



Ionis reports fourth quarter and full year 2023 financial results

February 21, 2024

WAINUA™ approved with launch underway; on track for EU and Canada approval decisions this year

Positive Phase 3 olezarsen and donidalorsen data, preparing regulatory submissions for FCS and HAE, respectively

Olezarsen granted Breakthrough Therapy designation by the FDA for FCS

Ionis provides full year 2024 financial guidance

CARLSBAD, Calif., Feb. 21, 2024 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the "Company"), today reported financial results for the fourth quarter and full year ended December 31, 2023.

"This past year included many remarkable achievements as we continued to advance our vision to bring better futures to people with serious diseases. Ionis achieved two FDA approvals, delivered three positive Phase 3 data readouts, expanded our rich Phase 3 pipeline to nine medicines and advanced our next wave of wholly owned medicines as well as our technology," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "In 2024, we anticipate building on our success with important catalysts and continued value creation. The WAINUA U.S. launch is underway for patients with hereditary ATTR polyneuropathy, and we expect additional approvals in other countries this year. We plan to present positive Phase 3 data for olezarsen in familial chylomicronemia syndrome and donidalorsen in hereditary angioedema, positioning Ionis to independently launch these two medicines. We also anticipate additional readouts from multiple mid-stage programs that, if positive, would advance into Phase 3 development, further strengthening our ability to deliver a steady cadence of potentially transformational medicines for years to come."

Fourth Quarter and Full Year 2023 Summary Financial Results⁽¹⁾:

	Three months ended		Year ended	
	December 31, 2023	December 31, 2022	December 31, 2023	December 31, 2022
	(amounts in millions)			
Total revenue	\$325	\$152	\$788	\$587
Operating expenses	\$331	\$360	\$1,141	\$998
Operating expenses on a non-GAAP basis	\$305	\$335	\$1,035	\$898
Loss from operations	(\$6)	(\$208)	(\$353)	(\$411)
Income (Loss) from operations on a non-GAAP basis	\$20	(\$183)	(\$247)	(\$311)

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

Financial Highlights

- Revenue more than doubled for the fourth quarter of 2023 compared to the same period in the prior year and increased 34% for the full year, driven by the successful progression of Ionis' pipeline and technology platform
- Operating expenses increased compared to the prior year, primarily due to strategic investments to bring eplontersen, olezarsen and donidalorsen to patients
- 2023 operating loss significantly improved over prior year due to substantial revenue earned during the year
- Cash and short-term investments of \$2.3 billion as of December 31, 2023 enables continued investments to drive increasing value, including supporting our potential upcoming launches

Recent Marketed Medicines Highlights

- WAINUA approved in the U.S., resulting in a \$50 million milestone payment from AstraZeneca; launch underway for treatment of adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTRv-PN)
- SPINRAZA continued to be the global market leader for the treatment of spinal muscular atrophy (SMA) with global sales of \$1.7 billion in 2023

Recent Late-Stage Pipeline Highlights

- Eplontersen granted Fast Track designation by the FDA for the treatment of patients with ATTR cardiomyopathy

(ATTR-CM)

- Olezarsen granted Breakthrough Therapy designation by the FDA for the treatment of patients with familial chylomicronemia syndrome (FCS)
- Olezarsen granted orphan drug designation by the FDA for the treatment of patients with FCS
- Achieved multiple milestones with donidalorsen for the treatment of patients with hereditary angioedema (HAE):
 - Reported positive topline data from the Phase 3 OASIS-HAE study in patients treated every four weeks or every eight weeks; preparing to submit NDA
 - Licensed European donidalorsen commercialization rights to Otsuka; Otsuka preparing to submit MAA
 - Donidalorsen granted orphan drug designation by EMA
 - Reported positive Phase 2 data from the open label extension study in patients with HAE treated for two years
- Bepirovirsen granted fast track designation by the FDA for the treatment of patients with chronic hepatitis B (CHB)

Recent Other Pipeline Highlights

- Achieved multiple milestones with ION582 (BIIB121) for the treatment of patients with Angelman syndrome:
 - Completed enrollment in the Phase 1/2 HALOS study in patients with Angelman syndrome; on track for data readout in mid-2024
 - Presented positive clinical update from ongoing HALOS study at the FAST (Foundation for Angelman Syndrome Therapeutics) Summit
 - Extended the long-term extension portion of HALOS study
- Sapablursen and ION356 granted fast track designation by the FDA for the treatment of patients with polycythemia vera (PV) and Pelizaeus-Merzbacher disease (PMD), respectively
- Initiated the Phase 1/2 PrProfile study of ION717 in patients with Prion disease
- AstraZeneca licensed ION826 for the treatment of heart failure, resulting in a \$36 million payment from AstraZeneca

Recent Technology Advancement Highlights

- Licensed Vect-Horus' blood-brain barrier crossing technology for the development of RNA-targeted neurological disease medicines

