge, there are no claims, judgments or settlements against or owed by any Third Party that is party to a Prior Agreement, or pending or threatened claims or litigation against any Third Party that is party to a Prior Agreement, in each case relating to the Licensed Technology that would impact activities under this Agreement.

9.2.4. SCHEDULE 9.2.4(a), SCHEDULE 9.2.4(b) and SCHEDULE 9.2.4(c) set forth true, correct and complete lists of all Ionis Core Technology Patents, Ionis Manufacturing and Analytical Patents, and Ionis Product-Specific Patents that, as of the Effective Date, are expected to apply to the Compounds contemplated under the R&D Plan as of the Effective Date, respectively, and indicates whether each such Patent Right is owned by Ionis or licensed by Ionis from a Third Party and if so, identifies the licensor or sublicensor from which the Patent Right is licensed. Ionis Controls such Patent Rights existing as of the Effective Date and is entitled to grant all rights and licenses (or sublicenses, as the case may be) under such Patent Rights it purports to grant to Roche under this Agreement.

9.2.5. (a) There is no fact or circumstance known by Ionis that would cause Ionis to reasonably conclude that any Licensed Patent is invalid or un-enforceable, (b) there is no fact or circumstance known by Ionis that would cause Ionis to reasonably conclude the inventorship of each Licensed Patent is not properly identified on each patent, (c) all official fees, maintenance fees and annuities for the Licensed Patents have been paid and all administrative procedures with governmental agencies have been completed, (d) none of the Ionis Product-Specific Patents that would be licensed by Ionis to Roche upon Handoff under this Agreement are currently involved in any interference, reissue, re- examination, cancellation or opposition proceeding and neither Ionis, nor any of its Affiliates, has received any written notice from any person, or has knowledge, of such actual or threatened Proceeding, and (e) to the best of Ionis' knowledge and belief, Roche's practice of the inventions claimed in the Ionis Product-Specific Patents in the performance of the Roche R&D Activities contemplated as of the Effective Date will not [***].

9.2.6. SCHEDULE 9.2.6 is a complete and accurate list of all agreements that create Third Party Obligations that affect the rights granted by Ionis to Roche under this Agreement with respect to Ionis Development Candidates contemplated by the R&D Plans on the Effective Date.

9.2.7. Ionis has all rights necessary to grant the Handoff and licenses contained in this Agreement, and has the ability to work exclusively with Roche as set forth in this Agreement, including the covenants granted in Section 4.1 (Exclusivity).

9.3. **Ionis Covenants**. Ionis hereby covenants to Roche that, except as expressly permitted under this Agreement:

9.3.1. Ionis will promptly amend SCHEDULE 9.2.4(a), SCHEDULE 9.2.4(b) and SCHEDULE 9.2.4(c) and submit such amended Schedules to Roche if Ionis becomes aware that any Ionis Core Technology Patents, Ionis Manufacturing and Analytical Patents or Ionis Product-Specific Patents are not properly identified on the respective Schedules;

9.3.2. during the Agreement Term, Ionis will maintain and not breach any agreements with Third Parties entered into after the Effective Date ("***New Third Party Licenses***") that provide a grant of rights from such Third Party to Ionis that are Controlled by Ionis and are licensed or may become subject to a license from Ionis to Roche for a Product under this Agreement;

9.3.3. Ionis will promptly notify Roche of any material breach by Ionis or a Third Party of any New Third Party License, and in the event of a breach by Ionis, will permit Roche to cure such breach on Ionis' behalf upon Roche's request;

9.3.4. Ionis will not amend, modify or terminate any New Third Party License in a manner that would adversely affect Roche's rights hereunder without first obtaining Roche's written consent, which [***];

9.3.5. Ionis will not enter into any new agreement or other obligation with any Third Party, or amend an existing agreement with a Third Party, in each case that restricts, limits or encumbers the rights granted to Roche under this Agreement;

9.3.6. Ionis will cause its Affiliates to comply with the terms of Section 4.1 (Exclusivity);

9.3.7. All employees and contractors of Ionis performing research and Development activities hereunder on behalf of Ionis will be obligated to assign all right, title and interest in and to any inventions (or grant a license to Ionis prior to or upon Handoff to obtain such a license) developed by them, whether or not patentable, to Ionis or such Affiliate, respectively, as the sole owner thereof; and

9.3.8. If, after the Effective Date, Ionis becomes the owner or otherwise acquires Control of any formulation or delivery devices that would be necessary or useful in order for Roche to further Develop, Manufacture or Commercialize a Product, and Roche has executed Handoff and the license granted to Roche under this Agreement is in effect, Ionis will make such technology available to Roche on commercially reasonable terms.

9.4. **Representations and Warranties of Roche**. Roche hereby represents and warrants to Ionis, as of the Effective Date, that all employees and contractors of Roche performing research and Development activities hereunder on behalf of Roche will be obligated to assign all right, title and interest in and to any inventions (or grant a license to Roche prior to or upon Handoff to obtain such a license) developed by them, whether or not patentable, to Roche or such Affiliate, respectively, as the sole owner thereof.

9.5. **DISCLAIMER. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY NOR ITS AFFILIATES MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. ROCHE AND IONIS UNDERSTAND THAT PRODUCTS ARE THE SUBJECT OF ONGOING RESEARCH AND DEVELOPMENT AND THAT NEITHER PARTY CAN ASSURE THE SAFETY, USEFULNESS OR COMMERCIAL OR TECHNICAL VIABILITY OF THE PRODUCTS.**

ARTICLE 10.
INDEMNIFICATION; INSURANCE

10.1. **Indemnification by Roche**. Roche will indemnify, defend and hold harmless Ionis and its Affiliates, and its or their respective directors, officers, employees and agents, from and against any and all liabilities, damages, losses, costs and expenses including the reasonable fees of attorneys (collectively "***Losses***") arising out of or resulting from any and all Third Party suits, claims, actions, proceedings or demands ("***Claims***") based upon:

10.1.1. the gross negligence or willful misconduct of Roche, its Affiliates or Sublicensees and its or their respective directors, officers, employees and agents, in connection with Roche's performance of its obligations or exercise of its rights under this Agreement;

10.1.2. any breach of any representation or warranty or express covenant made by Roche under ARTICLE 9 or any other provision under this Agreement;

10.1.3. the Development or Manufacturing activities that are conducted by or on behalf of Roche or its Affiliates or Sublicensees (which will exclude any Development or Manufacturing activities that are conducted by or on behalf of Ionis pursuant to this Agreement); or

10.1.4. the Commercialization of a Product by or on behalf of Roche or its Affiliates or Sublicensees;

except, in each case above, to the extent such Claim arose out of or resulted from or is attributable to any acts or omissions of Ionis or its Affiliates, licensees, Sublicensees or contractors, and its or their respective directors, officers, employees and agents or other circumstance for which Ionis has an indemnity obligation pursuant to Section 10.2 (Indemnification by Ionis).

10.2. **Indemnification by Ionis**. Ionis will indemnify, defend and hold harmless Roche and its Affiliates, and its or their respective directors, officers, employees and agents, from and against any and all Losses arising out of or resulting from any and all Claims based upon:

10.2.1. the gross negligence or willful misconduct of Ionis, its Affiliates or Sublicensees or its or their respective directors, officers, employees and agents, in connection with Ionis' performance of its obligations or exercise of its rights under this Agreement;

10.2.2. any breach of any representation or warranty or express covenant made by Ionis under ARTICLE 9 or any other provision under this Agreement;

10.2.3. any Development or Manufacturing activities that are conducted by or on behalf of Ionis or its Affiliates or Sublicensees (which will exclude any Development or Manufacturing activities that are conducted by or on behalf of Roche pursuant to this Agreement); or

10.2.4. any Development, Manufacturing or Commercialization activities that are conducted by or on behalf of Ionis or its Affiliates or Sublicensees with respect to a Discontinued Product;

except, in each case above, to the extent such Claim arose out of or resulted from or is attributable to any acts or omissions of Roche or its Affiliates, licensees, Sublicensees or contractors and its or their respective directors, officers, employees and agents or other circumstance for which Roche has an indemnity obligation pursuant to Section 10.1 (Indemnification by Roche).

10.3. **Procedure**. If a Person entitled to indemnification under Section 10.1 (Indemnification by Roche) or Section 10.2 (Indemnification by Ionis) (an "***Indemnitee***") seeks such indemnification, such Indemnitee will (i) inform the indemnifying Party in writing of a Claim as soon as reasonably practicable after such Indemnitee receives notice of such Claim, (ii) permit the indemnifying Party to assume direction and control of the defense of the Claim (including the sole right to settle such Claim at the sole discretion of the indemnifying Party, *provided that* such settlement or compromise does not admit any fault or negligence on the part of the Indemnitee, or impose any obligation on, or otherwise materially adversely affect, the Indemnitee or other Party), (iii) cooperate as reasonably requested (at the expense of the indemnifying Party) in the defense of the Claim, and (iv) undertake reasonable steps to mitigate any Losses with respect to the Claim. The provisions of Section 8.5 (Defense of Claims Brought by Third Parties) will govern the procedures for responding to a Claim of infringement described therein. Notwithstanding anything in this Agreement to the contrary, the indemnifying Party will have no liability under Section 10.1 (Indemnification by Roche) or Section 10.2 (Indemnification by Ionis), as the case may be, for Claims settled or compromised by the Indemnitee without the indemnifying Party's prior written consent.

10.4. **Insurance**.

10.4.1. **Ionis' Insurance Obligations**. Ionis hereby represents and warrants to Roche that it will maintain, at its cost, reasonable insurance against liability and other risks associated with its activities contemplated by this Agreement, including but not limited to its indemnification obligations herein, in such amounts and on such terms as are customary for prudent practices for biotech companies of similar size and with similar resources in the pharmaceutical industry for the activities to be conducted by it under this Agreement taking into account the scope of Development of Products. Ionis will furnish to Roche evidence of any insurance required under this Section 10.4.1 (Ionis' Insurance Obligations), upon request.

10.4.2. **Roche's Insurance Obligations**. Roche hereby represents and warrants to Ionis that it will maintain, at its cost, reasonable insurance – which may be through self-insurance – against liability and other risks associated with its activities contemplated by this Agreement (including product liability), including but not limited to its indemnification obligations herein, in such amounts and on such terms as are customary for prudent practices for large companies in the pharmaceutical industry for the activities to be conducted by Roche under this Agreement. Roche will maintain such insurance throughout the Agreement Term and for [***] thereafter, and will furnish to Ionis evidence of such insurance, upon request.

10.5. LIMITATION OF CONSEQUENTIAL DAMAGES. EXCEPT FOR (a) CLAIMS OF A THIRD PARTY THAT ARE SUBJECT TO INDEMNIFICATION UNDER THIS ARTICLE 10 (INDEMNIFICATION; INSURANCE), (b) CLAIMS ARISING OUT OF A PARTY'S WILLFUL MISCONDUCT OF THIS AGREEMENT, (c) A PARTY'S BREACH OF ARTICLE 4 (EXCLUSIVITY COVENANTS), OR A BREACH OF SECTION 11.4.2 (LICENSE TERMINATION) BY ROCHE OR ITS AFFILIATES OR (d) CLAIMS ARISING OUT OF A PARTY'S BREACH OF ITS CONFIDENTIALITY OBLIGATIONS UNDER THIS AGREEMENT, NEITHER PARTY NOR ANY OF ITS AFFILIATES WILL BE LIABLE TO THE OTHER PARTY TO THIS AGREEMENT OR ITS AFFILIATES FOR ANY INCIDENTAL, CONSEQUENTIAL, SPECIAL, PUNITIVE OR OTHER INDIRECT DAMAGES, WHETHER LIABILITY IS ASSERTED IN CONTRACT, TORT (INCLUDING NEGLIGENCE AND STRICT PRODUCT LIABILITY), INDEMNITY OR CONTRIBUTION, AND IRRESPECTIVE OF WHETHER THAT PARTY OR ANY REPRESENTATIVE OF THAT PARTY HAS BEEN ADVISED OF, OR OTHERWISE MIGHT HAVE ANTICIPATED THE POSSIBILITY OF, ANY SUCH LOSS OR DAMAGE.

ARTICLE 11.
TERM; TERMINATION

11.1. Agreement Term; Expiration. This Agreement is effective as of the Effective Date and, unless earlier terminated pursuant to the other provisions of this ARTICLE 11, will continue in full force and effect until this Agreement expires as follows:

11.1.1. on a country-by-country and Product-by-Product basis, on the date of expiration of all payment obligations by the Commercializing Party under this Agreement with respect to such Product (or such Discontinued Product) in such country; and

11.1.2. in its entirety upon the expiration of all payment obligations under this Agreement with respect to the last Product (or last Discontinued Product) in all countries pursuant to Section 11.1.1.

The period from the Effective Date until the date of expiration of this Agreement pursuant to this Section 11.1 (Agreement Term; Expiration) is the "***Agreement Term***." On a Product-by-Product basis, if with respect to a particular Product this Agreement expires (i.e., is not terminated early) under Section 11.1.1 or Section 11.1.2 in a particular country, then, effective upon such expiration, Ionis will and hereby does grant to Roche a fully paid-up, royalty-free, and irrevocable non-exclusive license under the Licensed Know-How to Manufacture, Develop and Commercialize the Product that is the subject of such expiration in such country.

