

Ionis reports third quarter financial results

November 9, 2022

Advanced key priorities: initiated manufacturing infrastructure project to support growth

Increased 2022 cash and investments guidance

CARLSBAD, Calif., Nov. 9, 2022 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the "Company") today reported financial results for the third quarter of 2022. Financial results are summarized below:

	Three months ended		Nine months ended	
	September 30,	September 30,	September 30,	September 30,
	2022	2021	2022	2021
	(amounts in millions)			
Total revenue	\$160	\$133	\$435	\$370
Operating expenses	\$219	\$219	\$637	\$621
Operating expenses on a non-GAAP basis	\$195	\$185	\$562	\$499
Net loss	(\$47)	(\$82)	(\$217)	(\$253)
Net loss on a non-GAAP basis	(\$23)	(\$48)	(\$142)	(\$131)

Financial Highlights

- Revenue increased 20% for the third quarter of 2022 and 18% on a year-to-date basis compared to the same periods last year driven by significant partner payments earned across multiple programs
- Non-GAAP operating expenses increased 5% for the third quarter of 2022 and 13% on a year-to-date basis compared to the same periods last year driven by advancing Phase 3 pipeline
- Entered into a long-term lease in October 2022 to construct a new manufacturing facility supporting continued growth
- Entered into a sale-leaseback transaction in October 2022 for several real estate assets, generating net proceeds of \$240 million plus full funding to expand R&D campus
- Reaffirmed 2022 P&L guidance; increased cash and investments guidance to approximately \$2.0 billion

Late-Stage Pipeline Highlights

- Presented positive data from the Phase 3 NEURO-TTRansform study of eplontersen in patients with polyneuropathy caused by hereditary TTR amyloidosis; on track to file U.S. New Drug Application this year
- Expanded enrollment in the Phase 3 CARDIO-TTRansform study of eplontersen in patients with ATTR cardiomyopathy; data still expected first half of 2025
- NDA for tofersen was accepted and granted priority review by the FDA; Prescription Drug User Fee Act date of April 25, 2023
- Initiated CORE2, a confirmatory Phase 3 study of olezarsen in patients with severe hypertriglyceridemia (SHTG)
- Initiated ESSENCE, a supporting Phase 3 study of olezarsen in patients with SHTG or hypertriglyceridemia and cardiovascular disease

Mid-Stage Pipeline Highlights

- GSK presented positive end of study data from the Phase 2b B-Clear study of bepirovirsen demonstrating potential for functional cures in patients with chronic hepatitis B; GSK plans to advance bepirovirsen into Phase 3 development in the first half of 2023
- Presented positive data from the Phase 2 study of IONIS-FB-L_{Rx} in patients with immunoglobulin A nephropathy; Roche plans to advance IONIS-FB-L_{Rx} into Phase 3 development in the first half of 2023
- Bayer presented positive data from the Phase 2b study of fesomersen in patients with end-stage renal disease; Ionis regained rights to fesomersen from Bayer and is assessing next steps
- Roche presented the Phase 2 GENERATION HD2 study design of tominersen in Huntington's disease patients; Roche plans to begin enrollment in early 2023
- Reported ION449 (AZD8233) targeting PCSK9 met the primary endpoint in Phase 2b SOLANO study in patients with hypercholesterolemia; based on pre-specified efficacy criteria, AstraZeneca is not advancing ION449

"We have made significant progress on our key priorities this year, building our commercial pipeline, delivering an abundance of new medicines to the market and expanding and diversifying our technology. We delivered positive data from eight key programs, positioning us to potentially add two new marketed medicines to our portfolio and expand our rich Phase 3 pipeline to eight medicines next year. Additionally, we have recently begun work on a manufacturing facility to support our pipeline growth," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "As we advance our near-term opportunities, including filing the NDA this year for eplontersen, and expanding our rich late-stage pipeline, we are well positioned to drive increasing value for all stakeholders."

