Ionis reports fourth quarter and full year 2022 financial results

February 22, 2023

Eplontersen NDA submitted to FDA; tofersen under regulatory review for marketing approval in U.S. and EU

Phase 3 data planned for eplontersen and olezarsen; robust late-stage pipeline expanding with two new Phase 3 programs

Ionis provides full year 2023 financial guidance

CARLSBAD, Calif., Feb. 22, 2023 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the "Company"), a genetic medicines company, today reported financial results for the fourth quarter and full year ended December 31, 2022. Financial results are summarized below:

	Three months ended December 31,		Year ended December 31,	
	2022	2021	2022	2021
	(amounts in millions)			
Total revenue	$152	$440	$587	$810
Operating expenses	$360	$219	$998	$840
Operating expenses on a non-GAAP basis	$335	$196	$898	$695
Net (loss) income	($52)	$225	($270)	($29)
Net (loss) income on a non-GAAP basis	($168)	$248	($311)	$116
Cash, cash equivalents and short-term investments[1]			$1,987	$2,115

[1] Balance at December 31, 2022 does not include $500 million received in January 2023 under royalty monetization transaction.

Financial Highlights

- 2022 revenue was in line with expectations, reflecting revenue from numerous diverse sources. The prior year fourth quarter and full year benefited from the $200 million earned from AstraZeneca to jointly develop and commercialize eplontersen
- 2022 operating expenses increased as planned compared to the prior year, reflecting investments in pipeline, technology and go-to-market activities for eplontersen, olezarsen and donidalorsen
- Further strengthened financial position with royalty monetization and sale and leaseback transactions worth up to $1.5 billion, including more than $700 million already received
- Initiated construction of a new manufacturing facility to support Ionis' goal to sustainably deliver genetic medicines to the market

Recent Late-Stage Pipeline Highlights

- Submitted the eplontersen NDA in the U.S. for patients with polyneuropathy caused by hereditary TTR amyloidosis
- FDA Advisory Committee meeting planned for March 22, 2023 to review Biogen's NDA for tofersen for patients with SOD1-ALS (PDUFA date of April 25, 2023); EMA accepted MAA for review
- FDA granted olezarsen Fast Track designation for the treatment of patients with FCS
- Reported positive Phase 2 data from the open label extension study of donidalorsen in patients with hereditary angioedema treated for one year, including new data showing clinically meaningful improvement in angioedema quality of life score; Phase 3 study expected to complete enrollment in 2023
- GSK advanced bepirovirsen into Phase 3 development in patients with chronic hepatitis B

Recent Additional Pipeline Highlights

- Biogen initiated a Phase 2 study of IONIS-MAPT$_{Rx}$ (BIIB080) in patients with mild cognitive impairment or mild dementia due to Alzheimer's disease
- Roche initiated a Phase 2 study of tominersen in patients with prodromal or early manifest Huntington's disease
- Biogen initiated a Phase 1 study of ION306 (BIIB115) for the treatment of spinal muscular atrophy with the potential for long interval dosing

Recent Technology Advancement Highlights

- Partnered with Metagenomi to add gene editing capabilities to Ionis' technology platform
- Advanced programs incorporating muscle LICA technology and MsPA backbone chemistry into preclinical development

"We made substantial progress in 2022, marked by important achievements, including the December submission of the eplontersen NDA for people with ATTRv-PN. We also delivered multiple positive data readouts, enabling us to advance and expand our rich late- and mid-stage pipeline. And we took important steps to expand and diversify our technology, including our Metagenomi collaboration to add DNA editing to our platform," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "As we start 2023, we are positioned to build upon our achievements by bringing our first near-term

commercial opportunities to the market. We look forward to reporting the 66-week results from the eplontersen NEURO-TTRansform study in the first half of this year. Importantly, we are prepared to co-commercialization eplontersen with our partner, AstraZeneca. We also look forward to Phase 3 data from olezarsen in FCS patients, positioning us for our first independent launch. With the talent and resources we have today, we anticipate a highly productive year that will enable us to drive increasing value for all stakeholders."

Fourth Quarter and Full Year 2022 Financial Results

Revenue

Ionis' revenue was comprised of the following:

	Three months ended December 31,		Year ended December 31,	
	2022	2021	2022	2021
Revenue:	(amounts in millions)			
Commercial revenue:				
SPINRAZA royalties	$67	$69	$242	$268
TEGSEDI and WAYLIVRA revenue, net	7	9	30	56
Licensing and royalty revenue	6	9	31	18
Total commercial revenue	80	87	303	342
Research and development revenue:				
Amortization from upfront payments	15	21	69	78
Milestone payments	14	40	74	88
License fees	-	290	37	291
Other services	22	2	27	11
Collaborative agreement revenue	51	353	207	468
Eplontersen joint development revenue	21	-	77	-
Total research and development revenue	72	353	284	468
Total revenue	$152	$440	$587	$810