11.2. Termination.

11.2.1. Roche's Termination for Convenience. Roche may terminate this Agreement for convenience as a whole or on a Program-by-Program basis, Target-by- Target basis, Product-by-Product basis or country-by-country basis by providing ninety (90) days written notice to Ionis of such termination.

11.2.2. Termination for Material Breach.

(a) **Roche's Right to Terminate**. If Roche believes that Ionis is in material breach of this Agreement (other than with respect to a failure to use Commercially Reasonable Efforts under Section 3.1.2 (Conducting the R&D Plans) or Section 3.1.9 (Performance Milestones During the Handoff Period), which are governed by Section 11.2.3 (Remedies for Failure to Use Commercially Reasonable Efforts) below), then Roche may deliver written notice of such material breach to Ionis. If the breach is curable, Ionis will have [***] to cure such breach. If Ionis fails to cure such breach within the [***] period, or if the breach is not subject to cure, Roche may terminate this Agreement in whole or on a Program-by-Program basis, Target-by-Target basis, Product-by-Product basis or country-by-country basis, as applicable, by providing written notice to Ionis.

(b) **Ionis' Right to Terminate**. If Ionis believes that Roche is in material breach of this Agreement (other than with respect to a failure to use Commercially Reasonable Efforts under Section 3.1.2 (Conducting the R&D Plans), Section 3.1.9 (Performance Milestones During the Handoff Period), or Section 6.2 (Diligence), which is governed by Section 11.2.3 (Remedies for Failure to Use Commercially Reasonable Efforts) below), then Ionis may deliver written notice of such material breach to Roche. If the breach is curable, Roche will have [***] days to cure such breach (except to the extent such breach involves the failure to make a payment when due, which breach must be cured within [***] days following such notice). If Roche fails to cure such breach within the [***] or [***] period, as applicable, or if the breach is not subject to cure, Ionis may terminate this Agreement by providing written notice to Roche in whole or on a Program-by-Program basis, Target-by-Target basis, Product-by-Product basis or country-by- country basis, as applicable, by proving written notice to Roche.

11.2.3. Remedies for Failure to Use Commercially Reasonable Efforts.

(a) If Ionis, in Roche's reasonable determination, fails to use Commercially Reasonable Efforts in the activities contemplated in Section 3.1.2 (Conducting the R&D Plans) or Section 3.1.9 (Performance Milestones During the Handoff Period), then Roche will notify Ionis and, within [***] thereafter, Ionis and Roche will meet and confer to discuss and resolve the matter in good faith, and attempt to devise a mutually agreeable plan to address any outstanding issues related to Ionis' use of Commercially Reasonable Efforts in Section 3.1.2 (Conducting the R&D Plans) or Section 3.1.9 (Performance Milestones During the Handoff Period), as applicable. Following such a meeting, if Ionis fails to use Commercially Reasonable Efforts as agreed, Roche will have the right to terminate this Agreement in whole or on a Program-by-Program basis, Target-by-Target basis, Product-by-Product basis or country-by-country basis, as applicable.

(b) If Roche, in Ionis' reasonable determination, fails to use Commercially Reasonable Efforts in the activities contemplated in Section 3.1.2 (Conducting the R&D Plans), Section 3.1.9 (Performance Milestones During the Handoff Period), or Section 6.2 (Diligence), then Ionis will notify Roche and, within [***] thereafter, [***]. Following [***], if Roche fails to use Commercially Reasonable Efforts as agreed and subject to Section 11.2.4 (Disputes Regarding Material Breach), Ionis will have the right to terminate this Agreement in whole or on a Program-by-Program basis, Target-by-Target basis, Product-by-Product basis or country-by-country basis, as applicable.

11.2.4. **Disputes Regarding Material Breach**. Notwithstanding the foregoing, if the Breaching Party in Section 11.2.2(a) (Roche's Right to Terminate) or Section 11.2.2(b) (Ionis' Right to Terminate) disputes in good faith the existence or materiality of, or failure to cure any such breach which is not a payment breach, and provides notice to the Non-Breaching Party of such dispute within such [***] or [***] period, as applicable, then the Non-Breaching Party will not have the right to terminate this Agreement in accordance with Section 11.2.2(a) (Roche's Right to Terminate) or Section 11.2.2(b) (Ionis' Right to Terminate), unless and until it has been determined in accordance with Section 13.1 (Dispute Resolution) that this Agreement was materially breached by the Breaching Party and the Breaching Party fails to cure such breach within [***] days following such determination. It is understood and acknowledged that during the pendency of such dispute, all the terms of this Agreement will remain in effect and the Parties will continue to perform all of their respective obligations hereunder, including satisfying any payment obligations.

11.2.5. **Termination for Insolvency**.

(a) Either Party may terminate this Agreement if, at any time, the other Party files in any court or agency pursuant to any statute or regulation of any state or country a petition in bankruptcy or insolvency or for reorganization or for an arrangement or for the appointment of a receiver or trustee of the Party or of substantially all of its assets; or if the other Party proposes a written agreement of composition or extension of substantially all of its debts; or if the other Party is served with an involuntary petition against it, filed in any insolvency proceeding, and such petition is not dismissed within ninety (90) days after the filing thereof; or if the other Party is a party to any dissolution or liquidation; or if the other Party makes an assignment of substantially all of its assets for the benefit of creditors.

(b) All rights and licenses granted under or pursuant to any section of this Agreement are and will otherwise be deemed to be for purposes of Section 365(n) of Title 11, United States Code (the "***Bankruptcy Code***") licenses of rights to "intellectual property" as defined in Section 101(35A) of the Bankruptcy Code. The Parties will retain and may fully exercise all of their respective rights and elections under the Bankruptcy Code. Upon the bankruptcy of any Party, the non-bankrupt Party will further be entitled to a complete duplicate of, or complete access to, any such intellectual property, and such, if not already in its possession, will be promptly delivered to the non-bankrupt Party, unless the bankrupt Party elects in writing to continue, and continues, to perform all of its obligations under this Agreement.

11.2.6. Termination if Ionis Development Candidate Not Identified or Designated.

(a) On a Target-by-Target basis, if, [***], then either Party will have the right to terminate the Agreement with regard to the applicable Program by providing [***] days' written notice to the other Party.

(b) If the JSC does not recommend a Compound for designation as an Ionis Development Candidate (and does not, as an alternative, recommend designation of a Related Compound) within [***] after Roche's receipt of the applicable Development Candidate Data Package, or Roche does not confirm the designation of a Compound (or Related Compound, as applicable) as an Ionis Development Candidate within [***] after the date of the JSC's recommendation (or a longer period as the Parties may mutually agree in writing), in each case in accordance with Section 3.1.3 (Ionis Development Candidate Designation; IND- Enabling Toxicology Study Costs), then Ionis will have the right to terminate the Agreement with regard to the applicable Program by providing [***] days' written notice to Roche.

(c) If this Agreement is terminated under this Section 11.2.6(a) (Termination if Ionis Development Candidate Not Identified or Designated) with respect to a Program, then Section 11.4 (General Consequences of Termination of the Agreement) will apply solely with respect to the applicable Program. Nothing in this Section 11.2.6 (Termination if Ionis Development Candidate Not Identified or Designated) will terminate or otherwise affect the provisions of another Program, which shall remain in full force and effect.

(d) If this Agreement is terminated under this Section 11.2.6 (Termination if Ionis Development Candidate Not Identified or Designated) with respect to a Program, then [***].

11.2.7. Termination for Cessation of Development. If, (a) prior to [***], Roche has suspended Development activities for a period of [***] but (i) has not [***], or (ii) has not [***], or (b) Section 3.1.7 (Failure of IND-Enabling Toxicology Study to Achieve Handoff Data Package Criteria; Disputes over Achievement of Handoff Data Package Criteria) becomes applicable under this Agreement, within the [***] period no Related Compound has been designated as a replacement Ionis Development Candidate, and Roche is not otherwise [***], then in each case ((a) or (b)) Ionis shall have the right to terminate this Agreement in accordance with Section 11.2.2(b) (Ionis' Right to Terminate). Ionis' rights under this Section 11.2.7 (Termination for Cessation of Development) are without prejudice to Roche's obligation to use Commercially Reasonable Efforts as set out in Section 6.2 (Diligence).

11.3. **Patent Challenge**. If, during the Agreement Term, solely with respect to rights to the Ionis Product-Specific Patents and the Ionis Core Technology Patents claiming technology incorporated in a Product, in each case that are included in a license granted to Roche under Section 5.1.2 (Development and Commercialization License Grant to Roche), Roche, its Affiliates or Sublicensees, in any country, (a) commence or otherwise voluntarily determine to participate in (other than as may be necessary or reasonably required to [***]) any action or proceeding, challenging or denying the enforceability or validity of any claim within an issued patent or patent application within such Ionis Product-Specific Patents or Ionis Core Technology Patents, or (b) direct, support or actively assist any other Person (other than as may be necessary or reasonably required to [***]) in bringing or prosecuting any action or proceeding challenging or denying the validity of any claim within an issued patent or patent application within such Ionis Product-Specific Patents or Ionis Core Technology Patents, then unless, within [***] after written notice from Ionis, Roche [***], Ionis may, to the extent permitted under Applicable Law, terminate this Agreement and the provisions of Section 11.4 (General Consequences of Termination of the Agreement) and Section 11.5 (Special Consequences of Termination of the Agreement) will apply, *provided, however*, [***].

11.4. **General Consequences of Termination of the Agreement**. If any portion of this Agreement or the whole Agreement is terminated by a Party in accordance with this ARTICLE 11 at any time and for any reason, the following terms will apply to any such termination, either in whole or on a Program-by-Program basis, Target-by-Target basis, Product-by-Product basis or country-by-country basis:

11.4.1. **Return of Information and Materials**. The Parties will return (or destroy, as directed by the other Party) all data, files, records and other materials containing or comprising the other Party's Confidential Information that are the subject of such termination to the extent separable from data, files, records and other materials (a) required for the continuation of the Program(s), Target, Product(s) or countries which have not been terminated or (b) that constitute the Confidential Information of the returning Party. Notwithstanding the foregoing, the Parties will be permitted to retain one copy of such data, files, records, and other materials for archival and legal compliance purposes.

11.4.2. **License Termination**. Upon termination but not expiration of the Agreement, except for the licenses granted under Section 5.1.3 (Cross-Licenses under Collaboration Intellectual Property) and Section 11.2.6(d), any licenses granted by Ionis to Roche under this Agreement will terminate and Roche, its Affiliates and Sublicensees will cease selling all Products that are the subject of such termination, unless Ionis elects to have Roche continue to sell the applicable Product(s) as part of the Transition Activities under Section 11.5.9 (Transition Activities).

11.4.3. **Exclusivity Covenants**. On a Target-by-Target basis, neither Party will have any further obligations under Section 4.1 (Exclusivity) of this Agreement.

11.4.4. **Accrued Rights**. Termination or expiration of this Agreement for any reason will be without prejudice to any rights or financial compensation that will have accrued to the benefit of a Party prior to such termination or expiration. Such termination or expiration will not relieve a Party from obligations that are expressly indicated to survive the termination or expiration of this Agreement. For purposes of clarification, milestone payments under ARTICLE 7 accrue as of the date the applicable Milestone Event is achieved even if the payment is not due at that time.

11.4.5. **Survival**. The following provisions of this Agreement will survive the expiration or termination of this Agreement: Section 3.10 (Failure to Identify or Designate an Ionis Development Candidate) (but only if this Agreement is terminated under Section 11.2.6 (Termination if Ionis Development Candidate Not Identified or Designated)), Section 5.1.3 (Cross-Licenses under Collaboration Intellectual Property), Section 5.1.5 (No Implied Licenses), Section 7.2 ([***]) through Section 7.6 (Mode of Payment) (in each case solely with respect to any financial compensation that has accrued prior to expiry or termination), Section 7.7 (Records Retention), Section 7.8 (Audits), Section 7.9 (Taxes), Section 7.10 (Interest), Section 8.1 (Ownership), Section 8.5.2 (Third Party Claims Regarding Discontinued Products), Section 8.5.3 (Interplay Between Enforcement of IP and Defense of Third Party Claims), Section 8.6.5 (Settlement), Section 9.5 (Disclaimer), ARTICLE 10 (Indemnification; Insurance), Section 11.1 (Agreement Term; Expiration), Section 11.2.5 (Termination for Insolvency), Section 11.2.6 (Termination if Ionis Development Candidate Not Identified or Designated), Section 11.4 (General Consequences of Termination of the Agreement), Section 11.5 (Special Consequences of Termination of the Agreement), Section 11.6 (Reverse Royalty Payments to Roche for Discontinued Products), Section 11.7 (Sublicensees), ARTICLE 12 (Confidentiality), ARTICLE 13 (Miscellaneous) and

11.4.6. APPENDIX 1 (Definitions) (to the extent definitions are embodied in the foregoing listed Articles and Sections).

11.5. **Special Consequences of Termination of the Agreement**. If Roche terminates the Agreement under Section 11.2.1 (Roche's Termination for Convenience), or Ionis terminates this Agreement under Section 11.2.2(b) (Ionis' Right to Terminate), Section 11.2.3 (Remedies for Failure to Use Commercially Reasonable Efforts), or Section 11.2.7 (Termination for Cessation of Development), then in addition to the terms set forth in Section 11.4 (General Consequences of Termination of the Agreement), the following additional terms will also apply:

11.5.1. **License to Ionis for Discontinued Products Comprising Ionis Development Candidates**. Roche will and hereby does grant to Ionis a sublicensable, royalty- bearing, worldwide, exclusive license or sublicense, as the case may be, under all Roche Technology (excluding Companion Diagnostic IP) Controlled by Roche as of the date of such reversion that Covers Discontinued Products comprising an Ionis Development Candidate solely as necessary to Develop, make, have made, use, sell, offer for sale, have sold, import and otherwise Commercialize such Discontinued Products in the Field;

11.5.2. **License to Ionis for Companion Diagnostic Products**. On request by Ionis, Roche will make available to Ionis, on commercially reasonable terms, any diagnostic products and/or services to select patients who will use Products (each, a "***Companion Diagnostic Product***") and any Patent Rights and Know- How Covering such Companion Diagnostic Products (such intellectual property, "***Companion Diagnostic IP***") Controlled by Roche as of the date of such reversion that is necessary to Develop or Commercialize such Companion Diagnostic Products;

11.5.3. **Know-How Transfer**. Within [***] following the date of termination, Roche will transfer to Ionis for use with respect to the Development and Commercialization of Discontinued Products, copies of any Roche Collaboration Know-How data, results, and regulatory information, and to the extent solely related to and necessary for the Development or Commercialization of such Discontinued Products, [***] in the possession of Roche as of the date of such reversion that relate to such Discontinued Products, and any other information or material specified in Section 3.5 (Technology Transfer Implementation);

11.5.4. **Regulatory Materials**. Within [***] following the date of the termination, Roche will assign, and hereby does assign, to Ionis all of Roche's right, title and interest in and to all regulatory materials for the Discontinued Product, including any IND, orphan drug designation and marketing authorizations that relate to the applicable Discontinued Product;

11.5.5. **Trademarks**. Roche will license to Ionis any trademarks that are specific to Discontinued Products solely for use with such Discontinued Products; *provided, however*, that in no event will Roche have any obligation to license to Ionis any trademarks used by Roche both in connection with a Product and in connection with the sale of any other product or service, including any Roche- or Roche-formative marks, company logos, or trademarks of its Affiliates or Sublicensees;

11.5.6. **Prosecution and Maintenance of Patents for Discontinued Products**. Ionis will control and be responsible at its sole cost for all aspects of the Prosecution and Maintenance of all Joint Collaboration Patents for Discontinued Products that claim Ionis Development Candidates and Ionis Product-Specific Patents for Discontinued Products, and Roche will provide Ionis with (and will instruct its counsel to provide Ionis with) all of the information and records in Roche's and its counsel's possession related to the Prosecution and Maintenance of such Joint Collaboration Patents for Discontinued Products that claim Ionis Development Candidates and Ionis Product-Specific Patents for Discontinued Products.

11.5.7. **Stocks of API and Finished Drug Product**. Ionis will have the right to purchase from Roche any or all of the inventory of API and/or Finished Drug Product for such Discontinued Product held by Roche as of the effective date of termination (that are not committed to be supplied to any Third Party or Sublicensee, in the ordinary course of business, as of the effective date of termination), if any, [***]. Ionis will notify Roche within [***] after the effective date of termination whether Ionis elects to exercise such right;

11.5.8. **Manufacturing Technology Transfer**. If Roche or Roche's CMO is manufacturing API and/or Finished Drug Product as of the termination triggering this provision, then Ionis may request Roche to conduct (or cause to be conducted by Roche's CMO) a technology transfer to Ionis (or Ionis' designated Third Party supplier) of any technology, information and data reasonably related to Roche's or such CMO's manufacturing and supply of API and/or Finished Drug Product for such Discontinued Product, and if so requested, Roche will conduct (or cause to be conducted by Roche's CMO) such a technology transfer, and Ionis [***], and Roche will (or will cause Roche's CMO to) continue to (i) provide reasonable support and cooperation with Ionis' regulatory filings and interactions with Regulatory Authorities related to Roche's or such CMO's API and/or Finished Drug Product manufacturing (including any required inspections), and (ii) supply (or cause to be supplied by Roche's CMO) API and/or Finished Drug Product to Ionis, [***] to enable Ionis to identify and contract with a suitable Third Party API and/or Finished Drug Product manufacturer; and

11.5.9. **Transition Activities**. For a period of up to [***] following the effective date of termination:

(a) The Parties wish to provide a mechanism to ensure that, assuming the Discontinued Product is available to patients as of the reversion date, patients who were being treated with the Discontinued Product prior to such termination or who desire access to the Discontinued Product can continue to have access to such Discontinued Product while the regulatory and commercial responsibilities for the Discontinued Product are transitioned from Roche to Ionis. As such, Ionis may request Roche to perform transition activities that are necessary or useful to (1) transition Roche's Commercialization activities (if any) to Ionis to minimize disruption to sales, (2) provide patients with continued access to the applicable Discontinued Products (if applicable), (3) enable Ionis (or Ionis' designee) to assume and execute the responsibilities under all Approvals and ongoing Clinical Studies for the applicable Discontinued Product, and (4) ensure long-term continuity of supply for the Discontinued Product (collectively, the "***Transition Activities***"), including, if applicable, the categories of services and deliverables listed on SCHEDULE 11.5.9, but no longer than [***] following the effective date of termination. If applicable, Roche will [***] SCHEDULE 11.5.9; *provided* Roche and Ionis may mutually agree in writing to [***].

(b) Ionis may elect to have Roche perform the applicable Transition Activities by providing written notice to Roche no later than [***] following the effective date of the termination. If Ionis requests Transition Activities, without limiting the provisions of Section 11.5 (Special Consequences of Termination of the Agreement), the Parties will mutually agree upon a transition plan for Roche to perform the applicable Transition Activities including delivery and transition dates. In addition, the Parties will establish a transition committee consisting of at least each Party's Alliance Managers, a representative from each Party's chemistry, manufacturing and controls ("***CMC***") group who was responsible for the Discontinued Product prior to the termination, and up to two (2) additional representatives from each Party who are from other relevant functional groups to facilitate a smooth transition. While Roche is providing applicable Transition Activities, Roche and Ionis will [***].

(c) Ionis will [***] to perform the Transition Activities. In addition, Ionis will [***] to perform the Transition Activities. Ionis will own [***].

11.6. Reverse Royalty Payments to Roche for Discontinued Products.

11.6.1. If either party terminates the Agreement with respect to a Product after payment of the applicable milestone amount for the "[***]" Milestone Event set forth in TABLE 1 of Section 7.3.1 (Development Milestones for [***]) or TABLE 2 of Section 7.3.2 (Development Milestones for [***]) but before the payment of the applicable milestone amount for the "[***]" Milestone Event set forth in TABLE 1 of Section 7.3.1 (Development Milestones for [***]) or TABLE 2 of Section 7.3.2 (Development Milestones for [***]) with respect to the Discontinued Product that is the subject of such termination, and Ionis or any of its Affiliates or Sublicensees Commercializes such Discontinued Product, then Ionis will pay Roche a reversion royalty of [***] of Annual worldwide Net Sales of such Discontinued Product [***].

11.6.2. If either Party terminates this Agreement with respect to a Product after payment of the applicable milestone amount for the "[***]" Milestone Event set forth in TABLE 1 of Section 7.3.1 (Development Milestones for [***]) or TABLE 2 of Section 7.3.2 (Development Milestones for [***]) but before the payment of the first applicable milestone amount for the "[***]" Milestone Event set forth in TABLE 1 of Section 7.3.1 (Development Milestones for [***]) or TABLE 2 of Section 7.3.2 (Development Milestones for [***]) with respect to the Product that is the subject of such termination, and Ionis or any of its Affiliates or Sublicensees Commercializes such Discontinued Product, then Ionis will pay Roche a reversion royalty of [***] of Annual worldwide Net Sales of such Discontinued Product [***].

11.6.3. If either Party terminates this Agreement with respect to a Product after payment of the first applicable milestone amount for the "[***]" Milestone Event set forth in TABLE 1 of Section 7.3.1 (Development Milestones for [***]) or TABLE 2 of Section 7.3.2 (Development Milestones for [***]) with respect to the Discontinued Product that is the subject of such termination, and Ionis or any of its Affiliates or Sublicensees Commercializes such Discontinued Product, then Ionis will pay Roche a reversion royalty of [***] of Annual worldwide Net Sales of such Discontinued Product [***].

11.6.4. Ionis will pay Roche reversion royalties under this Section 11.6 (Reverse Royalty Payments to Roche for Discontinued Products) in accordance with the provisions governing payment of royalties from Roche to Ionis in Section 7.4 (Royalties) (*mutatis mutandis*).

11.6.5. Limitations on Grant-Backs.

For purposes of clarity, irrespective of anything to the contrary in this Agreement:

(a) All transfers and licenses from Roche to Ionis (or other obligations of Roche) under Section 11.6 (Reverse Royalty Payments to Roche for Discontinued Products) are solely with respect to Product(s) [***]. Should at the effective date of termination (i) [***], or (ii) [***], then [***]. For clarity, Roche [***].

(b) In connection with research studies, Clinical Studies or other activities associated with the Development and Commercialization of Products, Roche may have collected (i) personally identifiable information about individual human subjects or (ii) human biological samples (collectively, "***PII/Samples***"). Legal and contractual restrictions may apply to such PII/Samples. Roche shall have no obligation to transfer such PII/Samples unless necessary for the continued development of the Product, in which case Roche shall not be obliged to transfer any PII/Samples that Roche in good faith believes would be prohibited or would subject Roche to potential liability by reason of Applicable Law, contractual restrictions or insufficient patient consent. If Roche transfers any such PII/Samples, the Parties will enter into the relevant agreements under applicable data privacy laws (such as a data transfer agreement) when required in accordance with Section 12.1 (Confidentiality; Exceptions). Upon the transfer of such PII/Samples by Roche, Ionis shall use such PII/Samples for the sole purpose of Developing and Commercializing the Product, and Ionis shall be responsible for the correct and lawful use of the PII/Sample in compliance with the applicable data protection laws, the informed consent forms and privacy notices (including but not limited to potential re-consenting of the patients at Ionis' costs if the legal basis for the processing of the patients' data was their explicit consent).

11.7. **Sublicensees**. If this Agreement terminates for any reason, any Sublicensee granted a sublicense by Roche to Develop or Commercialize Products will, from the effective date of such termination, automatically become a direct licensee of Ionis with respect to the rights sublicensed to the Sublicensee by Roche; *so long as* (i) such Sublicensee is not in breach of its sublicense agreement, (ii) such Sublicensee agrees in writing to comply with all of the terms of this Agreement to the extent applicable to the rights originally sublicensed to it by Roche, and (iii) such Sublicensee agrees to pay directly to Ionis such Sublicensee's payments under this Agreement to the extent applicable to the rights sublicensed to it by Roche. Roche agrees that it will confirm clause (i) of the foregoing in writing at the request and for the benefit of Ionis and if requested, the Sublicensee.

ARTICLE 12.
CONFIDENTIALITY

12.1. **Confidentiality; Exceptions**. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing, the Parties agree that, during the Agreement Term and for five years thereafter, the receiving Party (the "***Receiving Party***") and its Affiliates will keep confidential and will not publish or otherwise disclose or use for any purpose other than as provided for in this Agreement any confidential or proprietary information or materials, patentable or otherwise, in any form (written, oral, photographic, electronic, magnetic, or otherwise) which is disclosed to it by the other Party (the "***Disclosing Party***") or its Affiliates or otherwise received or accessed by a Receiving Party in the course of performing its obligations or exercising its rights under this Agreement, including trade secrets, Know-How, inventions or discoveries, proprietary information, formulae, processes, techniques and information relating to the past, present and future marketing, financial, and research and development activities of any product or potential product or useful technology of the Disclosing Party or its Affiliates and the pricing thereof (collectively, "***Confidential Information***"). Without limiting the foregoing, Roche agrees that it will not disclose or use Ionis' Confidential Information or the Licensed Know-How for any purpose other than as provided in this Agreement. Roche has procedures in place to protect such information and will ensure it implements such procedures appropriately to prevent Ionis' Confidential Information and the Licensed Know-How from being disclosed or used for any purpose other than as provided in this Agreement. In addition to the confidentiality obligations set forth in this Agreement, in the event that, during the implementation of the Agreement, one of the Parties processes any information that is protected by applicable data privacy laws, including without limitation, the Health Insurance Portability & Accountability Act of 1996 (HIPAA) in the US, the Swiss Data Protection Act, the European Union General Data Protection Regulation 2016/679 (GDPR), the Personal Information Protection and Electronic Documents Canada (PIPEDA) in Canada, and any other applicable data protection laws, the respective Party agrees to fully comply with such laws, as they may be applicable to the Party. If and as required by applicable data privacy laws, including but not limited to the EU GDPR, Swiss or United Kingdom laws, the Parties shall execute additional data protection documentation, such as the Standard Contractual Clauses issued by the European Commission to cover any cross-border transfers of personal data. If a Party to this Agreement becomes subject to an investigation by a data protection authority or any other competent authority in relation to the processing of personal data under this Agreement, then the Party affected will inform the other Party without any undue delay unless the Party is not permitted to provide such information. The Parties will inform each other without any undue delay and provide each other with reasonable support in case of a Data Subject Request (as such term is defined under the applicable data privacy law(s)) or in case of a Data Breach (as such term is defined under the applicable data privacy law(s)) that would potentially affect the other Party to this Agreement. If changes to the applicable data privacy laws affect the compliance of data processing activities under this Agreement, then the Parties will negotiate in good faith adjustments to the data privacy language in this Agreement, or additional data privacy documentation if and as required by applicable data privacy laws. The Parties warrant that they will implement and maintain adequate technical and organizational measures to ensure the integrity and security of personal data processed under this Agreement.

