Ionis reports third quarter 2024 financial results

November 6, 2024

WAINUA™ U.S. launch progressing well; approved in UK; positive CHMP opinion

Olezarsen FCS PDUFA December 19, 2024

Donidalorsen HAE PDUFA August 21, 2025; EU regulatory submission in process

On track to achieve 2024 P&L financial guidance; increased 2024 cash guidance

CARLSBAD, Calif., Nov. 6, 2024 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the "Company") today reported financial results for the third quarter of 2024.

"Today, we stand on the cusp of a new era for Ionis, with our first co-commercialization launch proceeding well with WAINUA, our first planned independent launch fast approaching and continued strong progress across our rich pipeline. With an upcoming December FDA action date, we are ready to independently bring olezarsen to people with familial chylomicronemia syndrome, a serious rare disease with no approved treatments in the U.S. We are similarly well positioned for our second independent launch for donidalorsen, which we believe could become a preferred treatment choice for people with hereditary angioedema, with an FDA action date of August 21, 2025," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "In parallel, we are making great progress across the rest of our rich Phase 3 pipeline. We expect Phase 3 results supporting olezarsen's second indication in severe hypertriglyceridemia and pelacarsen in Lp(a)-driven cardiovascular disease next year, as well as Phase 3 results supporting eplontersen's second indication in ATTR cardiomyopathy in the second half of 2026. We are also advancing our next wave of potentially transformational wholly owned medicines, including ION582 for Angelman syndrome, which we expect to enter Phase 3 development in the first half of next year following our positive end of Phase 2 discussion with the FDA. Our recent achievements, together with our advancing and expanding pipeline, position Ionis to deliver on our goal to bring a steady cadence of transformational medicines to people with serious diseases."

Third Quarter 2024 Summary Financial Results[(1)]:

	Three months ended September 30,		Nine months ended September 30,	
	2024	2023	2024	2023
	(amounts in millions)			
Total revenue	$134	$144	$479	$463
Operating expenses	$282	$287	$843	$811
Operating expenses on a non-GAAP basis	$250	$261	$749	$732
Loss from operations	($148)	($143)	($364)	($348)
Loss from operations on a non-GAAP basis	($116)	($117)	($270)	($269)

(1) Reconciliation of GAAP to non-GAAP basis contained later in this release.

Financial Highlights

- Revenue for the three and nine months ended September 30, 2024 decreased by 7% and increased by 3% compared to the same periods last year, respectively. Ionis continued to generate revenue from diverse sources, including a new source of royalty revenue with the launch of WAINUA in the U.S in the first quarter
- Operating expenses for the three and nine months ended September 30, 2024 increased as planned compared to the same periods last year, excluding certain one-time costs in 2023, reflecting continued investments in late-stage development, including WAINUA for ATTR cardiomyopathy (ATTR-CM) and olezarsen for severe hypertriglyceridemia (sHTG), and commercialization efforts for WAINUA, olezarsen and donidalorsen
- Reaffirmed 2024 P&L financial guidance, increased cash guidance to $2.2 billion reflecting proceeds from equity offering

Recent Marketed Medicines Highlights

- WAINUA (WAINZUA in Europe) for the treatment of adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTRv-PN) achieved multiple commercial and regulatory milestones:
    - Generated sales of $23 million and $44 million resulting in royalty revenue of $5 million and $10 million in the three and nine months ended September 30, 2024, respectively
    - Received positive Committee for Medicinal Products for Human Use (CHMP) opinion from European Medicines Agency (EMA) for the treatment of hereditary transthyretin-mediated amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy
    - Approved in UK by the Medicines and Healthcare products Regulatory Agency (MHRA) with an accelerated National Institute for Health and Care Excellence (NICE) recommendation; earning $30 million from AstraZeneca
    - Launch underway in Canada, following approval and reimbursement from Health Canada
- SPINRAZA® (nusinersen) for the treatment of spinal muscular atrophy (SMA) generated global sales of $381 million and $1.2 billion resulting in royalty revenue of $57 million and $152 million in the three and nine months ended September 30, 2024, respectively
    - Positive Phase 2/3 DEVOTE study data presented from higher dose nusinersen; global regulatory applications planned
- QALSODY® (tofersen) granted marketing approval in China for the treatment of SOD1-ALS