Fourth Quarter, Full Year 2023 Financial Results and 2024 Financial Guidance

"In 2023, we earned substantial revenues due to continued success with our pipeline and technology. As a result, we exceeded our 2023 revenue guidance, which drove a smaller than anticipated operating loss," said Elizabeth L. Hougen, chief financial officer of Ionis. "In 2024, with WAINUA's launch for ATTRv-PN underway, we are adding a new stream of royalty revenue to our substantial and sustained revenues. We will continue to deploy our capital resources toward growth opportunities that can enable Ionis to unlock next-level value. This includes continuing to make significant investments in near-term commercial opportunities, the expansion of our wholly owned pipeline, and advancing our technology, all of which should empower future growth."

Revenue

Ionis' revenue was comprised of the following:

	Three months ended		Year ended	
	December 31,		December 31,	
	2023	2022	2023	2022
Revenue:	(amounts in millions)			
Commercial revenue:				
SPINRAZA royalties	\$62	\$67	\$240	\$242
Other commercial revenue:				
TEGSEDI and WAYLIVRA revenue, net	9	7	35	30
Licensing and royalty revenue	8	6	34	31
Total commercial revenue	79	80	309	303
Research and development revenue:				
Amortization from upfront payments	76	15	125	69
Milestone payments	11	14	101	74
License fees	92	-	117	37
Other services	-	22	10	27
Collaborative agreement revenue	179	51	353	207
WAINUA joint development revenue	67	21	126	77
Total research and development revenue	246	72	479	284
Total revenue	\$325	\$152	\$788	\$587

Commercial revenues in 2023 were comparable to 2022. Commercial revenue for 2023 included \$240 million from SPINRAZA royalties, which was comparable to 2022. Ionis' commercial revenue in 2023 also included royalties from QALSODY U.S. product sales.

R&D revenue significantly increased in 2023 compared to 2022 primarily due to continued success with Ionis' pipeline and technology. As a result, Ionis earned significant partner payments, including \$50 million from AstraZeneca for the FDA approval of WAINUA for ATTRv-PN in the U.S., \$36 million from AstraZeneca for licensing ION826 and payments from Ionis' new collaborations with Otsuka, Roche and Novartis.

Operating Expenses

Ionis' operating expenses increased for the year ended December 31, 2023 compared to 2022 primarily due to certain one-time costs, including a non-cash charge associated with a lease exit and the license fee Ionis paid to Vect-Horus. As Ionis advanced its robust pipeline, study costs increased compared to the same periods in 2022 as many of the Company's Phase 3 studies are either fully enrolled or approaching full enrollment, resulting in higher R&D expenses year over year. R&D expenses for the fourth quarter of 2023 were lower compared to the fourth quarter of 2022, primarily due to the \$80 million upfront payment Ionis paid to Metagenomi in 2022. Ionis' SG&A expenses increased year over year primarily due to launch preparation activities for WAINUA, olezarsen and donidalorsen.

Balance Sheet

As of December 31, 2023, Ionis' cash, cash equivalents and short-term investments increased to \$2.3 billion compared to \$2.0 billion at December 31, 2022 primarily due to the \$500 million Ionis received from Royalty Pharma in January 2023 and significant partner payments throughout 2023. Ionis' working capital also increased over the same period primarily due to the Company's higher cash and short-term investments balance. In 2023, the Company recorded a long-term liability for future royalties due to Royalty Pharma. In June 2023, Ionis issued \$575 million of senior convertible notes due in June 2028 with an interest rate of 1.75%. The Company used the majority of the proceeds to repurchase \$504 million of its 0.125% convertible notes.

2024 Financial Guidance

The Company's 2024 guidance reflects its plan to deploy its capital resources toward growth opportunities, including continued investments in its near-term commercial opportunities, expanding its wholly owned pipeline and advancing its technology platform. Additionally, the Company expects to continue earning substantial revenue from its commercial portfolio and partnered programs.

Full Year 2024 Guidance

Revenue	>\$575 million
Operating loss on a non-GAAP basis	<\$475 million
Cash, cash equivalents and short-term investments	~\$1.7 billion

Webcast

Management will host a conference call and webcast to discuss Ionis' fourth quarter and full year 2023 results at 11:30 a.m. Eastern time on Wednesday, February 21, 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 fourth quarter and full year 2023 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 ($\geq 9\%$ 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 ionispharma.com and follow us on X (Twitter) and LinkedIn.

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, 2022, 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. QALSODY[™] is a trademark of Biogen. SPINRAZA[®] is a registered trademark of Biogen. WAINUA[™] is a registered trademark of the AstraZeneca group of companies.