12.2. **Prior Confidentiality Agreement**. The Non-Disclosure Agreement executed by Ionis and Roche on November 11, 2021 (including any and all amendments thereto) (the "***CDA***") will govern disclosures of Information (as defined in the CDA) between the Parties prior to the Effective Date. All Confidential Information exchanged between the Parties on or after the Effective Date under this Agreement will be subject to the terms of this ARTICLE 12.

12.3. **Authorized Disclosure**. Except as expressly provided otherwise in this Agreement, a Receiving Party or its Affiliates may use and disclose to Third Parties Confidential Information of the Disclosing Party as follows: (i) solely in connection with the performance of its obligations or exercise of rights granted or reserved in this Agreement under confidentiality provisions no less restrictive than those in this Agreement, *provided,* a Receiving Party may disclose Confidential Information to a governmental entity or agency without requiring such entity or agency to enter into a confidentiality agreement; (ii) to the extent reasonably necessary to file or prosecute patent, copyright and trademark applications (subject to Section 12.4 (Press Release; Publications; Disclosure of Agreement) below), complying with applicable governmental regulations, obtaining Approvals, conducting Pre-Clinical Studies or Clinical Studies, marketing a Product, or as otherwise required by Applicable Law, regulation, rule or legal process (including the rules of the SEC and any stock exchange); *provided, however*, that if a Receiving Party or any of its Affiliates is required by law or regulation to make any such disclosure of a Disclosing Party's Confidential Information it will, except where impracticable for necessary disclosures, give reasonable advance notice to the Disclosing Party of such disclosure requirement and will use its reasonable efforts to secure confidential treatment of such Confidential Information required to be disclosed; (iii) in communication with actual or potential lenders, investors, merger partners, acquirers, consultants, or professional advisors on a need-to-know basis, in each case under confidentiality provisions no less restrictive than those of this Agreement; (iv) to the extent such disclosure is required to comply with existing expressly stated contractual obligations owed to such Party's or its Affiliates' licensor with respect to any intellectual property licensed to the other Party under this Agreement; or (v) as mutually agreed to in writing by the Parties. Notwithstanding the foregoing, if either Party concludes based on the reasonable opinion of counsel that a copy of this Agreement must be filed with the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States, such Party will, within a reasonable time prior to any such filing (and to the extent possible at least [***] prior to any such filing), provide the other Party with a copy of this Agreement showing any provisions hereof as to which such Party proposes to request confidential treatment, and the Parties shall coordinate with each other and will use good faith efforts to mutually agree on the redaction of certain provisions of this Agreement (together with all exhibits and schedules) before filing such copy of this Agreement, provided that notwithstanding the foregoing, the filing Party shall retain final decision-making authority over the redactions to be made in its filed copy of this Agreement.

12.4. **Press Release; Publications; Disclosure of Agreement**.

12.4.1. **Public Announcements – Generally**. Either Party may issue a press release announcing the execution of this Agreement and disclosing selected key terms, subject to prior agreement of the Parties on the final draft of press release to be issued. Except to the extent required to comply with Applicable Law, regulation, rule or legal process or as otherwise permitted in accordance with this Section 12.4 (Press Release; Publications; Disclosure of Agreement), each Party agrees not to issue any other press release or other public statement disclosing other information relating to this Agreement or the terms of this Agreement or the transactions contemplated hereby without the prior written consent of the other Party, which consent will not be unreasonably withheld or delayed.

12.4.2. **Use of Name**. Except as set forth in Section 12.4.8 (Acknowledgement; Commercial Materials), neither Party will use the other Party's name in a press release or other publication without first obtaining the prior written consent of the Party to be named.

12.4.3. **Notice of Significant Events**. Each Party will notify (no later than [***] after the information or results are obtained) the other Party of any significant event related to a Product (including any data, serious adverse event or regulatory advice or approval) so that the Parties may analyze the need to or desirability of publicly disclosing or reporting such event. Notwithstanding Section 12.4.1 (Public Announcements – Generally) above, any press release or other similar public communication by either Party related to a Product's efficacy or safety data and/or results, will be submitted to the other Party for review and approval at least [***] in advance of such proposed public disclosure, which approval will not be unreasonably withheld or delayed.

12.4.4. **Press Releases**. Roche will have the sole right, consistent with its practice with its other compounds and products, to issue press releases, publish, present or otherwise disclose the progress and results regarding the Products to the public; *provided*, that with respect to any proposed press release or other similar public communication by Roche disclosing regulatory discussions, the efficacy or safety data or results related to the Products or Roche's sales projections, (i) Roche will submit such proposed communication to Ionis for review at least [***] in advance of such proposed public disclosure, (ii) Ionis will have the right to review and recommend changes to such communication, and (iii) Roche will in good faith consider any changes that are timely recommended by Ionis.

12.4.5. **Scientific or Clinical Presentations**. Regarding any proposed scientific publications related to results from any Clinical Studies of a Product, the Parties agree to use Commercially Reasonable Efforts to control public scientific disclosures of such results to prevent any adverse effect of any premature public disclosure of such results. The Parties will establish a procedure for publication review and each Party will first submit to the other Party through the JPC an early draft of all such publications or presentations, at least [***] prior to submission for publication including to facilitate the publication of any summaries of Clinical Studies data and results as required on the clinical trial registry of each respective Party. Each Party will review such proposed publication to avoid the unauthorized disclosure of a Party's Confidential Information and to preserve the patentability of inventions arising from an R&D Plan. If, during such [***] period, the other Party informs such Party that its proposed publication contains Confidential Information of the other Party, then such Party will delete such Confidential Information from its proposed publication. In addition, if during such [***] period, the other Party informs such Party that its proposed publication discloses non-public inventions made by either Party in the course of the Development under this Agreement, or the public disclosure of such proposed publication may have a material adverse effect on any Patent Rights or Know-How solely owned or Controlled by such other Party, then such Party will either (i) delay such proposed publication for up to [***] from the date of such Party's objection, to permit the timely first filing of patent application(s), or (ii) remove the identified disclosures prior to publication.

12.4.6. **SEC Filings**. Each Party will give the other Party a reasonable opportunity to review all material filings with the SEC describing the terms of this Agreement prior to submission of such filings, and will give due consideration to any reasonable comments by the non-filing Party relating to such filing.

12.4.7. **Subsequent Disclosure**. Notwithstanding the foregoing, to the extent information regarding this Agreement or a Product has already been publicly disclosed, either Party (or its Affiliates) may subsequently disclose the same information to the public without the consent of the other Party.

12.4.8. **Acknowledgment; Commercial Materials**. Each Party will acknowledge in any press release, public presentation, publication or commercial marketing materials regarding the collaboration or a Product, the other Party's role in discovering and Developing a Product or Discontinued Product, as applicable, that the Product is under license from Ionis and otherwise acknowledge the contributions from the other Party, and each Party's stock ticker symbol (e.g., Ionis: Nasdaq: IONS; Roche: SIX: RO, ROG; OTCQX: RHHBY). Ionis may include the Products (and identify Roche as its partner for the Product) in Ionis' drug pipeline. In addition, subject to Applicable Law, the words "Discovered by Ionis" will be included in Product communications, *provided* that Roche will have final decision-making authority regarding the applicability of any legal and regulatory requirements for such acknowledgement.

ARTICLE 13.
MISCELLANEOUS

13.1. Dispute Resolution.

13.1.1. **Escalation**. If any dispute occurs under this Agreement (other than a dispute regarding the construction, validity or enforcement of either Party's Patent Rights, which disputes will be resolved pursuant to Section 13.2 (Governing Law; Jurisdiction; Venue; Service of Process)), then either Party may request in writing that the dispute be referred for resolution to the Head of Roche Pharma Partnering and the Chief Executive Officer of Ionis (the "***Executives***"). Within [***] after such a request, the Executives will meet in person at a mutually acceptable time and location or by means of telephone or video conference to negotiate a settlement of the dispute. Each Party's JSC representatives may participate in such meeting if desired. If the Executives fail to resolve the dispute within such [***] period, then the dispute will be referred to binding arbitration under Section 13.1.2 (Binding Arbitration).

13.1.2. **Binding Arbitration**. If a dispute subject to Section 13.1.1 (Escalation) is not resolved pursuant to Section 13.1.1 (Escalation), except as otherwise set forth in this Agreement such dispute will be resolved through binding arbitration in accordance with this Section 13.1.2 (Binding Arbitration) and under the Commercial Arbitration Rules of the [***] then in effect, including application of the "*Expedited Procedures*" (sections E-1, et al) of the Commercial Arbitration Rules of the [***]. The proceedings and decisions of the arbitrator will be confidential, final and binding on the Parties, and judgment upon the award of such arbitrators may be entered in any court having jurisdiction thereof. The arbitration will take place in Boston, Massachusetts USA and will be conducted by three (3) arbitrators. Each of Roche and Ionis shall appoint one (1) arbitrator within thirty (30) days after the notice that initiated the arbitration. These two (2) arbitrators shall in turn appoint a third arbitrator who will be reasonably acceptable to the Parties and who will be appointed in accordance with [***] rules. Each arbitrator chosen hereunder will have educational training and industry experience sufficient to demonstrate a reasonable level of scientific, financial, medical and industry knowledge relevant to the particular dispute.

13.2. Governing Law; Jurisdiction; Venue; Service of Process.

13.2.1. This Agreement and any dispute will be governed by and construed and enforced in accordance with the laws of [***], without reference to conflicts of laws principles.

13.2.2. Each Party hereby agrees that service of process: (a) made in any manner permitted by [***] law, or (b) made by overnight express courier service (signature required), prepaid, at its address specified pursuant to Section 13.7 (Notices), will constitute good and valid service of process in any such action and (c) waives and agrees not to assert (by way of motion, as a defense, or otherwise) in any such action any claim that service of process made in accordance with clause (a) or (b) does not constitute good and valid service of process.

13.3. **Remedies**. Notwithstanding anything to the contrary in this Agreement, each Party will be entitled to seek, in addition to any other right or remedy it may have, at law or in equity, a temporary restraining order or a preliminary injunction, without the posting of any bond or other security, enjoining or restraining the other Party from any violation or threatened violation of this Agreement, and the Parties agree that in the event of a threatened or actual material breach of this Agreement injunctive relief would be appropriate. Neither Party may recover any Losses relating to any matter arising under one provision of this Agreement to the extent that such Party has already recovered Losses with respect to such matter pursuant to other provisions of this Agreement (including recoveries under Section 10.1 (Indemnification by Roche) or Section 10.2 (Indemnification by Ionis)). Except for the offsets and credits explicitly set forth in Section 7.4.3(f)(i) (Additional Ionis Core Intellectual Property) and Section 7.8 (Audits), neither Party will have the right to set-off any amount it is owed or believes it is owed against payments due or payable to the other Party under this Agreement.

13.4. **Assignment and Successors**. Neither this Agreement nor any obligation of a Party hereunder may be assigned by either Party without the consent of the other, except that each Party may assign this Agreement and the rights, obligations and interests of such Party, in whole or in part, without the other Party's consent, to any of its Affiliates, to any purchaser of all or substantially all of its assets or all or substantially all of its assets to which this Agreement relates or to any successor corporation resulting from any merger, consolidation, share exchange or other similar transaction; *provided*, if a Party transfers or assigns this Agreement to [***], then such transferring Party (or such Affiliate) ("***Transferring Party***"), will [***] any payment that the Transferring Party is obligated to pay to the non-transferring Party ("***Non-Transferring Party***") under ARTICLE 7 for the taxes withheld such that the Non-Transferring Party receives [***]. In addition, Ionis may assign or transfer its rights to receive payments under this Agreement (but no liabilities), without Roche's consent, to an Affiliate or to a Third Party in connection with a payment factoring transaction. Any purported assignment or transfer made in contravention of this Section 13.4 (Assignment and Successors) will be null and void. To the extent the Non-Transferring Party utilizes [***], the Non- Transferring Party will [***] to the Transferring Party [***]. To assist the Transferring Party in determining when [***], beginning with the first Annual tax return for the year in which the Transferring Party [***], and each year thereafter (including, for clarity, all years in which the Non-Transferring Party utilizes [***], the Non-Transferring Party will provide the Transferring Party with the Non-Transferring Party's' Annual tax returns (federal and state) and, in years in which the Non-Transferring Party utilizes [***], supporting documentation for such [***].

13.5. **Change of Control**. If Ionis undergoes a Change of Control, then Roche shall have the right at any time after Handoff to disband the JSC and make unilateral decisions with respect to the R&D Plans, and the Development and Commercialization of Products with no obligation to seek input from Ionis or its successor, if applicable.