Ionis' 2022 revenue continued to be derived from diverse sources, with just over half coming from commercial products and the balance from numerous partnered programs. SPINRAZA royalties, the largest contributor to the Company's commercial revenue, increased each quarter in 2022. Total SPINRAZA product sales increased six percent in the fourth quarter of 2022 compared to the prior quarter and also increased four percent compared to the same quarter in 2021. The increases were driven by stabilization in the U.S. and growth in Asian markets partially offset by competition in Europe. Total SPINRAZA product sales decreased six percent year-over-year due to foreign currency exchange and competition in Europe. TEGSEDI and WAYLIVRA revenue in 2022 reflected the shift to distribution fees.

R&D revenue for 2022 included $112 million from Biogen for advancing several neurology disease programs, $77 million from AstraZeneca for its share of the global Phase 3 development costs for eplontersen and $64 million from Roche for licensing and advancing IONIS-FB-L_{Rx}, among other partner payments. R&D revenue was higher in 2021 compared to 2022 primarily due to the $200 million Ionis earned in the fourth quarter of 2021 from AstraZeneca to jointly develop and commercialize eplontersen.

Operating Expenses

Ionis' operating expenses increased for the three months and year ended December 31, 2022 compared to the same periods in 2021, in line with expectations. For both periods, higher R&D expenses were driven by the increased number of Phase 3 studies the Company is conducting, which doubled from three to six studies in 2021, and the $80 million upfront payment for Ionis' collaboration with Metagenomi. SG&A expenses increased for the three months ended December 31, 2022 compared to the same period in 2021 driven by Ionis' go-to-market activities for eplontersen, olezarsen and donidalorsen. SG&A expenses were lower for 2022 compared to 2021 largely due to the substantial savings the Company achieved from integrating Akcea and restructuring the Company's commercial operations in 2021.

Gain on Sale of Property and Related Tax Impact

In October 2022, Ionis entered into a sale and leaseback transaction for several of its real estate assets. Under the agreement, Ionis received net proceeds of $200 million, with the potential to receive additional payments of up to $40 million plus funding to expand the Company's R&D campus. As a result, the Company recognized a $150 million gain on sale of property and $9 million in related income tax expense in the fourth quarter of 2022. In conjunction with the sale and leaseback transaction, the Company extinguished its mortgage debt for the related properties and recorded a new right of lease asset and liability on its balance sheet.

Balance Sheet

As of December 31, 2022, Ionis had cash, cash equivalents and short-term investments of $2.0 billion compared to $2.1 billion at December 31, 2021. Ionis' year-end cash balance does not include the $500 million the Company received from Royalty Pharma in January 2023. From December 31, 2021 to December 31, 2022, Ionis' debt obligations decreased by $50 million because the Company repaid its mortgage debt and Ionis' working capital decreased modestly driven by the Company's slightly lower cash and short-term investments balance.

2023 Financial Guidance

The Company's 2023 guidance reflects its ability to earn substantial revenue from its commercial portfolio and partnered programs. It also reflects the Company's commitment to investing in advancing its rich late-stage pipeline and preparing to commercialize its near-term commercial opportunities, eplontersen, olezarsen and donidalorsen, while maintaining a healthy balance sheet to continue investing for future growth.

Full Year 2023 Guidance

Revenue	>$575 million
Operating expenses on a non-GAAP basis	~$970 - $995 million
Net operating loss on a non-GAAP basis	<$425 million
Cash, cash equivalents and short-term investments	~$2.0 billion

"Our solid 2022 financial results reflected our ability to earn substantial revenues while investing in key programs with the potential to drive substantial future growth, including our near-term commercial opportunities," said Elizabeth L. Hougen, chief financial officer of Ionis. "Additionally, we recently bolstered our balance sheet with more than $700 million from our royalty monetization and sale and leaseback transactions. With approximately $2.5 billion in pro forma cash, we have the resources to continue to advance our innovative pipeline and achieve commercial readiness for eplontersen, olezarsen and donidalorsen."

Webcast

Management will host a conference call and webcast to discuss Ionis' fourth quarter and full year 2022 results at 11:30 a.m. Eastern time on Wednesday, February 22, 2022. Interested parties may access the webcast here. A webcast replay will be available for a limited time at the same address. To access the Company's fourth quarter and full year 2022 earnings slides click here.

About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been the leader in RNA-targeted therapy, pioneering new markets and changing the standards of care with its novel antisense technology. Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry leading cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming the leader in genetic medicine, utilizing a multi-platform approach to discover, develop and deliver life-transforming therapies.

To learn more about Ionis visit www.ionispharma.com or follow us on Twitter @ionispharma.

