SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

FORM 8-K

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

Date of report (Date of earliest event reported): February 22, 2023

IONIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125

(Commission File No.)

33-0336973 (IRS Employer Identification No.)

2855 Gazelle Court Carlsbad, CA 92010 (Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: (760) 931-9200

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

□ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

D Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

□ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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 is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (Section 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (Section 240.12b-2 of this chapter).

Emerging growth company \Box

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.

Item 2.02 Results of Operations and Financial Condition.

On February 22, 2023, Ionis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter and fiscal year ended December 31, 2022. In addition to disclosing results that are determined in accordance with Generally Accepted Accounting Principles ("GAAP"), the Company also discloses pro forma or non-GAAP results of operations, which are adjusted from GAAP to exclude non-cash compensation expense related to equity awards and the related tax effects. In addition, in 2022, the Company's non-GAAP net loss excluded the gain on property related to the Company's sale leaseback transaction and the related tax effects. In 2021, all non-GAAP manunts excluded expenses related to the Company's merger transaction with Akcea Therapeutics, Inc. and expenses related to the Company's restructured commercial operations. The Company is presenting pro forma information with such exclusions because the Company believes it is useful for investors in assessing the company's operations, 3-8216 and 34-47583.

The information in this Current Report on Form 8-K and the Exhibit attached hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "*Exchange Act*") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, regardless of any general incorporation language in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit No.</u>	Description
<u>99.1</u>	Press Release dated February 22, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

IONIS PHARMACEUTICALS, INC.

Dated: February 22, 2023

By: /s/ Patrick R. O'Neil Раткиск R. O'Neil Executive Vice President, Chief Legal Officer and General Counsel



Ionis reports fourth quarter and full year 2022 financial results 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., February 22, 2023 – 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 n end Decemb	ed			Year o Decem	ended ber 31,		
	 2022		2021	20)22		2021	
			(amounts in	n 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 i	n millio	ons)		
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 lonis' business, financial guidance and the therapeutic and commercial potential of SPINRAZA (nusinersen), TEGSEDI (inotersen), WAYLIVRA (volanesorsen), epleatersen, bepirovirsen, lonis' technologies and lonis' other products in development. Any statement describing lonis' 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. These and factors currently known by Ionis. As a result, you are cautioned not to rely on these forward-looking statements. These and other documents are variable 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. WAYLIVRA[®] is a registered trademark of Akcea Therapeutics, Inc. SPINRAZA[®] is a registered trademark of Biogen.

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

		Three mon Decem 2022	ber 31,	021		ended iber 31,	2021
		(unau	dited)				
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)	. <u></u>		 (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	<u></u>	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 r end Decem	led			Year of Decem		
	2	022		2021		2022		2021
				(unau	dited)			
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	S	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	s	(208)	\$	221	\$	(411)	S	(30)
Excluding compensation expense related to equity awards	Ŷ	(25)	Ψ	(23)	Ψ	(100)	Ŷ	(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	S	(52)	\$	225	\$	(270)	s	(29)
Excluding compensation expense related to equity awards	ψ	(25)	Ψ	(23)	Ψ	(100)	Ψ	(121)
Excluding Akcea merger and restructured commercial operation costs*		(25)		(25)		(100)		(121)
Excluding gain on sale of real estate assets**		150		-		150		(2-1)
Excluding income tax effect related to gain on sale of real estate assets		(9)		-		(9)		-
Non-GAAP net income (loss)	-	(168)	-	248	*	(311)	0	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 Epiontersen 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: onis 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				
onis reads and conducts	Development Expenses (R&D Expenses)	\$147M	100% of Ionis' Phase 3 development expenses				

Ph Ior

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 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 (unaudited)			2021 cember 31,
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			
Tofarran	SOD1-ALS	NDA approval			
Tofersen	SODI-ALS	EU approval			
Enlantarian (TTD)	ATTDy polynouropathy	NDA approval			
Eplontersen (TTR)	ATTRv polyneuropathy	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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