13.6. **Force Majeure**. No Party will be held responsible to the other Party nor be deemed to be in default under, or in breach of any provision of, this Agreement for failure or delay in performing any obligation of this Agreement when such failure or delay is due to force majeure, and without the fault or negligence of the Party so failing or delaying. For purposes of this Agreement, force majeure means a cause beyond the reasonable control of a Party, which may include acts of God; acts, regulations, or laws of any government; war; terrorism; civil commotion; fire, flood, earthquake, tornado, tsunami, explosion or storm; pandemic; epidemic and failure of public utilities or common carriers. In such event the Party so failing or delaying will immediately notify the other Party of such inability and of the period for which such inability is expected to continue. The Party giving such notice will be excused from such of its obligations under this Agreement as it is thereby disabled from performing for so long as it is so disabled for up to a maximum of ninety (90) days, after which time the Parties will negotiate in good faith any modifications of the terms of this Agreement that may be necessary to arrive at an equitable solution, unless the Party giving such notice has set out a reasonable timeframe and plan to resolve the effects of such force majeure and executes such plan within such timeframe. To the extent possible, each Party will use reasonable efforts to minimize the duration of any force majeure.

13.7. **Notices**. Any notice or request required or permitted to be given under or in connection with this Agreement will be deemed to have been sufficiently given if in writing and personally delivered or sent by certified mail (return receipt requested), facsimile transmission (receipt verified), or overnight express courier service (signature required), prepaid, to the Party for which such notice is intended, at the address set forth for such Party below:

If to Ionis, addressed to:	Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010 Attention: Chief Executive Officer
with a copy to:	Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010 Attention: General Counsel Email: [***]
If to Roche, addressed to:	F. Hoffmann-La Roche Ltd Grenzacherstrasse 124 4070 Basel, Switzerland Attention: Corporate Legal Department Fax: [***]
If to Roche, addressed to:	Hoffmann-La Roche Inc. 150 Clove Road, Suite 8 Little Falls, New Jersey 07424 Attention: Corporate Secretary Fax: [***]
with a copy to:	F. Hoffmann-La Roche Ltd Grenzacherstrasse 124 4070 Basel, Switzerland Attention: Alliance Manager Fax: [***]

or to such other address for such Party as it will have specified by like notice to the other Party; *provided that* notices of a change of address will be effective only upon receipt thereof. If delivered personally or by facsimile transmission, the date of delivery will be deemed to be the date on which such notice or request was given. If sent by overnight express courier service, the date of delivery will be deemed to be the next Business Day after such notice or request was deposited with such service. If sent by certified mail, the date of delivery will be deemed to be the third Business Day after such notice or request was deposited with the U.S. Postal Service.

13.8. **Invoices**. All invoices that are required or permitted hereunder shall be in writing and sent by Ionis to Roche at the following address or any other address that Roche may later provide:

F. Hoffmann-La Roche AG
Kreditorenbuchhaltung
Grenzacherstrasse 124
CH - 4070 Basel

Upon Ionis' request, Roche's Alliance Manager will provide Ionis' Alliance Manager with any additional information reasonably requested by Ionis to facilitate the prompt delivery of invoices to Roche, including an email address for sending invoices.

13.9. **Export Clause**. Each Party acknowledges that the laws and regulations of the United States restrict the export and re-export of commodities and technical data of United States origin. Each Party agrees that it will not export or re-export restricted commodities or the technical data of the other Party in any form without the appropriate United States and foreign government licenses.

13.10. **Waiver**. Neither Party may waive or release any of its rights or interests in this Agreement except in writing. The failure of either Party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement will not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition. No waiver by either Party of any condition or term in any one or more instances will be construed as a continuing waiver or subsequent waiver of such condition or term or of another condition or term.

13.11. **Severability**. If any provision hereof should be held invalid, illegal or unenforceable in any jurisdiction, the Parties will negotiate in good faith a valid, legal and enforceable substitute provision that most nearly reflects the original intent of the Parties and all other provisions hereof will remain in full force and effect in such jurisdiction and will be liberally construed in order to carry out the intentions of the Parties hereto as nearly as may be possible. Such invalidity, illegality or unenforceability will not affect the validity, legality or enforceability of such provision in any other jurisdiction.

13.12. **Entire Agreement**. This Agreement, together with the Schedules and Appendices hereto, sets forth all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties regarding the subject matter hereof and supersedes and terminates all prior agreements and understanding between the Parties pertaining to the subject matter hereof. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties regarding the subject matter hereof other than as set forth in this Agreement and the Schedules and Appendices hereto. No subsequent alteration, amendment, change or addition to this Agreement will be binding upon the Parties hereto unless reduced to writing and signed by the respective authorized representatives of the Parties.

13.13. **Independent Contractors**. Nothing herein will be construed to create any relationship of employer and employee, agent and principal, partnership or joint venture between the Parties. Each Party is an independent contractor. Neither Party will assume, either directly or indirectly, any liability of or for the other Party. Neither Party will have the authority to bind or obligate the other Party and neither Party will represent that it has such authority.

13.14. **Interpretation**. Except as otherwise explicitly specified to the contrary, (a) references to a section, exhibit or schedule means a section of, or schedule or exhibit to this Agreement, unless another agreement is specified, (b) the word "including" (in its various forms) means "including without limitation," (c) the words "will" and "shall" have the same meaning, (d) references to a particular statute or regulation include all rules and regulations thereunder and any predecessor or successor statute, rules or regulation, in each case as amended or otherwise modified from time to time, (e) words in the singular or plural form include the plural and singular form, respectively, (f) references to a particular Person include such Person's successors and assigns to the extent not prohibited by this Agreement, (g) unless otherwise specified, "$" is in reference to United States dollars, and (h) the headings contained in this Agreement, and in any Appendix or Schedule to this Agreement are for convenience only and will not in any way affect the construction of or be taken into consideration in interpreting this Agreement.

13.15. **Further Actions**. Each Party will execute, acknowledge and deliver such further instruments, and do all such other acts, as may be necessary or appropriate in order to carry out the expressly stated purposes and the clear intent of this Agreement.

13.16. **Construction of Agreement**. The terms and provisions of this Agreement represent the results of negotiations between the Parties and their representatives, each of which has been represented by counsel of its own choosing, and neither of which has acted under duress or compulsion, whether legal, economic or otherwise. Accordingly, the terms and provisions of this Agreement will be interpreted and construed in accordance with their usual and customary meanings, and each of the Parties hereto hereby waives the application in connection with the interpretation and construction of this Agreement of any rule of law to the effect that ambiguous or conflicting terms or provisions contained in this Agreement will be interpreted or construed against the Party whose attorney prepared the executed draft or any earlier draft of this Agreement.

13.17. **Supremacy**. In the event of any express conflict or inconsistency between this Agreement and any Schedule or Appendix hereto, the terms of this Agreement will apply. The Parties understand and agree that the Schedules and Appendices hereto are not intended to be the final and complete embodiment of any terms or provisions of this Agreement, and are to be updated from time to time during the Agreement Term, as appropriate and in accordance with the provisions of this Agreement.

13.18. **Counterparts.** This Agreement may be executed in one or more counterparts, each of which shall be deemed an original and all of which taken together shall be deemed to constitute one and the same agreement. The Parties agree that execution of this Agreement by e-Signatures or by exchanging executed signature pages in .pdf format shall have the same legal force and effect as the exchange of original signatures. As used in this Section, "e-Signature" shall mean a signature that consists of one or more letters, characters, numbers or other symbols in digital form incorporated in, attached to or associated with the electronic document, that (a) is unique to the person executing the signature; (b) the technology or process used to make the signature is under the sole control of the person making the signature; (c) the technology or process can be used to identify the person using the technology or process; and (d) the electronic signature can be linked with an electronic document in such a way that it can be used to determine whether the electronic document has been changed since the electronic signature was incorporated in, attached to or associated with the electronic document.

[SIGNATURE PAGES FOLLOW]

* - * - * - *

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their representatives thereunto duly authorized as of the Effective Date.

F. HOFFMANN-LA ROCHE LTD

By: */s/ James Sabry*
Name: James Sabry
Title: Global Head – Roche Pharma Partnering
Date: September 26, 2023

By: */s/ Stephanie Harloff*
Name: Stephanie Harloff
Title: Legal Counsel – Legal Pharma Partnering
Date: September 26, 2023

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their representatives thereunto duly authorized as of the Effective Date.

HOFFMANN-LA ROCHE INC.

By: */s/ Gerald Bohm*
Name: Gerald Bohm
Title: Principal Counsel Associate General Counsel
Date: September 26, 2023

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their representatives thereunto duly authorized as of the Effective Date.

IONIS PHARMACEUTICALS, INC.

By: */s/ Brett Monia*
Name: Brett Monia
Title: Chief Executive Officer
Date: September 26, 2023

LIST OF APPENDICES AND SCHEDULES

APPENDIX 1

DEFINITIONS

For purposes of this Agreement, the following capitalized terms will have the following meanings:

"**[***]**" means [***].

"***Acceptance***" means, with respect to an NDA, BLA, MAA or JNDA filed for a Product, (a) in the United States, the receipt of written notice from the FDA that such NDA or BLA is officially "*filed*," (b) in the European Union, receipt of written notice of acceptance by the EMA of such MAA for filing under the centralized European procedure in accordance with any feedback received from European Regulatory Authorities; *provided that* if the centralized filing procedure is not used, then Acceptance will be determined upon the acceptance of such MAA by the applicable Regulatory Authority in a Major Market in the EU, and (c) in Japan, receipt of written notice of acceptance of filing of such JNDA from the Koseisho (i.e., the Japanese Ministry of Health and Welfare, or any successor agency thereto).

"***Accounting Standard***" means (a) the United States Generally Accepted Accounting Principles ("GAAP") or (b) International Financial Reporting Standards of the International Accounting Standards Boards ("IFRS"), in each case ((a) and (b)) as generally and consistently applied throughout the applicable Person's organization. Each Party will promptly notify the other Party in writing if such Party changes the Accounting Standards pursuant to which its records are maintained.

"***Additional Ionis Core IP***" has the meaning set forth in Section 7.4.3(f)(i)(1).

"***Affiliate***" of an entity means any corporation, firm, partnership or other entity which directly or indirectly through one or more intermediaries controls, is controlled by or is under common control with a Party to this Agreement. An entity will be deemed to control another entity if it
(i) owns, directly or indirectly, more than fifty percent (50%) of the outstanding voting securities or capital stock (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) of such other entity, or has other comparable ownership interest with respect to any entity other than a corporation; or (ii) has the power, whether pursuant to contract, ownership of securities or otherwise, to direct the management and policies of the entity. Anything to the contrary in this paragraph notwithstanding, Chugai Pharmaceutical Co., Ltd, a Japanese corporation ("***Chugai***"), shall not be deemed an Affiliate of Roche unless Roche provides written notice to Ionis of its desire to include Chugai as an Affiliate of Roche.

"***Agreement***" has the meaning set forth in the Preamble of this Agreement.

"***Agreement Term***" has the meaning set forth in Section 11.1 (Agreement Term; Expiration).

"***Alliance Manager***" has the meaning set forth in Section 3.3.3 (Alliance Managers).

"***Alzheimer's Disease***" means a neurodegenerative disease associated with cognitive disorders as per ICD 11.

"***Annual***" means the period covering a Calendar Year or occurring once per Calendar Year, as the context requires.

"***API***" means the bulk active pharmaceutical ingredient manufactured in accordance with cGMP (unless stated otherwise herein) for a Product. The quantity of API will be the as-is gross mass of the API after lyophilization (*i.e.*, including such amounts of water, impurities, salt, heavy metals, etc., within the limits set forth in the API specifications) and before release, retention, stability or characterization samples are removed (if needed).

"[***]" ([***]) means [***].

"***Applicable Law***" or "***Law***" means all applicable laws, statutes, rules, regulations and other pronouncements having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, agency or other body, domestic or foreign, including any applicable rules, regulations, guidelines, or other requirements of the Regulatory Authorities that may be in effect from time to time.

"***Approval***" means (i) with respect to a Product in the EU, the earlier to occur of (A) approval from the applicable Regulatory Authority in at least one member state in the EU sufficient for the manufacture, distribution, use, marketing and sale of such Product, including pricing and reimbursement approval, in such jurisdiction in accordance with Applicable Laws, or (B) the First Commercial Sale of a Product in the EU; and (ii) with respect to a Product in any regulatory jurisdiction other than the EU, approval sufficient for the manufacture, distribution, use, marketing and sale of such Product in such jurisdiction in accordance with Applicable Laws.

"***ASO***" means a compound comprising a [***] Oligonucleotide.

"***Audit Report***" has the meaning set forth in Section 7.8 (Audits).

"***Bankruptcy Code***" has the meaning set forth in Section 11.2.5(b).

"***BLA***" means a biologics license application that is submitted to the FDA for a Product, pursuant to 21 C.F.R. § 601.2.

"***Breaching Party***" means the Party that is believed by the Non-Breaching Party to be in material breach of this Agreement.

"***Business Day***" means any day other than a Saturday or Sunday on which banking institutions in New York, New York are open for business.

"***Calendar Quarter***" means a period of three consecutive months ending on the last day of March, June, September, or December, respectively, and will also include the period beginning on the Effective Date and ending on the last day of the Calendar Quarter in which the Effective Date falls.

"***Calendar Year***" means a year beginning on January 1 (or, with respect to 2023, the Effective Date) and ending on December 31.