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business, financial guidance and the therapeutic and commercial potential of SPINRAZA (nusinersen), TEGSEDI (inotersen), WAYLIVRA (volanesorsen), eplontersen, olezarsen, donidalorsen, ION363, tofersen, pelacarsen, bepirovirsen, Ionis' technologies and Ionis' other products in development. Any statement describing Ionis' 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. Ionis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' annual report on Form 10-K for the year ended December 31, 2021, and most recent Form 10-Q, which are on file with the Securities and Exchange Commission. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Ionis," "Company," "we," "our" and "us" all refer to Ionis Pharmaceuticals and its subsidiaries.

Ionis Pharmaceuticals® is a registered trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutics® is a registered trademark of Akcea Therapeutics, Inc. TEGSEDI® is a registered trademark of Akcea Therapeutics, Inc. WAYLIVRA® is a registered trademark of Akcea Therapeutics, Inc. SPINRAZA® is a registered trademark of Biogen.

IONIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION
Condensed Consolidated Statements of Operations
(In Millions, Except Per Share Data)

	Three months ended, December 31,		Year ended December 31,	
	2022	2021	2022	2021
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$67	$69	$242	$268
TEGSEDI and WAYLIVRA revenue, net	7	9	30	56
Licensing and royalty revenue	6	9	31	18
Total commercial revenue	80	87	303	342
Research and development revenue:				
Collaborative agreement revenue	51	353	207	468
Eplontersen joint development revenue	21	-	77	-
Total research and development revenue	72	353	284	468
Total revenue	152	440	587	810
Expenses:				
Cost of sales	4	2	14	11
Research, development and patent	308	179	833	643

Selling, general and administrative	48	38	151	186
Total operating expenses	360	219	998	840
Income (loss) from operations	(208)	221	(411)	(30)
Other income (expense):				
Gain on sale of real estate assets	150	-	150	-
Other income, net	14	4	3	-
Income (loss) before income tax benefit (expense)	(44)	225	(258)	(30)
Income tax benefit (expense)	(8)	-	(12)	1
Net income (loss)	($52)	$225	($270)	($29)
Basic net income (loss) per share	($0.37)	$1.59	($1.90)	($0.20)
Diluted net income (loss) per share	($0.37)	$1.41	($1.90)	($0.20)
Shares used in computing basic net income (loss) per share	142	141	142	141
Shares used in computing diluted net income (loss) per share	142	160	142	141

IONIS PHARMACEUTICALS, INC.
Reconciliation of GAAP to Non-GAAP Basis:
Condensed Consolidated Operating Expenses, Income (Loss) From Operations, and Net Income (Loss)
(In Millions)

	Three months ended December 31,		Year ended December 31,	
	2022	2021	2022	2021
	(unaudited)			
As reported research, development and patent expenses according to GAAP	$308	$179	$833	$643
Excluding compensation expense related to equity awards	(19)	(16)	(74)	(88)
Excluding Akcea merger and restructured commercial operation costs*	-	(1)	-	(9)
Non-GAAP research, development and patent expenses	$289	$162	$759	$546
As reported selling, general and administrative expenses according to GAAP	$48	$38	$151	$186
Excluding compensation expense related to equity awards	(7)	(7)	(26)	(33)
Excluding Akcea merger and restructured commercial operation costs*	-	1	-	(15)
Non-GAAP selling, general and administrative expenses	$41	$32	$125	$138
As reported operating expenses according to GAAP	$360	$219	$998	$840
Excluding compensation expense related to equity awards	(25)	(23)	(100)	(121)
Excluding Akcea merger and restructured commercial operation costs*	-	-	-	(24)
Non-GAAP operating expenses	$335	$196	$898	$695
As reported income (loss) from operations according to GAAP	($208)	$221	($411)	($30)
Excluding compensation expense related to equity awards	(25)	(23)	(100)	(121)
Excluding Akcea merger and restructured commercial operation costs*	-	-	-	(24)
Non-GAAP income (loss) from operations	($183)	$244	($311)	$115
As reported net income (loss) according to GAAP	($52)	$225	($270)	($29)
Excluding compensation expense related to equity awards	(25)	(23)	(100)	(121)
Excluding Akcea merger and restructured commercial operation costs*	-	-	-	(24)
Excluding gain on sale of real estate assets**	150	-	150	-
Excluding income tax effect related to gain on sale of real estate assets	(9)	-	(9)	-
Non-GAAP net income (loss)	($168)	$248	($311)	$116

*In October 2020, Ionis completed a merger transaction with Akcea such that following the completion of the merger Akcea became a wholly owned subsidiary of Ionis. Additionally, in December 2020 and April 2021, Ionis restructured its European operations and its North American TEGSEDI operations, respectively, as a result of entering into distribution agreements with Sobi. The Company excluded the Akcea merger and restructured commercial operation costs from its non-GAAP amounts for the applicable periods.