Third Quarter 2022 Financial Results

Revenue

Ionis' revenue was comprised of the following:

	Three months ended		Nine months ended	
	September 30,		September 30,	
	2022	2021	2022	2021
Revenue:	(amounts in millions)			
Commercial revenue:				
SPINRAZA royalties	\$62	\$67	\$175	\$199
TEGSEDI and WAYLIVRA revenue, net	6	15	23	47
Licensing and royalty revenue	5	3	25	9
Total commercial revenue	73	85	223	255
Research and development revenue:				
Amortization from upfront payments	18	17	54	57
Milestone payments	15	28	60	48
License fees	35	-	37	-
Other services	1	3	6	10
Collaborative agreement revenue	69	48	157	115
Eplontersen joint development revenue	18	-	55	-
Total research and development revenue	87	48	212	115
Total revenue	\$160	\$133	\$435	\$370

Total revenue for the three and nine months ended September 30, 2022 increased 20 percent and 18 percent compared to the same periods last year, respectively. The increase was driven by significant payments Ionis earned across multiple partnered programs. R&D revenue for the nine months ended September 30, 2022 included \$85 million from Biogen for advancing several neurology disease programs, \$63 million from Roche for licensing and advancing IONIS-FB-LR_x and \$55 million from AstraZeneca for its share of the global Phase 3 development costs for eplontersen.

Commercial revenue for the three and nine months ended September 30, 2022 decreased 15 percent and 13 percent compared to the same periods last year, respectively. SPINRAZA royalties for the three and nine months ended September 30, 2022 decreased 7 percent and 12 percent compared to the same periods last year, respectively. In the U.S., SPINRAZA sales were flat in the first nine months of 2022 compared to the same period last year. Outside of the U.S. SPINRAZA royalties were lower due to lower SPINRAZA product sales primarily due to decreased pricing, foreign currency exchange and competition. TEGSEDI and WAYLIVRA revenue was also lower due to the shift to distribution fees in 2021.

Operating Expenses

Ionis' non-GAAP operating expenses increased for the three and nine months ended September 30, 2022 compared to the same periods in 2021, in line with expectations. For both periods, higher R&D expenses were driven by the expanded number of Phase 3 studies the Company is conducting, which doubled from three to six studies in 2021. SG&A expenses increased for the three months ended September 30, 2022 compared to the same period last year driven by Ionis' go-to-market activities for eplontersen, donidalorsen and olezarsen. SG&A expenses were lower for the nine months ended September 30, 2022 compared to the same period last year largely due to the substantial savings the Company achieved from integrating Akcea and restructuring its commercial operations in 2021.

Balance Sheet

As of September 30, 2022, Ionis had cash, cash equivalents and short-term investments of \$2.0 billion, compared with \$2.1 billion at December 31, 2021. Ionis' debt obligations and working capital did not change significantly from December 31, 2021 to September 30, 2022.

In October 2022, Ionis entered into a sale and leaseback transaction for several of its real estate assets. Under the agreement, Ionis will receive net proceeds of approximately \$240 million plus full funding to expand the Company's R&D campus. The net proceeds reflect the Company's extinguishment of its mortgage debt for the related properties. Ionis' fourth quarter financial results will reflect the impact this transaction.

2022 Financial Guidance

The Company reaffirmed its full year 2022 guidance for total revenue, operating expenses and net loss, on a non-GAAP basis. The Company's 2022 operating expense guidance, compared to the prior year, includes increasing R&D expenses between 25% and 30% and consistent SG&A expenses. Ionis expects to recognize a substantial gain on the sale of its real estate assets in the fourth quarter. The gain will not impact the Company's non-GAAP results since the sale was non-recurring and not part of the Company's normal business operations.

The Company increased its full year 2022 cash and investments guidance to approximately \$2.0 billion from the previous guidance of \$1.7 billion.

	Current	Previous
Full Year 2022 Guidance	As of 3Q22	As of 2Q22
Revenue	>\$575 million	>\$575 million
Operating expenses on a non-GAAP basis	\$825-\$850 million	\$825-\$850 million
Net loss on a non-GAAP basis	<\$275 million	<\$275 million
Cash, cash equivalents and short-term investments	~\$2.0 billion	~\$1.7 billion

"Our strong year-to-date results, including year-over-year revenue growth of nearly 20 percent, keep us on track to meet our 2022 P&L guidance," said Elizabeth L. Hougen, chief financial officer of Ionis. "Additionally, we recently bolstered our balance sheet when we unlocked net proceeds of

approximately \$240 million plus full funding to expand our R&D campus by capitalizing on the favorable life sciences real estate market and monetizing several of our facilities through a sale and leaseback transaction. As a result, we are increasing our 2022 cash and short-term investment guidance to approximately \$2 billion."