"***CDA***" has the meaning set forth in Section 12.2.

"***cGMP***" means current Good Manufacturing Practices as specified in the United States Code of Federal Regulations, ICH Guideline Q7A, or equivalent laws, rules, or regulations of an applicable Regulatory Authority at the time of manufacture.

"***Change of Control***" means, with respect to a Party: (a) the acquisition by any Third Party of beneficial ownership of more than fifty percent (50%) of the then outstanding common shares or voting power of such Party, other than acquisitions by employee benefit plans sponsored or maintained by such Party; (b) the consummation of a business combination involving such Party, unless, following such business combination, the stockholders of such Party immediately prior to such business combination beneficially own directly or indirectly more than fifty percent (50%) of the then outstanding common shares or voting power of the entity resulting from such business combination.

"***Claims***" has the meaning set forth in Section 10.1 (Indemnification by Roche).

"***Clinical Study***" or "***Clinical Studies***" means a Phase 1 Trial, Phase 2 Trial, Phase 3 Trial, Pivotal Trial or Phase 4 Trial, or such other study in humans that is conducted in accordance with good clinical practices and is designed to generate data in support or maintenance of an NDA, BLA, MAA, JNDA or other similar marketing application.

"***CMC***" has the meaning set forth in Section 11.5.9(b).

"***CMO***" means a Third Party contract manufacturer Manufacturing API or Finished Drug Product for any purpose under this Agreement.

"***Combination Product***" means a Product that will be [***].

"***Commercialize***," "***Commercialization***" or "***Commercializing***" means any and all activities directed to marketing, promoting, detailing, distributing, importing, having imported, exporting, having exported, selling or offering to sell a Product following receipt of Approval for a Product in the applicable country, including conducting pre-and post-Approval activities, including studies reasonably required to increase the market potential of a Product and studies to provide improved formulation and Product delivery, and launching and promoting a Product in each country.

"***Commercializing Party***" means (a) Roche, with respect to a Product that is being Developed and Commercialized by or on behalf of Roche, its Affiliates or Sublicensees hereunder, and (b) Ionis, with respect to a Discontinued Product that is being Developed and Commercialized by or on behalf of Ionis, its Affiliates or Sublicensees hereunder.

"***Commercially Reasonable Efforts***" means the carrying out of discovery, research, development or commercialization activities using good-faith commercially reasonable [***] efforts that the applicable Party would reasonably devote to a compound or product of similar market potential or profit potential at a similar stage in development or product life resulting from its own research efforts, based on conditions then prevailing and taking into account, without limitation, issues of safety and efficacy, regulatory authority-approved labeling, product profile, the competitiveness of alternative products in the marketplace, the likely timing of the product's entry into the market, the patent and other proprietary position, the likelihood of approval and other relevant scientific, technical and commercial factors. The R&D Plans attached to this Agreement as of the Effective Date as APPENDIX 2 exemplify a level of diligence that meets the Commercially Reasonable Efforts standard required under this Agreement. Without limiting any of the foregoing, (A) Commercially Reasonable Efforts as it applies to Roche's Development or Commercialization of a Product hereunder includes the use of Commercially Reasonable Efforts to perform the Roche R&D Activities designated under the R&D Plans [***]; and (B) Commercially Reasonable Efforts as it applies to Ionis' Development of an Ionis Development Candidate hereunder includes the use of Commercially Reasonable Efforts to perform the Ionis R&D Activities designated under the R&D Plans in accordance with the timelines set forth therein. Roche [***].

"***Companion Diagnostic IP***" has the meaning set forth in Section 11.5.2 (License to Ionis for Companion Diagnostic Products).

"***Companion Diagnostic Product***" has the meaning set forth in Section 11.5.2 (License to Ionis for Companion Diagnostic Products).

"***Competitive Infringement***" has the meaning set forth in Section 8.6.1 (Duty to Notify of Competitive Infringement).

"***Compound***" means an Oligonucleotide that is designed to bind to (a) the RNA that encodes [***], or (b) the RNA that encodes [***], in each case ((a) and (b)) that are (1) discovered by Ionis prior to the Effective Date or by Ionis on its own or in collaboration with Roche in the performance of the applicable R&D Plan or (2) designated as a Compound according to Section 3.6 (Follow-On Ionis Development Candidates).

"***Compulsory Sublicense***" means a sublicense granted to a Third Party, through the order, decree or grant of a governmental authority having competent jurisdiction, authorizing such Third Party to manufacture, use, sale, offer for sale, import or export a Product in any country.

"***Compulsory Sublicensee***" means a Third Party that was granted a Compulsory Sublicense.

"***Confidential Information***" has the meaning set forth in Section 12.1 (Confidentiality; Exceptions). "*Confidential Information*" does not include information that:

(a) was in the lawful knowledge and possession of the Receiving Party or its Affiliates prior to the time it was disclosed to, or learned by, the Receiving Party or its Affiliates, or was otherwise developed independently by the Receiving Party or its Affiliates, as evidenced by written records kept in the ordinary course of business, or other documentary proof of actual use by the Receiving Party or its Affiliates;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party or its Affiliates;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the Receiving Party or its Affiliates in breach of this Agreement; or

(d) was disclosed to the Receiving Party or its Affiliates, other than under an obligation of confidentiality, by a Third Party who had no obligation to the Disclosing Party or its Affiliates not to disclose such information to others.

"***Control***" or "***Controlled***" means possession of the ability to grant a license or sublicense hereunder without violating the terms of any agreement with any Third Party; *provided*, *however*, that if a Party has a right to grant a license or sublicense, with respect to an item of intellectual property to the other Party only upon payment of compensation (including milestones or royalties) to a Third Party ("***Third Party Compensation***"), then the first Party will be deemed to have "*Control*" of the relevant item of intellectual property only if the other Party agrees to bear the cost of such Third Party Compensation. Notwithstanding anything to the contrary under this Agreement, with respect to any Third Party that becomes an Affiliate of a Party after the Effective Date (including a Third Party acquirer), no intellectual property of such Third Party will be included in the licenses granted hereunder by virtue of such Third Party becoming an Affiliate of such Party.

"***Costs***" means, with respect to particular activities performed, or to be performed, by Ionis, Ionis' time incurred in performing such activities, at the FTE Rate, and the out-of-pocket expenses incurred by or on behalf of Ionis in connection with the performance of such activities.

"***Cover***," "***Covered***" or "***Covering***" means, with respect to a patent, that the act of making, using or selling by an unauthorized Person would infringe a Valid Claim included in such patent, or in the case of a patent that is a patent application, would infringe a Valid Claim in such patent application if it were to issue as a patent.

"***Develop***," "***Developing***" or "***Development***" means with respect to a Product, any and all preclinical (i.e., IND-Enabling Toxicology Studies), clinical, or regulatory activity with respect to a Product to seek Approval (including the submission of all necessary filings with applicable Regulatory Authorities to support such preclinical and clinical activities and Approval), including human clinical trials conducted after Approval of a Product to seek Approval for additional indications for a Product.

"***Development Candidate Data Package***" means, with respect to a Compound, either (a) the data package Ionis presents to the JSC as the basis for deciding whether to designate such Compound an Ionis Development Candidate; *provided* such package meets the Success Criteria listed in APPENDIX 3.

"***Development Candidate Data Package Deficiency Notice***" has the meaning set forth in Section 3.1.3(a).

"***Disclosing Party***" has the meaning set forth in Section 12.1 (Confidentiality; Exceptions).

"***Discontinued Product***" means a Product that is the subject of a termination under this Agreement.

"***Effective Date***" has the meaning set forth in the Preamble of this Agreement.

"***EMA***" means the European Medicines Agency and any successor entity thereto.

"***European Union***" or "***EU***" means each and every country or territory that is officially part of the European Union.

"***Executives***" has the meaning set forth in Section 13.1.1 (Escalation).

"[***]" has the meaning set forth in Section 7.3.2(b) ([***]).

"[***]" has the meaning set forth in Section 7.3.1(b) ([***]).

"***FDA***" means the United States Food and Drug Administration and any successor entity thereto.

"***FDCA***" shall mean the United States Food, Drug and Cosmetics Act.

"***Field***" means all prophylactic or therapeutic uses for any indication in humans.

"***Finished Drug Product***" means any drug product containing API as an active ingredient in finished bulk form for the Development or Commercialization of a Product by a Party under this Agreement.

"***First Commercial Sale***" means, on a country-by-country basis, the first invoiced sale of a Product to a Third Party by Roche following the receipt of any Regulatory Approval (including pricing and reimbursement approvals) required for the sale of such Product, or if no such Regulatory Approval is required, the date of the first invoiced sale of a Product to a Third Party by Roche in such country.

"***Follow-On Ionis Development Candidate***" means a Compound comprising [***] that is designated as a Follow-On Ionis Development Candidate under either Section 3.6.1 (Follow-On Ionis Development Candidate [***]) or Section 3.6.2 (Follow-On Development Candidates [***]), as applicable, and that, in each case, is reasonably likely to be Covered by a composition of matter patent that is different from the composition of matter patent within the Patent Rights Covering another Compound directed to the same Target.

"***FTE***" means a total of [***] weeks or [***] hours per year of work on the Development of a Product carried out by employees of a Party having the appropriate relevant expertise to conduct such activities. For clarity, the FTE Rate and out-of-pocket costs must not include duplicative costs.

"***FTE Rate***" means the amount of $[***] per FTE, on a fully burdened cost basis. The FTE Rate will be increased each Calendar Year after [***] by the [***].

"***Fully Burdened Manufacturing Cost***" or "FBMC" means for the Manufacture of the Product or Ionis Development Candidate the following: [***].

"***Generic Product***" shall mean, with respect to a Product in a country, a pharmaceutical product (other than such Product) that (a) is sold by a Third Party other than a Sublicensee under license from Roche in such country, (b) is authorized for use in such country in one or more of the indications for which such Product has Regulatory Approval in such country, and (c) either (i) contains the same active pharmaceutical ingredient(s) as such Product or (ii) is a product approved by way of an abbreviated regulatory mechanism by the Regulatory Authority in such country that, in each case, meets the equivalency determination by the applicable Regulatory Authority (including a determination that the produce is "comparable," "interchangeable," "bioequivalent," "biosimilar," or other term of similar meaning, if applicable, with respect to such Product). A product shall not be considered to be a Generic Product if (x) Roche or any of its Affiliates or Sublicensees was involved in or authorized the development or commercialization of such product, (y) Roche or any of its Affiliates or Sublicensees has granted a license to such Third Party in respect of such product, or (z) such product is commercialized by any Person who obtained such product in a chain of distribution that included Roche or any of its Affiliates or Sublicensees.

"***Group Sublicensee***" means any individual, corporation, association or other business entity:

(i) to which Roche has granted a sublicense or license under any Licensed Technology or Roche Technology, as the case may be, in accordance with the terms of this Agreement;

(ii) that is not an Affiliate of Roche; and

(iii) that is consolidated within Roche's externally published audited financial statements,

(iv) excluding Chugai unless Roche explicitly includes Chugai as an Affiliate pursuant to the "*Affiliate*" definition.

"***Handoff***" has the meaning set forth in Section 3.1.5 (Ionis Development Candidate Handoff).

"***Handoff Data Package***" means, with respect to an Ionis Development Candidate, the pharmacology, toxicology, histology and pharmacokinetic data generated from the IND- Enabling Toxicology Studies under the R&D Plan for such Ionis Development Candidate.

"***Handoff Data Package Criteria***" means the criteria a Handoff Data Package must meet in order for Handoff to occur in accordance with Section 3.1.5 (Handoff), which criteria are set forth as of the Effective Date in APPENDIX 4.

"***Handoff Period***" has the meaning set forth in Section 2.1.

"***Huntington's Disease***" means the hereditary disorder caused by mutation associated with trinucleotide repeat expansion in the Huntingtin gene on chromosome 4p as defined in the ICD 11.

"***IND***" means an Investigational New Drug Application (as defined in the Food, Drug and Cosmetic Act, as amended) filed with the FDA or its foreign counterparts.

"***IND-Enabling Toxicology Studies***" means the pre-clinical toxicology studies conducted in compliance with current Good Laboratory Practice ("***cGLP***") which are required to file an IND, which will consist of one 13-week cGLP rodent toxicology study and one 5-week cGLP non- human primate toxicology study.

"***Indemnitee***" has the meaning set forth in Section 10.3 (Procedure).

"[***]" or "[***]" means [***].

"***Initiation***" or "***Initiate***" means, (i) with respect to any IND-Enabling Toxicology Study, dosing of the first animal subject in such IND-Enabling Toxicology Study, and (ii) with respect to any Clinical Study performed by Roche, its Affiliates or Sublicensees, the date the first patient is dosed with a Product in such Clinical Study.

"***Ionis***" has the meaning set forth in the Preamble of this Agreement.

"***Ionis Collaboration Know-How***" means Know-How discovered, developed, invented or created solely by or on behalf of Ionis or its Affiliate or a Third Party acting on their behalf in the performance of activities under this Agreement, that is necessary or useful to Develop, Manufacture or Commercialize a Product in the Field.

"***Ionis Collaboration Patents***" means Patent Rights invented solely by or on behalf of Ionis or its Affiliate or a Third Party acting on their behalf in the performance of activities under this Agreement, that are necessary or useful to Develop, Manufacture or Commercialize a Product in the Field. Ionis Collaboration Patents do not include the Ionis Product-Specific Patents.

