

Ionis reports first quarter 2021 financial results and recent business achievements

May 5, 2021

On track to achieve 2021 guidance
Webcast today, May 5, 2021, at 11:30 a.m. Eastern Time

CARLSBAD, Calif., May 5, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today reported its financial results for the first quarter of 2021 and recent business highlights.



"In the first quarter, we took important steps to maximize the value of our wholly owned pipeline. We recently initiated pivotal studies with our wholly owned FUS-ALS and Alexander disease programs. We delivered positive results from our IONIS-PKK-L_{RX} program, demonstrating its potential to change the standard of care for patients with hereditary angioedema. We also further strengthened the business and continued executing on our strategic priorities," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "This summer, we expect data from our IONIS-MAPT_{RX} program in Alzheimer's disease patients. And later this year, we look forward to data from the Phase 3 VALOR study of tofersen in patients with SOD1-ALS. If results from the VALOR study are positive, we expect tofersen to be our next commercial medicine. These key upcoming catalysts, together with our recent achievements, position us well to have 12 or more products on the market in 2026."

First Quarter 2021 and Recent Summary Financial Results

- On track to achieve 2021 financial guidance reflecting investments in Ionis' wholly owned pipeline, based on the following first quarter results
 - \$112 million in total revenues
 - \$159 million of operating expenses on a non-GAAP basis⁽¹⁾ and \$204 million on a GAAP basis
 - Net loss of \$45 million on a non-GAAP basis⁽¹⁾ and \$90 million on a GAAP basis
- Further strengthened the Company's balance sheet with pro forma cash of \$2.1 billion, after reflecting the convertible notes transaction
 - Enables expansion of manufacturing and R&D capacity
 - \$632.5 million principal due in April 2026 with 0% interest and an effective conversion price of \$76.39 after the purchase of a call spread
 - Will realize interest expense savings while keeping potential future dilution nearly flat
 - Repurchased approximately 80% of previously outstanding 1% convertible notes due in November 2021

"So far this year, we have taken important steps in support of developing and commercializing our wholly owned medicines. In addition to completing the restructuring of our European operations, we expanded our Sobi distribution agreement to include North America. These transactions unlocked significant resources that we are now redirecting towards our highest priority programs, including IONIS-TTR-L_{RX} and IONIS-APOCIII-L_{RX}," said Elizabeth L. Hougen, chief financial officer of Ionis. "We are on track to meet our 2021 financial guidance. In the second half of this year, we expect R&D revenue to increase as many of our partnered programs continue to advance. Importantly, we are well-capitalized with the resources we need to expand our manufacturing and R&D capacity to support the future needs of our wholly owned pipeline. This large capital project, which is now underway, is necessary to successfully execute on our goal to drive growth."

(1) All non-GAAP amounts referred to in this press release exclude non-cash compensation expense related to equity awards and expenses related to

the Akcea acquisition and restructured European operations and the related tax effects. Please refer to the section below titled "Financial Impacts of Akcea Acquisition and Restructured Operations" for a summary of the costs specific to these transactions. Additionally, please refer to the detailed reconciliation of non-GAAP and GAAP measures, which is provided later in this release.

First Quarter 2021 Marketed Products Highlights

- SPINRAZA: a global foundation-of-care for the treatment of spinal muscular atrophy (SMA) patients of all ages
 - \$521 million in worldwide sales in the first quarter
 - More than 11,000 patients worldwide were on therapy at the end of the first quarter across post-marketing, expanded access and clinical trial settings
 - Higher-dose SPINRAZA demonstrated safety and tolerability consistent with the currently approved dose in the open-label safety cohort of the DEVOTE study, enabling enrollment in the blinded, pivotal cohort to get underway
- TEGSEDI and WAYLIVRA: important medicines approved for the treatment of patients with severe rare diseases
 - Completed the transition of European operations to Swedish Orphan Biovitrum AB (Sobi) and expanded the distribution agreement to include North American TEGSEDI operations

First Quarter 2021 and Recent Pipeline Events

- Phase 3 Pipeline: growing and positioned for 12 or more products on the market in 2026
 - Advanced ION363 into a Phase 3 study in patients with FUS-ALS
 - Advanced tofersen into the Phase 3 ATLAS study in presymptomatic SOD1-ALS patients
 - Roche reported tominersen data related to the dosing halt in the Phase 3 program
- Mid-stage Pipeline: advancing multiple medicines with potential to change the standard of care for patients with severe diseases
 - Reported positive topline IONIS-PKK-LRx results in patients with hereditary angioedema
 - Advanced ION373 into the Phase 2 portion of a pivotal study in patients with Alexander disease
 - Advanced the IONIS-AGT-LRx development program:
 - Reported positive Phase 2 data in *JACC: Basic to Translational Science*
 - Advanced into a Phase 2b study in patients with hypertension uncontrolled with three or more antihypertensive medications
 - Advanced into a Phase 2 study in patients with chronic heart failure with reduced ejection fraction
 - Advanced the ongoing Phase 2 study of ION541 in patients with ALS regardless of family history, resulting in a \$10 million payment from Biogen