Webcast

Management will host a conference call and webcast to discuss Ionis' third quarter 2022 results at 11:30 a.m. Eastern time on Wednesday, November 9, 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 third quarter 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 a leading, fully integrated biotechnology company.

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, pelacarsen, tofersen, 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 related to the impact COVID-19 could have on our business, and 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, Nine months ended			
	September 30,		September 30,	
	2022	2021	2022	2021
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$62	\$67	\$175	\$199
TEGSEDI and WAYLIVRA revenue, net	6	15	23	47
Licensing and royalty revenue	5	3	25	9
Total commercial revenue	73	85	223	255
Research and development revenue:				
Collaborative agreement revenue	69	48	157	115
Eplontersen joint development revenue	18	-	55	-
Total research and development revenue	87	48	212	115
Total revenue	160	133	435	370
Expenses:				
Cost of sales	2	3	10	9
Research, development and patent	183	185	525	464
Selling, general and administrative	34	31	102	148
Total operating expenses	219	219	637	621
Loss from operations	(59)	(86)	(202)	(251)
Other expense (income)	12	2	(12)	(3)
Loss before income tax benefit (expense)	(47)	(84)	(214)	(254)
Income tax benefit (expense)	-	2	(3)	1

Net loss	<u>(\$47)</u>	<u>(\$82)</u>	<u>(\$217)</u>	<u>(\$253)</u>
Basic and diluted net loss per share	<u>(\$0.33)</u>	<u>(\$0.58)</u>	<u>(\$1.53)</u>	<u>(\$1.80)</u>
Shares used in computing basic and diluted net loss per share	<u>142</u>	<u>141</u>	<u>142</u>	<u>141</u>

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		Nine months ended	
	September 30, 2022	2021	September 30, 2022	2021
	(unaudited)			
As reported research, development and patent expenses according to GAAP	\$183	\$185	\$525	\$464
Excluding compensation expense related to equity awards	(18)	(23)	(55)	(72)
Excluding Akcea merger and restructured commercial operation costs*	-	(2)	-	(8)
Non-GAAP research, development and patent expenses	<u>\$165</u>	<u>\$160</u>	<u>\$470</u>	<u>\$384</u>
As reported selling, general and administrative expenses according to GAAP	\$34	\$31	\$102	\$148
Excluding compensation expense related to equity awards	(6)	(7)	(19)	(26)
Excluding Akcea merger and restructured commercial operation costs*	-	(1)	-	(16)
Non-GAAP selling, general and administrative expenses	<u>\$28</u>	<u>\$23</u>	<u>\$83</u>	<u>\$106</u>
As reported operating expenses according to GAAP	\$219	\$219	\$637	\$621
Excluding compensation expense related to equity awards	(24)	(31)	(75)	(98)
Excluding Akcea merger and restructured commercial operation costs*	-	(3)	-	(24)
Non-GAAP operating expenses	<u>\$195</u>	<u>\$185</u>	<u>\$562</u>	<u>\$499</u>
As reported loss from operations according to GAAP	(\$59)	(\$86)	(\$202)	(\$251)
Excluding compensation expense related to equity awards	(24)	(31)	(75)	(98)
Excluding Akcea merger and restructured commercial operation costs*	-	(3)	-	(24)
Non-GAAP loss from operations	<u>(\$35)</u>	<u>(\$52)</u>	<u>(\$127)</u>	<u>(\$129)</u>
As reported net loss according to GAAP	(\$47)	(\$82)	(\$217)	(\$253)
Excluding compensation expense related to equity awards	(24)	(31)	(75)	(98)
Excluding Akcea merger and restructured commercial operation costs*	-	(3)	-	(24)
Non-GAAP net loss	<u>(\$23)</u>	<u>(\$48)</u>	<u>(\$142)</u>	<u>(\$131)</u>

*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.