"***Ionis Collaboration Technology***" means Ionis Collaboration Know-How and Ionis Collaboration Patents, and Ionis' interest in any Joint Collaboration Technology.

"***Ionis Core Technology Patents***" means all Patent Rights owned, used, developed by, or licensed to Ionis or its Affiliates, in each case to the extent Controlled by Ionis or its Affiliates on the Effective Date or at any time during the Agreement Term, claiming subject matter generally applicable to Oligonucleotides, other than Ionis Product-Specific Patents or Ionis Manufacturing and Analytical Patents. A representative list of Ionis Core Technology Patents as of the Effective Date is set forth on SCHEDULE 9.2.4(a) attached hereto.

"***Ionis Development Candidate***" means a Compound discovered by Ionis in performing the R&D Plan that is reasonably determined by the JSC as ready to start IND-Enabling Toxicology Studies in accordance with Section 3.1.3 (Ionis Development Candidate Designation; IND- Enabling Toxicology Study Costs).

"***Ionis' Fully Absorbed Cost of Goods***" means the costs incurred by Ionis as determined using the methodology set forth in SCHEDULE 3.4.1(b), fairly applied and as employed on a consistent basis throughout Ionis' operations.

"***Ionis Internal Oligonucleotide Safety Database***" has the meaning set forth in Section 6.3.2(a).

"***Ionis Know-How***" means any Know-How, including Ionis' interest in any Joint Collaboration Know-How, owned, used, developed by, or licensed to Ionis or its Affiliates, in each case to the extent Controlled by Ionis or its Affiliates on the Effective Date or at any time during the Agreement Term. Ionis Know-How does not include the Ionis Manufacturing and Analytical Know-How.

"***Ionis Manufacturing and Analytical Know-How***" means Know-How, including Ionis' interest in any Joint Collaboration Know-How, that relates to the synthesis or analysis of a Product regardless of sequence or chemical modification, owned, used, developed by, or licensed to Ionis or its Affiliates, in each case to the extent Controlled by Ionis or its Affiliates on the Effective Date or at any time during the Agreement Term. Ionis Manufacturing and Analytical Know-How does not include the Ionis Know-How.

"***Ionis Manufacturing and Analytical Patents***" means Patent Rights, including Ionis' interest in any Joint Collaboration Patents, that claim methods and materials used in the synthesis or analysis of a Product regardless of sequence or chemical modification, owned, used, developed by, or licensed to Ionis or its Affiliates, in each case to the extent Controlled by Ionis or its Affiliates on the Effective Date or at any time during the Agreement Term. A representative list of Ionis Manufacturing and Analytical Patents as of the Effective Date is set forth on SCHEDULE 9.2.4.(b) attached hereto. Ionis Manufacturing and Analytical Patents do not include the Ionis Product-Specific Patents or the Ionis Core Technology Patents.

"***Ionis Product-Specific Patents***" means Patent Rights Controlled by Ionis or any of its Affiliates on or after the Effective Date claiming (i) the specific composition of matter of an Ionis Development Candidate; (ii) methods of using an Ionis Development Candidate as a prophylactic or therapeutic; or (iii) the specific mechanism of action of an Ionis Development Candidate, in each case to the extent necessary to Develop, Manufacture or Commercialize an Ionis Development Candidate; *provided however*, Patent Rights Controlled by Ionis or any of its Affiliates that (y) include claims that are directed to subject matter applicable to Oligonucleotides in general, or (z) include an Oligonucleotide, the sequence of which targets both (1) the RNA that encodes [***] or [***] and (2) Oligonucleotides that do not target the RNA encoding [***] or [***], will not be considered Ionis Product-Specific Patents, and in the case of (y) and (z), such Patent Rights will be considered Ionis Core Technology Patents. A list of Ionis Product-Specific Patents as of the Effective Date is set forth on SCHEDULE 9.2.4(c) attached hereto.

"***Ionis R&D Activities***" means the research and/or pre-clinical activities for which Ionis is designated as responsible under an R&D Plan.

"[***]" has the meaning set forth in Section 7.4.3(e) ([***]).

"***Japan NDA***" or "***JNDA***" means the Japanese equivalent of an NDA filed with the Koseisho (i.e., the Japanese Ministry of Health and Welfare, or any successor agency thereto).

"***JMC***" has the meaning set forth in Section 3.3.2(a) (Establishment; Composition; Dissolution).

"***JNDA Approval***" means the Approval of a JNDA by the Koseisho (i.e., the Japanese Ministry of Health and Welfare, or any successor agency thereto) for the applicable Product in Japan.

"***Joint Patent Committee***" or "***JPC***" has the meaning set forth in Section 8.2.1 (Establishment).

"***Joint Collaboration Know-How***" means Know-How discovered, developed, invented or created jointly in the performance of activities under this Agreement by or on behalf of both Parties or their respective Affiliates or Third Parties acting on their behalf that is necessary or useful to Develop, Manufacture or Commercialize a Product in the Field.

"***Joint Collaboration Patents***" means any Patent Rights invented jointly in the performance of activities under this Agreement by or on behalf of both Parties or their respective Affiliates or Third Parties acting on their behalf that is necessary or useful to Develop, Manufacture or Commercialize a Product in the Field.

"***Joint Collaboration Technology***" means Joint Collaboration Know-How and Joint Collaboration Patents.

"***JSC***" has the meaning set forth in Section 3.3.1(a) (Establishment; Composition; Working Groups; Dissolution).

"[***] ***Communications***" means [***].

"***Key Regulatory Submissions***" means, with respect to a Product, (a) [***], (b) [***], (c) [***], (d) [***], and (e) [***].

"***Know-How***" means unpatented inventions, technical information, know-how and materials, including technology, data, compositions, formulas, biological materials, assays, reagents, constructs, compounds, discoveries, procedures, processes, practices, protocols, methods, techniques, results of experimentation or testing, knowledge, trade secrets, skill and experience.

"***Lead Party***" has the meaning set forth in Section 8.5.1 (Third-Party Claims Regarding Products).

"***Licensed CMO***" has the meaning set forth in Section 5.1.4(a)(ii).

"***Licensed Know-How***" means Ionis Manufacturing and Analytical Know-How, Ionis Know- How, Ionis Collaboration Know-How, and Ionis' interest in any Joint Collaboration Know- How. For clarity, Licensed Know-How does not include any Know-How covering formulation technology or delivery devices *unless* such Know-How is included in any Ionis Collaboration Know-How or Joint Collaboration Know-How.

"***Licensed Patents***" means the Ionis Product-Specific Patents, Ionis Core Technology Patents, Ionis Manufacturing and Analytical Patents, Ionis Collaboration Patents, and Ionis' interest in any Joint Collaboration Patents. For clarity, Licensed Patents do not include any Patent Rights claiming formulation technology or delivery devices *unless* such Patent Rights are included in any Ionis Collaboration Patents or Joint Collaboration Patents.

"***Licensed Technology***" means any and all Licensed Patents and Licensed Know-How, in each case to the extent necessary or useful to Develop, Manufacture or Commercialize a Product.

"***Losses***" has the meaning set forth in Section 10.1 (Indemnification by Roche).

"[***]" ([***]) means [***].

"***MAA***" means a marketing authorization application filed with the EMA after completion of Clinical Studies to obtain Approval for a Product under the centralized European filing procedure or, if the centralized EMA filing procedure is not used, filed using the applicable procedures in any European Union country.

"***MAA Approval***" means the Approval of an MAA by the EMA for a Product in any country in the EU.

"***Major Market***" means any of the following countries: the United States, the United Kingdom, Germany, France, Italy, Spain.

"***Manufacture***" or "***Manufactured***" or "***Manufacturing***" means any activity involved in or relating to the manufacturing, quality control testing (including in-process, release and stability testing), releasing or packaging, for pre-clinical and clinical purposes, of API or a Product in finished form.

"***Milestone Event***" means a milestone event listed in TABLE 1 of Section 7.3.1 (Development Milestones for [***]), TABLE 2 of Section 7.3.2 (Development Milestones for [***]), or TABLE 3 of Section 7.3.3 (Milestone Payments for First Achievement of Sales Milestone Event by an [***] Product).

"***NDA***" means a New Drug Application filed with the FDA after completion of Clinical Studies to obtain Approval for a Product in the United States.

"***NDA Approval***" means the Approval of an NDA by the FDA for a Product in the U.S.

"***Net Sales***" of a Product in a particular period will mean the amount calculated by subtracting from the Sales of such Product for such period: (A) a lump sum deduction of [***] of Sales under item (i) of the "*Sales*" definition in lieu of those deductions that are not accounted for on a Product-by-Product basis (e.g., freight, postage charges, transportation insurance, packing materials for dispatch of goods, custom duties); (B) uncollectible amounts accrued during such period based on a proportional allocation of the total bad debts accrued during such period; (C) credit card charges (including processing fees) accrued during such period on such Sales; and (D) government mandated fees and taxes and other government charges accrued during such period for such Product including, for example, any fees, taxes or other charges that become due in connection with any healthcare reform, change in government pricing or discounting schemes, or other action of a government or regulatory body; provided that the foregoing deductions under (A) to (D) were not already taken as a gross-to-net deduction in accordance with the then currently used International Financial Reporting Standards (IFRS) in the calculation of Sales of such Product for such period.

"***New Third Party Licenses***" has the meaning set forth in Section 9.3.2.

"***Non-Breaching Party***" means the Party that believes the Breaching Party is in material breach of this Agreement.

"***Non-Transferring Party***" has the meaning set forth in Section 13.4 (Assignment and Successors).

"***Oligonucleotide***" means an oligonucleotide compound, or analog or variant thereof, having [***] and is designed to inhibit expression of a gene target via the binding, partially or wholly, of such compound to the RNA transcript of such gene target. For clarity, [***].

"[***]" means [***].

"***Party***" or "***Parties***" means Roche and Ionis individually or collectively.

"***Patent Costs***" means the reasonable fees and expenses paid to outside legal counsel, and filing, maintenance and other reasonable out-of-pocket expenses paid to Third Parties, incurred in connection with the Prosecution and Maintenance of Patent Rights.

"***Patent Rights***" means (a) patents, patent applications and similar government-issued rights protecting inventions in any country or jurisdiction however denominated, (b) all priority applications, divisionals, continuations, substitutions, continuations-in-part of and similar applications claiming priority to any of the foregoing, and (c) all patents and similar government-issued rights protecting inventions issuing on any of the foregoing applications, together with all registrations, reissues, renewals, re-examinations, confirmations, supplementary protection certificates, and extensions of any of (a), (b) or (c).

"***Permitted Licenses***" means (1) licenses granted by Ionis before or after the Effective Date to any Third Party under the Ionis Core Technology Patents, the Ionis Manufacturing and Analytical Patents, or the Ionis Manufacturing and Analytical Know-How (but not under the Ionis Product-Specific Patents) to (a) use oligonucleotides (or supply oligonucleotides to end users) solely to conduct pre-clinical research, or (b) enable such Third Party to manufacture or formulate oligonucleotides, where Ionis does not assist such Third Party to identify, discover or make a Compound or Product; and (2) material transfer agreements with academic collaborators or non-profit institutions solely to conduct noncommercial research. A list of relevant Permitted Licenses as of the Effective Date is set forth on APPENDIX 5 attached hereto.

"***Person***" will mean any corporation, limited or general partnership, limited liability company, joint venture, trust, unincorporated association, governmental body, authority, bureau or agency, any other entity or body, or an individual.

"***Phase 1 Trial***" means the initial clinical testing of a Product in humans (first-in-humans study) in any country that is designed to satisfy the requirements of 21 C.F.R. § 312.21(a), as amended from time to time, or a foreign equivalent thereof.

"***Phase 2 Trial***" means, with respect to a Product, a human clinical study for which the primary endpoints include a determination of safety, dose ranges, or an indication of efficacy of such Product in patients being studied as described in 21 C.F.R. § 312.21(b), as amended from time to time, or a foreign equivalent thereof.

"***Phase 3 Trial***" means, with respect to a Product, a human clinical study that is prospectively designed, along with other Phase 3 Trials, to demonstrate statistically whether such Product is safe and efficacious for use in humans in the indication being investigated as described in 21 C.F.R. § 312.21(c), as amended from time to time, or a foreign equivalent thereof.

"***Phase 4 Trial***" means (i) any Clinical Study conducted to satisfy a requirement of a Regulatory Authority in order to maintain Approval, or (ii) any Clinical Study conducted after the first Approval in the same disease state for which a Product received Approval other than for purposes of obtaining Approval.

"***PII/Samples***" has the meaning set forth in Section 11.6.5(b).

"***Pivotal Trial***" means (a) a Phase 3 Trial, or (b) a human Clinical Study of a Product that satisfies the requirements of 21 C.F.R. § 312.21(c) and is a registration trial on a sufficient number of patients designed to establish statistically significant efficacy and safety of such Product for its target patient population, and to determine warnings, precautions and adverse reactions that are associated with such Product in the dosage range to be prescribed, for the purpose of enabling the preparation and submission of an application for an NDA, BLA, MAA or similar application for marketing approval to the competent Regulatory Authorities in a given country, as evidenced by (i) an agreement with or statement from the FDA on a Special Protocol Assessment or equivalent in another country, or (ii) other guidance or minutes issued by the FDA, for such registration trial or equivalent in another country, or (iii) Roche's public statements, with respect to each, where the results of such clinical trial are intended (if supportive) to be used to establish both safety and efficacy of such product in patients that are the subject of such trial and serve as the basis for obtaining initial or supplemental Approval in the United States of such Product.