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,	
	2023	2022	2023	2022
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$62	\$67	\$240	\$242
Other commercial revenue	17	13	69	61
Total commercial revenue	79	80	309	303
Research and development revenue:				
Collaborative agreement revenue	179	51	353	207
WAINUA joint development revenue	67	21	126	77
Total research and development revenue	246	72	479	284
Total revenue	325	152	788	587
Expenses:				
Cost of sales	3	4	9	14
Research, development and patent	257	308	900	833
Selling, general and administrative	71	48	232	151
Total operating expenses	331	360	1,141	998
Loss from operations	(6)	(208)	(353)	(411)
Other income (expense):				
Interest expense related to the sale of future royalties	(18)	-	(69)	-
Gain on sale of real estate assets	-	150	-	150
Other income (expense), net	21	14	88	3
Loss before income tax expense	(3)	(44)	(334)	(258)
Income tax expense	(6)	(8)	(32)	(12)
Net loss	(\$9)	(\$52)	(\$366)	(\$270)
Basic and diluted net loss per share	(\$0.06)	(\$0.37)	(\$2.56)	(\$1.90)
Shares used in computing basic and diluted net loss per share	144	142	143	142

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,	
	2023	2022	2023	2022
	(unaudited)			
As reported research, development and patent expenses according to GAAP	\$257	\$308	\$900	\$833

Excluding compensation expense related to equity awards	(20)	(19)	(78)	(74)
Non-GAAP research, development and patent expenses	<u>\$237</u>	<u>\$289</u>	<u>\$822</u>	<u>\$759</u>
As reported selling, general and administrative expenses according to GAAP	\$71	\$48	\$232	\$151
Excluding compensation expense related to equity awards	(6)	(7)	(27)	(26)
Non-GAAP selling, general and administrative expenses	<u>\$65</u>	<u>\$41</u>	<u>\$205</u>	<u>\$125</u>
As reported operating expenses according to GAAP	\$331	\$360	\$1,141	\$998
Excluding compensation expense related to equity awards	(26)	(25)	(106)	(100)
Non-GAAP operating expenses	<u>\$305</u>	<u>\$335</u>	<u>\$1,035</u>	<u>\$898</u>
As reported loss from operations according to GAAP	(\$6)	(\$208)	(\$353)	(\$411)
Excluding compensation expense related to equity awards	(26)	(25)	(106)	(100)
Non-GAAP income (loss) from operations	<u>\$20</u>	<u>(\$183)</u>	<u>(\$247)</u>	<u>(\$311)</u>
As reported net loss according to GAAP	(\$9)	(\$52)	(\$366)	(\$270)
Excluding compensation expense related to equity awards and related tax effects	(26)	(25)	(106)	(100)
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)	<u>\$17</u>	<u>(\$168)</u>	<u>(\$260)</u>	<u>(\$311)</u>

*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 real estate assets related to the sale and leaseback transaction and the related tax effects. 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)

	December 31, 2023	December 31, 2022
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	\$2,331	\$1,987
Contracts receivable	98	26
Other current assets	213	190
Property, plant and equipment, net	71	74
Right-of-use assets	172	182
Other assets	105	75
Total assets	<u>\$2,990</u>	<u>\$2,534</u>
Liabilities and stockholders' equity:		
Current portion of deferred contract revenue	\$151	\$91
0.125% convertible senior notes, net – short-term	44	-
Other current liabilities	253	221
1.75% convertible senior notes, net	562	-
0% convertible senior notes, net	625	622
0.125% convertible senior notes, net – long-term	-	545
Liability related to sale of future royalties, net	514	-
Long-term lease liabilities	171	178
Long-term obligations, less current portion	42	16
Long-term deferred contract revenue	241	288
Total stockholders' equity	<u>387</u>	<u>573</u>

Total liabilities and stockholders' equity \$2,990 \$2,534

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	NDA filing	
		FDA approval decision	
		EU filing	
		Canada filing	
Donidalorsen	HAE	NDA filing	
QALSODY	SOD1-ALS	EMA approval decision	

Key Phase 3 Clinical Data Events			
Program	Indication	Event	Achieved
Donidalorsen	HAE	OASIS-HAE topline data	•
Donidalorsen	HAE	OASIS-HAE full data	
Donidalorsen	HAE	OASIS-Plus: OLE + Switch data	
Olezarsen	FCS	Balance study full data	

Key Phase 2 Clinical Data Events			
Program	Indication	Event	Achieved
Donidalorsen	HAE	3-year 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	

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

 View original content to download multimedia: <https://www.prnewswire.com/news-releases/ionis-reports-fourth-quarter-and-full-year-2023-financial-results-302066729.html>

SOURCE Ionis Pharmaceuticals, Inc.

Ionis Investor Contact: D. Wade Walke, Ph.D., info@ionisph.com, 760-603-2331; Ionis Media Contact: Hayley Soffer, CorporateCommunications@ionisph.com, 760-603-4679