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. 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 Nine Months Ended, September 30, 2022
(Unaudited)

Collaboration Activities	Financial Statement Line	Impact of Cost-Sharing Provisions on Ionis' Statement of Operations
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Phase 3 Development: lonis leads and conducts	Eplontersen Joint Development Revenue (R&D Revenue)	\$55M	55% of Total Phase 3 development expenses, including internal+external costs & CMC costs, net of lonis' share of AstraZeneca's Phase 3 development expenses
	Development Expenses (R&D Expenses)	\$107M	100% of lonis' Phase 3 development expenses

lonis' financial results for the nine months ended September 30, 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 paying 55 percent of the costs associated with the ongoing global Phase 3 development program. Because lonis is leading and conducting the Phase 3 development program, lonis is recognizing the 55 percent of cost-share funding AstraZeneca is responsible for, net of lonis' share of AstraZeneca's development expenses, as R&D revenue in the same period lonis incurs the related development expenses. For the nine months ended September 30, 2022 lonis earned \$55 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 bringing eplontersen to market outside the U.S., lonis 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 nine months ended September 30, 2022 lonis recognized \$1.4 million and \$1.5 million of medical affairs expenses and commercialization expenses for eplontersen, respectively, net of cost-share funding from AstraZeneca. lonis expects its medical affairs and commercialization expenses to increase as this collaboration progresses.

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

	September 30, 2022	December 31, 2021
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	\$1,982	\$2,115
Contracts receivable	7	62
Other current assets	164	168
Property, plant and equipment, net	181	178
Other assets	88	89
Total assets	<u>\$2,422</u>	<u>\$2,612</u>
Liabilities and stockholders' equity:		
Other current liabilities	\$184	\$143
Current portion of deferred contract revenue	100	98
0% convertible senior notes, net	621	619
0.125% convertible senior notes, net	544	542
Long-term obligations, less current portion	84	86
Long-term deferred contract revenue	295	352
Total stockholders' equity	<u>594</u>	<u>772</u>
Total liabilities and stockholders' equity	<u>\$2,422</u>	<u>\$2,612</u>

2022 Pipeline Milestones⁽¹⁾

Anticipated 2022 Regulatory Updates

Program	Regulatory Action	Anticipated Indication	H1	H2
Tofersen	NDA acceptance	SOD1-ALS		✓
Eplontersen (TTR)	NDA filing	ATTRv polyneuropathy		•

Anticipated Key 2022 Data Readouts

Program	Data Readout	Anticipated Indication	H1	H2
Eplontersen (TTR)	Phase 3	ATTRv polyneuropathy	✓	
Tofersen	Phase 3 OLE	SOD1-ALS	✓	
Tominersen (HTT)	Phase 3 post hoc	Huntington's disease	✓	
ION449 (PCSK9)	Phase 2b (ETESIAN)	Cardiovascular disease	✓	
Bepirovirsen (HBV)	Phase 2b	Hepatitis B virus infection	✓	
Donidalorsen (PKK)	Phase 2	HAE	✓	
IONIS-C9 _{Rx} (BIIB078)	Phase 1/2	C9-ALS	✓	

Fesomersen (FXI)	Phase 2b	Thrombosis		✓
IONIS-FB-L _{Rx}	Phase 2	Immunoglobulin A nephropathy		✓
ION449 (PCSK9)	Phase 2b (SOLANO)	Cardiovascular disease		✓
Donidalorsen (PKK)	Phase 2 OLE	HAE		•
IONIS-AGT-L _{Rx}	Phase 2b	Treatment-resistant hypertension		•
Cimdelirsen (GHR)	Phase 2 (monotherapy)	Acromegaly		•

Anticipated Key 2022 Study Initiations

Program	Phase	Anticipated Indication	H1	H2
Sapablursen (TMPRSS6)	2	Polycythemia vera	✓	
ION904 (AGT)	2	Uncontrolled hypertension	✓	
IONIS-MAPT _{Rx} (BIIB080)	2	Alzheimer's disease		•
ION717 (PRNP)	1/2	Prion disease		•

Anticipated Key 2022 Technology Advancements

Program	Anticipated Advancement	H1	H2
SMA	Advance follow-on program	✓	
Muscle LICA	Advance into preclinical development (IND-supporting)		✓
MsPA Backbone	Advance into preclinical development (IND-supporting)		✓

✓ = achieved • = planned

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

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Ionis Pharmaceuticals Investor Contact: 760-603-2331 OR Ionis Pharmaceuticals Media Contact: 760-603-4679