"***Pre-Clinical Studies***" means *in vitro* and *in vivo* studies of a Product, not in humans, including those studies conducted in whole animals and other test systems, designed to determine the toxicity, bioavailability, and pharmacokinetics of a Product and whether a Product has a desired effect.

"[***]" has the meaning set forth in Section 4.1.1 ([***] Exclusivity Covenants Before Handoff).

"***Prior Agreements***" means the agreements listed on SCHEDULE 9.2.6 attached hereto.

"***Proceeding***" means an action, suit or proceeding.

"***Product***" means a product, including without limitation any Combination Product, containing an Ionis Development Candidate, a Follow-On Ionis Development Candidate or a Compound as an active pharmaceutical ingredient, regardless of its finished form, formulation or dosage. One Product may be distinguished from another Product by the Compound being a distinctive active pharmaceutical ingredient.

"***Program***" means, respectively, the research program to be carried out under the R&D Plan for (a) the Ionis Development Candidates for [***], or (b) the Ionis Development Candidates for [***].

"***Program Patents***" has the meaning set forth in Section 8.2.1 (Establishment).

"***Prosecution and Maintenance***" or "***Prosecute and Maintain***" means, with regard to a Patent Right, the preparing, filing, prosecuting and maintenance of such Patent Right, as well as handling re-examinations, reissues, and requests for patent term extensions with respect to such Patent Right, together with the conduct of interferences, the defense of oppositions and other similar proceedings with respect to the particular Patent Right. For clarification, "***Prosecution and Maintenance***" or "***Prosecute and Maintain***" will not include any other enforcement actions taken with respect to a Patent Right.

"***R&D Plan***" means, for each Target, the research and preclinical development plan attached hereto as APPENDIX 2 (as may be amended in accordance with this Agreement) to conduct certain research, pre-clinical, and clinical activities for the purpose of designating at least one Ionis Development Candidate directed against such Target and delivering a Handoff Data Package with respect to such Ionis Development Candidate.

"***Receiving Party***" has the meaning set forth in Section 12.1 (Confidentiality; Exceptions).

"***Regulatory Approval***" means any approvals, licenses, registrations or authorizations by a Regulatory Authority, necessary for the sale of a Product in the Field in a regulatory jurisdiction in the Territory.

"***Regulatory Authority***" shall mean any national, supranational (e.g., the European Commission, the Council of the European Union, the European Medicines Agency), regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity including the FDA, in each country involved in the granting of regulatory approval for the Product.

"***Related Compound***" means, with respect to an Ionis Development Candidate, all other Compounds Ionis' RMC considered as possible Ionis Development Candidates in connection
with its review of Compounds generated under the applicable R&D Plan to propose a potential Ionis Development Candidate.

"[***]" has the meaning set forth in Section 7.4.3(a)(i).

"[***]" has the meaning set forth in Section 7.4.3(a)(ii).

"***RMC***" has the meaning set forth in Section 3.1.3(a).

"***Roche***" has the meaning set forth in the Preamble of this Agreement.

"[***]" has the meaning set forth in Section 2.2.

"***Roche Collaboration Know-How***" means Know-How discovered, developed, invented or created solely by or on behalf of Roche or its Affiliate or a Third Party acting on their behalf in the performance of activities under this Agreement, that is necessary or useful to Develop, Manufacture or Commercialize a Product in the Field.

"***Roche Collaboration Patents***" means Patent Rights discovered, developed, invented or created solely by or on behalf of Roche or its Affiliate or a Third Party acting on their behalf in the performance of activities under this Agreement, that are necessary or useful to Develop, Manufacture or Commercialize a Product in the Field.

"***Roche Collaboration Technology***" means Roche Collaboration Know-How, Roche Collaboration Patents, Roche interest in any Joint Collaboration Technology.

"***Roche Know-How***" means any Know-How that (i) did not arise in connection with the performance of an R&D Plan, (ii) is owned, used, developed by, or licensed to Roche or its Affiliates, and (iii) is necessary or useful to Develop, Manufacture or Commercialize a Product in the Field, in each case to the extent Controlled by Roche or its Affiliates on the Effective Date or at any time during the Agreement Term.

"***Roche Patents***" means any Patent Rights that are owned, used, developed by, or licensed to Roche or its Affiliates, and are necessary or useful to Develop, Manufacture or Commercialize a Product in the Field, in each case to the extent Controlled by Roche or its Affiliates on the Effective Date or at any time during the Agreement Term. Roche Patents include the Roche Collaboration Patents and Roche's interest in any Joint Collaboration Patent.

"***Roche-Prosecuted Patents***" has the meaning set forth in Section 8.3.4(b).

"***Roche R&D Activities***" means the research, pre-clinical and/or clinical activities for which Roche is designated as responsible under an R&D Plan.

"***Roche Technology***" means Roche's interest in Roche Collaboration Technology, Roche Know-How, Roche Patents and any trademarks described in Section 5.1.7 (Trademarks for Products), owned, used, developed by, or licensed to Roche or its Affiliates that is necessary or useful to Develop, Manufacture or Commercialize a Product.

"***Royalty Term***" has the meaning set forth in Section 7.4.2 (Royalty Term).

"***Sales***" of a Product in a particular period will mean the sum of (i) and (ii):

(i) the amount stated in Roche sales line of its externally published audited financial statements with respect to such Product for such period (excluding sales to any Sublicensee that are used for research or Development or re-sold by such Sublicensee as sales under item (ii) below). This amount reflects the gross invoice price at which such Product was sold or otherwise disposed of (other than for use as clinical supplies or free samples) by Roche/Genentech, its Affiliates and Group Sublicensees to Third Parties (excluding sales to any Sublicensee that are used for research or Development or re-sold by such Sublicensee as sales under item (ii) below) in such period reduced by gross-to- net deductions, if not previously deducted from such invoiced amount, taken in accordance with the then currently used International Financial Reporting Standards (IFRS).

For clarity, any sales by a Compulsory Sublicensee are excluded from Sales (but sharing of Compulsory Sublicense compensation received by Roche or any of its Affiliates or Sublicensees will be subject to Section 7.3.3 (Milestone Payments for First Achievement of Sales Milestone Event by an [***] Product) and Section 8.6.4 (Share of Recoveries)).

By way of example, the gross-to-net deductions taken in accordance with International Financial Reporting Standards (IFRS) as of the Effective Date include the following:

(a) credits, reserves or allowances granted for (w) damaged, outdated, returned, rejected, withdrawn or recalled Product, (x) wastage replacement and short-shipments, (y) billing errors and (z) indigent patient and similar programs (e.g., price capitation);

(b) governmental price reductions and government mandated rebates;

(c) chargebacks, including those granted to wholesalers, buying groups and retailers;

(d) customer rebates, including cash sales incentives for prompt payment, cash and volume discounts; and

(e) taxes, duties and any other governmental charges or levies imposed upon or measured by the import, export, use, manufacture or sale of a Product (excluding income or franchise taxes).

For the purpose of clarity, sales by Roche/Genentech and its Affiliates to any Sublicensee and/or Group Sublicensee that are used for research or Development or re- sold by such Sublicensee or Group Sublicensee as sales under item (ii) below will be excluded from "*Sales*" calculated under this item (i).

(ii) Sublicensee (excluding Compulsory Sublicensee) sales amounts reported to Roche and its Affiliates in accordance with Sublicensee contractual terms and their then currently used accounting standards. For the purpose of clarity, any Sublicensee sales as reported to Roche in accordance with Compulsory Sublicense agreements will be excluded from the Sales amount.

"***Step-In Party***" has the meaning set forth in Section 8.5.1 (Third-Party Claims Regarding Products).

"***Sublicensee***" means a Third Party to whom a Party or its Affiliates or Sublicensees has granted a sublicense or license under any Licensed Technology or Roche Technology, as the case may be, licensed to such Party in accordance with the terms of this Agreement.

"***Submission***" has the meaning set forth in SCHEDULE 7.4.3(a)(ii).

"[***]" has the meaning set forth in Section 7.3.2(b) ([***]).

"[***]" has the meaning set forth in Section 7.3.1(b) ([***]).

"[***]" means either a [***] or a [***], as applicable.

"***Success Criteria***" means the success criteria for an Ionis Development Candidate for the applicable Program as set out in APPENDIX 3.

"***Target***" has the meaning set forth in Section 2.1.

"***Technology Transfer Plan***" has the meaning set forth in Section 3.5 (Technology Transfer Implementation).

"***Territory***" means worldwide.

"***Third Party***" means a Person or entity other than the Parties or their respective Affiliates.

"***Third Party Obligations***" means any financial and non-financial encumbrances, obligations, restrictions, or limitations imposed by an agreement between Ionis and a Third Party that relate to a Product, [***] or [***], including field or territory restrictions, covenants, milestone payments, diligence obligations, sublicense revenue, royalties, or other payments.

"***Transferring Party***" has the meaning set forth in Section 13.4 (Assignment and Successors).

"***Transition Activities***" has the meaning set forth in Section 11.5.9 (Transition Activities).

"***United States***" or "***U.S.***" means the fifty states of the United States of America and all of its territories and possessions and the District of Columbia.

"***Valid Claim***" means a claim (i) of any issued, unexpired United States or foreign Patent Right, which will not, in the country of issuance, have been donated to the public, disclaimed, nor held invalid or unenforceable by a court of competent jurisdiction in an unappealed or unappealable decision, or (ii) of any United States or foreign patent application within a Patent Right, which will not, in the country in question, have been cancelled, withdrawn, abandoned nor been pending for more than seven (7) years, not including in calculating such seven-year period of time in which such application is in interference or opposition or similar proceedings or time in which a decision of an examiner is being appealed. Notwithstanding the foregoing, on a country-by-country basis, a patent application pending for more than seven years will not be considered to have any Valid Claim for purposes of this Agreement unless and until a patent meeting the criteria set forth in clause (i) above with respect to such application issues.

APPENDIX 2

R&D Plan(s)

[***]

APPENDIX 3

Success Criteria

[***]

APPENDIX 4

Handoff Data Package Criteria

[***]

APPENDIX 5

Relevant Permitted Licenses as of the Effective Date

1. [***].
2. [***].
3. [***].
4. [***].
5. [***].
6. [***].
7. [***].
8. [***].
9. [***].
10. [***].
11. [***].
12. [***].
13. [***].
14. [***].

SCHEDULE 2.2

[***]

SCHEDULE 3.4.1(a)

Ionis' Fully Absorbed Cost of Goods

[***]

SCHEDULE 7.4.3(a)(ii)

[***]

SCHEDULE 9.2.4(a)

Representative Ionis Core Technology Patents

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]

SCHEDULE 9.2.4 (b)

Ionis Manufacturing and Analytical Patents

Ionis Docket Number	Country	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]

Ionis Docket Number	Country	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]

Ionis Docket Number	Country	Application/ Patent Number	Grant Date	Title
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]
[***]	[***]	[***]		[***]

SCHEDULE 9.2.4 (c)

Ionis Product-Specific Patents

Ionis File No.	Country	Status	Application No.	Filing Date	Title
[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]	[***]	[***]

SCHEDULE 9.2.6

Prior Agreements

1. [***].

SCHEDULE 11.5.9

Transition Activities

[***]

EXHIBIT 31.1

CERTIFICATION

I, Brett P. Monia, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ionis Pharmaceuticals, Inc.;

2. Based on my knowledge, this quarterly report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this quarterly report;

3. Based on my knowledge, the condensed consolidated financial statements, and other financial information included in this quarterly report, fairly present in all material respects the financial condition, condensed consolidated results of operations and condensed consolidated cash flows of the registrant as of, and for, the periods presented in this quarterly report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: November 2, 2023

/s/ BRETT P. MONIA
Brett P. Monia, Ph.D.
Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION

I, Elizabeth L. Hougen, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ionis Pharmaceuticals, Inc.;

2. Based on my knowledge, this quarterly report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this quarterly report;

3. Based on my knowledge, the condensed consolidated financial statements, and other financial information included in this quarterly report, fairly present in all material respects the financial condition, condensed consolidated results of operations and condensed consolidated cash flows of the registrant as of, and for, the periods presented in this quarterly report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: November 2, 2023

/s/ ELIZABETH L. HOUGEN
Elizabeth L. Hougen
Chief Financial Officer

Exhibit 32.1

CERTIFICATION

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Brett P. Monia, the Chief Executive Officer of Ionis Pharmaceuticals, Inc., (the "Company"), and Elizabeth L. Hougen, the Chief Financial Officer of the Company, each hereby certifies that, to the best of his or her knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended September 30, 2023, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition of the Company at the end of the period covered by the Periodic Report and the results of operations of the Company for the period covered by the Periodic Report.

Dated: November 2, 2023

/s/ BRETT P. MONIA
Brett P. Monia, Ph.D.
Chief Executive Officer

/s/ ELIZABETH L. HOUGEN
Elizabeth L. Hougen
Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to Ionis Pharmaceuticals, Inc. and will be retained by Ionis Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.