Recent Late-Stage Pipeline Highlights

- Olezarsen positioned to potentially treat two patient populations with urgent unmet need, familial chylomicronemia syndrome (FCS) and severe hypertriglyceridemia (sHTG):
    - NDA for patients with FCS under FDA Priority Review with a PDUFA date of December 19, 2024
    - Marketing authorization application (MAA) under regulatory review by the EMA
    - Ongoing pivotal development program for sHTG on track for data in H2:2025
- Donidalorsen Phase 3 data position it to potentially launch next year as the first RNA-targeted prophylactic treatment for people with hereditary angioedema (HAE):
    - FDA accepted the NDA for patients with HAE with a PDUFA date of August 21, 2025; Otsuka, Europe and Asia Pacific partner, preparing to submit MAA
    - Presented positive Phase 2 open label extension (OLE) study data in patients treated up to three years with every four weeks or every eight weeks dosing
- Zilganersen Phase 3 study fully enrolled as a potential treatment for Alexander disease; on track for data in 2025
    - Granted Fast Track designation by the FDA
- ION582 achieved important clinical and regulatory milestones enabling initiation of Phase 3 development in Angelman syndrome (AS) in H1:2025:
    - Presented positive Phase 1/2 data in patients with AS at Angelman Syndrome Foundation (ASF) Family Conference
    - Completed positive End-of-Phase 2 discussion with FDA, included alignment on Phase 3 design
- Reported positive data from the Phase 2 study of IONIS-FB-L_{Rx} in patients with immunoglobulin A nephropathy (IgAN); Roche continues to advance IONIS-FB-L_{Rx} in the Phase 3 IMAGINATION study

Recent Other Pipeline Updates

- Sapablursen for the treatment of polycythemia vera granted orphan drug designation by FDA; enrollment complete in Phase 2 IMPRSSION study with data expected in 2025
- IONIS-MAPT$_{Rx}$ (BIIB080) enrollment complete in Phase 2 CELIA study in patients with early Alzheimer's disease (AD); data expected in 2026
- Initiated first in human studies with multiple medicines from neurological disease pipeline:
    - Phase 1/2 Orbit study of ION356 (PLP1) in patients with Pelizaeus-Merzbacher disease (PMD)
    - Phase 1/2 HERO study of ION269 (APP), for the potential treatment of Alzheimer's disease (AD), which is initially being evaluated in patients with Down syndrome (DS) who have a genetic risk for developing AD
    - Phase 1/2 ATTUNE study of ION440 (MECP2) in patients with MECP2 duplication syndrome

Third Quarter 2024 Financial Results

"This year has been marked by strong delivery on our pipeline and business goals, which position Ionis to deliver on our vision of bringing a steady cadence of innovative medicines to patients in need. Fully realizing these significant opportunities requires

substantial investment. As a result, we recently executed an equity offering that extends our cash runway, enabling us to continue to invest in the numerous attractive opportunities ahead of us, including our near-term commercial launches with multi-billion-dollar revenue potential and our rich late and mid-stage pipeline," said Elizabeth L. Hougen, chief financial officer of Ionis. "Looking beyond this year, we will continue to invest in go-to-market preparations for our planned olezarsen and donidalorsen launches. Additionally, with our increased confidence in the potential of WAINUA and olezarsen to address broader patient populations, we plan to scale our capabilities in line with the significant potential of these important medicines. At the same time, we are investing in our next wave of medicines, including pre-commercialization activities and Phase 3 development for ION582 for Angelman syndrome and zilganersen for Alexander disease. We expect our investments today will position Ionis for sustainable growth for years to come."

Revenue

Ionis' revenue was comprised of the following:

	Three months ended September 30,		Nine months ended September 30,	
	2024	2023	2024	2023
Revenue:	(amounts in millions)			
Commercial revenue:				
SPINRAZA royalties	$57	$67	$152	$179
WAINUA royalties	5	-	10	-
Other commercial revenue:				
TEGSEDI and WAYLIVRA revenue, net	9	8	26	25
Licensing and other royalty revenue	5	9	19	26
Total commercial revenue	76	84	207	230
Research and development revenue:				
Amortization from upfront payments	28	18	105	47
Milestone payments	16	16	76	90
License fees	-	5	38	25
Other services	1	5	18	11
Collaborative agreement revenue	45	44	237	173
WAINUA joint development revenue	13	16	35	60
Total research and development revenue	58	60	272	233
Total revenue	$134	$144	$479	$463

Commercial revenue for the three and nine months ended September 30, 2024 included a new source of royalty revenue with the launch of WAINUA in the U.S. in late January 2024. Ionis' commercial revenue for the three and nine months ended September 30, 2024 and 2023 also included royalties from the net sales of QALSODY, which Biogen launched in the U.S. in the second quarter of 2023 and in the EU in the second quarter of 2024. SPINRAZA product sales for the three months ended September 30, 2024 compared to the same period last year increased slightly in the U.S. and decreased outside of the U.S. primarily due to an annual order from a single country that did not recur in 2024.