**In October 2022, Ionis entered into a sale and leaseback transaction for several of its real estate assets. As a result, the Company recognized a $150 million gain on sale of real estate assets in the fourth quarter of 2022. The Company excluded the gain on sale of real estate assets and the related tax effect from its non-GAAP amounts for the applicable periods.

Reconciliation of GAAP to Non-GAAP Basis

As illustrated in the Selected Financial Information in this press release, non-GAAP operating expenses, non-GAAP income (loss) from operations, and non-GAAP net income (loss) were adjusted from GAAP to exclude compensation expense related to equity awards and the related tax effects. Compensation expense related to equity awards are non-cash. In 2022 Ionis' non-GAAP net loss excluded the gain on property related to the sale and leaseback transaction and the related tax effect. In 2021 all non-GAAP amounts also excluded expenses related to the Akcea merger and restructured commercial operations. Expenses related to the Akcea merger and restructured commercial operations included: severance costs, retention costs and other costs related to commercial operations. Ionis has regularly reported non-GAAP measures for operating results as non-GAAP results. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. Ionis reports these non-GAAP results to better enable financial statement users to assess and compare its historical performance and project its future operating results and cash flows. Further, the presentation of Ionis' non-GAAP results is consistent with how Ionis' management internally evaluates the performance of its operations.

IONIS PHARMACEUTICALS, INC.
Summary of the Financial Impacts of the Eplontersen Collaboration with AstraZeneca
For the Year Ended, December 31, 2022
(Unaudited)

Collaboration Activities	Financial Statement Line		Impact of Cost-Sharing Provisions on Ionis' Statement of Operations
Phase 3 Development: Ionis leads and conducts	Eplontersen Joint Development Revenue (R&D Revenue)	$77M	55% of Total Phase 3 development expenses, including internal+external costs & CMC costs, net of Ionis' share of AstraZeneca's Phase 3 development expenses
	Development Expenses (R&D Expenses)	$147M	100% of Ionis' Phase 3 development expenses

Ionis' financial results for the year ended December 31, 2022 reflected the cost-sharing provisions related to its 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 Ionis is leading and conducting the Phase 3 development program, Ionis is recognizing the 55 percent of cost-share funding AstraZeneca is responsible for, net of Ionis' share of AstraZeneca's development expenses, as R&D revenue in the same period Ionis incurs the related development expenses. For the year ended December 31, 2022 Ionis earned $77 million in joint development revenue under this collaboration.

Because AstraZeneca is responsible for the majority of the medical affairs and commercial costs in the U.S. and all costs associated with commercializing eplontersen outside the U.S., Ionis is recognizing cost-share funding it receives from AstraZeneca related to these activities as a reduction of its medical affairs (R&D expenses) and commercialization expenses (SG&A expenses). For the year ended December 31, 2022 Ionis recognized $2.0 million and $2.6 million of medical affairs expenses and commercialization expenses for eplontersen, respectively, net of cost-share funding from AstraZeneca. Ionis expects its medical affairs and commercialization expenses to increase as this collaboration progresses.

IONIS PHARMACEUTICALS, INC.
Condensed Consolidated Balance Sheets
(In Millions)

	December 31, 2022	December 31, 2021
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$1,987	$2,115
Contracts receivable	26	62
Other current assets	190	168
Property, plant and equipment, net	74	178
Right-of-use assets	182	18
Other assets	75	71
Total assets	$2,534	$2,612
Liabilities and stockholders' equity:		
Other current liabilities	$221	$143
Current portion of deferred contract revenue	91	98
0% convertible senior notes, net	622	619
0.125% convertible senior notes, net	545	542
Long-term lease liabilities	178	19
Long-term obligations, less current portion	16	67
Long-term deferred contract revenue	288	352
Total stockholders' equity	573	772
Total liabilities and stockholders' equity	$2,534	$2,612

2023 Key Value Driving Events(1)

Regulatory Actions		
Program	**Indication**	**Regulatory Action**
Tofersen	SOD1-ALS	NDA approval
		EU approval
Eplontersen (TTR)	ATTRv polyneuropathy	NDA approval
		OUS filings

Key Clinical Achievements		
Program	**Indication**	**Event**
Eplontersen (TTR)	ATTRv polyneuropathy	Phase 3 data (week 35 & 66)
Olezarsen	FCS	Phase 3 data
Eplontersen (TTR)	ATTR cardiomyopathy	Phase 3 full enrollment
Donidalorsen (PKK)	HAE	Phase 3 full enrollment

Phase 3 Initiations		
Program	**Indication**	**Timing**
Bepirovirsen (HBV)	Hepatitis B virus infection	H1:23 (achieved)
IONIS-FB-L_{Rx}	Immunoglobulin A nephropathy	H1:23

(1) Timing expectations based on current assumptions and subject to change.

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