R&D revenue was relatively consistent for the three months ended September 30, 2024 compared to the same period last year. R&D revenue increased for the nine months ended September 30, 2024 compared to the same period last year primarily due to the amortization of upfront payments from the new collaborations with Roche and Novartis that Ionis entered into during the second half of last year. In addition, license fees increased year over year as a result of new collaborations Ionis entered into during the second quarter of 2024, including the expanded donidalorsen licensing agreement with Otsuka, which now includes the Asia-Pacific region in addition to Europe. These increases were partially offset by the decrease in WAINUA joint development revenue, which decreased as development activities relating to ATTRv-PN wound down with the launch of WAINUA for this indication.

Operating Expenses

Ionis' operating expenses, excluding one-time costs associated with a lease exit in the third quarter of 2023, increased for the three and nine months ended September 30, 2024 compared to the same periods in 2023, consistent with expectations. SG&A expenses increased year over year primarily due to the launch of WAINUA in the U.S. and launch preparation activities for olezarsen and donidalorsen, including establishing the field team for olezarsen in the second quarter of 2024. R&D expenses were essentially flat for the three and nine months ended September 30, 2024 compared to the same periods last year as several late-stage studies have ended.

Balance Sheet

As of September 30, 2024, Ionis' cash, cash equivalents and short-term investments increased to $2.5 billion compared to $2.3

billion at December 31, 2023. In September 2024, Ionis issued 11.5 million shares of its common stock at a public offering price of $43.50 per share that generated gross proceeds of $500 million, before deducting underwriting discounts and commissions and other offering expenses payable by Ionis. The Company plans to continue deploying its capital resources toward growth opportunities, and projects to end 2024 with $2.2 billion in cash, cash equivalents and short-term investments. Ionis' working capital also increased over the same period primarily due to the Company's higher cash and short-term investments balance. As a result of Ionis' advancing pipeline that has delivered several positive data readouts, Ionis expects to make increased investments in the years ahead with the goal to realize the value of these opportunities, with a focus on its wholly owned late-stage and next wave of innovative medicines.

Webcast

Management will host a conference call and webcast to discuss Ionis' third quarter 2024 results at 11:30 a.m. Eastern time on Wednesday, November 6, 2024. 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 third quarter 2024 earnings slides click here.

For more information about SPINRAZA and QALSODY, visit https://www.spinraza.com/ and https://www.qalsody.com/, respectively. QALSODY is approved under accelerated approval based on reduction in plasma neurofilament light chain (NfL) observed in patients treated with QALSODY. Continued approval may be contingent upon verification of clinical benefit in confirmatory trial(s).

INDICATION for WAINUA™ (eplontersen)
WAINUA injection, for subcutaneous use, 45 mg is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

IMPORTANT SAFETY INFORMATION for WAINUA™ (eplontersen)

WARNINGS AND PRECAUTIONS
Reduced Serum Vitamin A Levels and Recommended Supplementation WAINUA leads to a decrease in serum vitamin A levels. Supplement with recommended daily allowance of vitamin A. Refer patient to an ophthalmologist if ocular symptoms suggestive of vitamin A deficiency occur.

ADVERSE REACTIONS
Most common adverse reactions (≥9% in WAINUA-treated patients) were vitamin A decreased (15%) and vomiting (9%).

Please see link to U.S. Full Prescribing Information for WAINUA.

About Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has five marketed medicines and a leading pipeline in neurology, cardiology, and other areas of high patient need. As the pioneer in RNA-targeted medicines, Ionis continues to drive innovation in RNA therapies in addition to advancing new approaches in gene editing. A deep understanding of disease biology and industry-leading technology propels our work, coupled with a passion and urgency to deliver life-changing advances for patients. To learn more about Ionis, visit Ionis.com and follow us on X (Twitter), LinkedIn and Instagram.

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business, financial guidance and the therapeutic and commercial potential of our commercial medicines, additional medicines in development and technologies. 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. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. 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, 2023, 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 Investor Contact:
D. Wade Walke, Ph.DD.
IR@ionis.com
760-603-2331

Ionis Media Contact:
Hayley Soffer
media@ionis.com
760-603-4679

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

	Three months ended September 30,		Nine months ended September 30,	
	2024	2023	2024	2023
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$57	$67	$152	$179
WAINUA royalties	5	-	10	-
Other commercial revenue	14	17	45	51
Total commercial revenue	76	84	207	230
Research and development revenue:				
Collaborative agreement revenue	45	44	237	173
WAINUA joint development revenue	13	16	35	60
Total research and development revenue	58	60	272	233
Total revenue	134	144	479	463
Expenses:				
Cost of sales	1	2	7	6
Research, development and patent	220	215	656	643
Selling, general and administrative	61	70	180	162
Total operating expenses	282	287	843	811
Loss from operations	(148)	(143)	(364)	(348)
Other income (expense):				
Interest expense related to the sale of future royalties	(19)	(18)	(55)	(51)
Other income, net	23	20	66	68
Loss before income tax benefit (expense)	(144)	(141)	(353)	(331)
Income tax benefit (expense)	4	(6)	3	(26)
Net loss	($140)	($147)	($350)	($357)
Basic and diluted net loss per share	($0.95)	($1.03)	($2.38)	($2.50)
Shares used in computing basic and diluted net loss per share	149	143	147	143

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

	Three months ended September 30,		Nine months ended September 30,	
	2024	2023	2024	2023
	(unaudited)			
As reported research, development and patent expenses according to GAAP	$220	$215	$656	$643
Excluding compensation expense related to equity awards	(22)	(19)	(67)	(58)
Non-GAAP research, development and patent expenses	$198	$196	$589	$585
As reported selling, general and administrative expenses according to GAAP	$61	$70	$180	$162
Excluding compensation expense related to equity awards	(10)	(7)	(26)	(22)
Non-GAAP selling, general and administrative expenses	$51	$63	$154	$140
As reported operating expenses according to GAAP	$282	$287	$843	$811
Excluding compensation expense related to equity awards	(32)	(26)	(94)	(79)
Non-GAAP operating expenses	$250	$261	$749	$732
As reported loss from operations according to GAAP	($148)	($143)	($364)	($348)
Excluding compensation expense related to equity awards	(32)	(26)	(94)	(79)
Non-GAAP loss from operations	($116)	($117)	($270)	($269)
As reported net loss according to GAAP	($140)	($147)	($350)	($357)
Excluding compensation expense related to equity awards and related tax effects	(32)	(26)	(94)	(79)
Non-GAAP net loss	($108)	($121)	($256)	($278)

Reconciliation of GAAP to Non-GAAP Basis

As illustrated in the Selected Financial Information in this press release, non-GAAP operating expenses, non-GAAP loss from operations, and non-GAAP net 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. 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.
Condensed Consolidated Balance Sheets
(In Millions)

	September 30, 2024	December 31, 2023
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$2,483	$2,331
Contracts receivable	18	98
Other current assets	213	213
Property, plant and equipment, net	83	71
Right-of-use assets	164	172
Other assets	120	105
Total assets	$3,081	$2,990
Liabilities and stockholders' equity:		
Current portion of deferred contract revenue	$76	$151
0.125% convertible senior notes, net – short-term	44	44

Other current liabilities	184	253
1.75% convertible senior notes, net	564	562
0% convertible senior notes, net	628	625
Liability related to sale of future royalties, net	538	514
Long-term lease liabilities	168	171
Long-term obligations, less current portion	43	42
Long-term deferred contract revenue	174	241
Total stockholders' equity	662	387
Total liabilities and stockholders' equity	$3,081	$2,990

Key 2024 Value Driving Events[(1)]

New Product Launches		
Program	**Indication**	**Achieved**
WAINUA	ATTRv-PN	•
Olezarsen	FCS	
QALSODY (EU)	SOD1-ALS	•

Regulatory Actions			
Program	**Indication**	**Regulatory Action**	**Achieved**
Eplontersen	ATTRv-PN	Additional OUS filings	•
		EMA approval decision	
		Additional OUS approval decision(s)	•
Olezarsen	FCS	FDA approval decision	
		NDA filing	•
		EU filing	•
		Canada filing	
Donidalorsen	HAE	NDA filing	•
QALSODY	SOD1-ALS	EMA approval decision	•
		China approval	•

Key Phase 3 Clinical Data Events			
Program	**Indication**	**Event**	**Achieved**
Olezarsen	FCS	Balance study full data	•
Donidalorsen	HAE	OASIS-HAE topline data	•
Donidalorsen	HAE	OASIS-HAE full data	•
Donidalorsen	HAE	OASIS-Plus: OLE + Switch data	•
Nusinersen	SMA	DEVOTE study data (higher dose)	•

Key Phase 2 Clinical Data Events			
Program	**Indication**	**Event**	**Achieved**
Donidalorsen	HAE	3-year Phase 2 OLE data	•
IONIS-FB-L_{Rx}	IgAN	Phase 2 data	•
IONIS-FB-L_{Rx}	GA	GOLDEN study data	--
ION224 (DGAT2)	NASH	Phase 2 data	•
ION582 (UBE3A)	Angelman syndrome	HALOS study data	•
ION541 (ATXN2)	ALS	ALSpire study data	--
Sapablursen (TMPRSS6)	Polycythemia vera	IMPRSSION study full enrollment	•
IONIS-MAPT$_{Rx}$ (Tau)	Alzheimer's disease	CELIA study full enrollment	•

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

• Milestone achieved

-- Milestone achieved, however program discontinued

View original content to download multimedia:https://www.prnewswire.com/news-releases/ionis-reports-third-quarter-2024-financial-results-302297131.html

SOURCE Ionis Pharmaceuticals, Inc.