Upcoming 2021 Pipeline Catalysts⁽²⁾

Anticipated 2021 Data Readouts

Program	Phase	Anticipated Indication	H1	H2
IONIS-PKK-LRx	2	Hereditary angioedema (top-line data)	√	
IONIS-AGT-LRx	2	Hypertension	√	
Tominersen	3	Huntington's disease	√	
IONIS-ENAC-2.5Rx	2	Cystic fibrosis	•	
IONIS-GHR-LRx	2+OLE	Acromegaly		•
IONIS-MAPT _{Rx}	1/2	Alzheimer's disease		•
IONIS-PKK-LRx	2	Hereditary angioedema (full data)		•
Vupanorsen	2b	sHTG/CVD risk reduction		•
Tofersen	3 (VALOR study)	SOD1-ALS		•

Anticipated 2021 Study Initiations

Program	Phase	Anticipated Indication	H1	H2
SPINRAZA	4 (RESPOND)	SMA, suboptimal gene therapy response	√	
Tofersen	3 (ATLAS study)	Presymptomatic SOD1-ALS	√	
ION363	3	FUS-ALS	√	
IONIS-AGT-LRx	2b	Resistant hypertension	√	
IONIS-AGT-LRx	2	Heart failure with reduced ejection fraction	√	
ION373	2/3	Alexander disease	√	
ION224	2b	NASH	•	
IONIS-APOCIII-LRx	3	Second TG indication (sHTG)		•

(2) Timing of partnered program catalysts based on partners' most recent publicly available disclosures

First Quarter 2021 Financial Results

Revenue

Ionis' revenue was comprised of the following (amounts in millions):

	Three months ended, March 31,	
	2021	2020
Revenue:		
Commercial revenue:		
SPINRAZA royalties	\$60	\$66
TEGSEDI and WAYLIVRA revenue, net	20	15
Licensing and royalty revenue	5	3
Total commercial revenue	85	84
R&D Revenue:		
Amortization from upfront payments	20	21
Milestone payments	5	23
Other services	2	5
Total R&D revenue	27	49
Total revenue	\$112	\$133

The Company's commercial revenue in the first quarter of 2021 was consistent with the same period last year. As the Company completes its transition of TEGSEDI operations in North America to Sobi, the Company's commercial revenue from product sales will shift to distribution fees based on net sales generated by Sobi.

The Company's R&D revenue decreased in the first quarter of 2021 compared to the same period last year primarily because the Company earned more milestone payments in the first quarter of 2020 than the same period this year. The Company expects its R&D revenue to increase in the second half of 2021 compared to the first half.

Financial Impacts of Akcea Acquisition and Restructured Operations

In conjunction with the Akcea acquisition and restructured European operations, in the first quarter of 2021, the Company incurred \$7 million of costs, which it excluded from its non-GAAP amounts for the period. Refer to the detailed reconciliation of non-GAAP and GAAP measures that is provided later in this release. The Company expects to incur additional expenses in the range of \$11 million to \$14 million related to the restructuring of its North American TEGSEDI operations from the expanded distribution agreement with Sobi. The company will reflect the North American TEGSEDI restructuring costs primarily in the second quarter of 2021.

Operating Expenses

Ionis' operating expenses for the first quarter of 2021 increased compared to the same period last year driven primarily by the Company's investments in advancing its late-stage wholly owned pipeline.

Net Loss Attributable to Ionis Common Stockholders

Ionis' net loss attributable to Ionis' common stockholders for the first quarter of 2021 increased compared to the same period in the prior year for the reasons discussed above.

Balance Sheet

Ionis ended March 2021 with cash, cash equivalents and short-term investments of \$1.8 billion, compared to \$1.9 billion at December 31, 2020. In April 2021, Ionis issued \$632.5 million of 0% senior convertible notes due in April 2026 and repurchased \$247.9 million of its 1% senior convertible notes. After reflecting these transactions, Ionis' pro forma cash, cash equivalents and short-term investments was \$2.1 billion.

The Company revised its 2020 amounts to reflect the simplified convertible instruments guidance the Company adopted retrospectively on January 1, 2021.

Webcast

Today, at 11:30 a.m. Eastern Time, Ionis will conduct a live webcast to discuss this earnings release and related activities. Interested parties may access the webcast [here](#). A webcast replay will be available for a limited time at the same address.

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 neurological and cardiometabolic franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming one of the most successful biotechnology companies.

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) and WAYLIVRA (volanesorsen) and Ionis' technologies and 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, 2020, and the most recent Form 10-Q quarterly filing, which are on file with the SEC. 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" refers to Ionis Pharmaceuticals and its subsidiaries.

Ionis Pharmaceuticals™ is a 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, March 31,	
	2021	2020
	(as revised*)	
	(unaudited)	
Revenue:		
Commercial revenue:		
SPINRAZA royalties	\$60	\$66
TEGSEDI and WAYLIVRA revenue, net	20	15
Licensing and royalty revenue	5	3
Total commercial revenue	85	84
Research and development revenue under collaborative agreements	27	49
Total revenue	112	133
Expenses:		
Cost of sales	3	3
Research, development and patent	140	116
Selling, general and administrative	61	75
Total operating expenses	204	194
Loss from operations	(92)	(61)
Other income, net	2	8
Loss before income tax benefit	(90)	(53)
Income tax benefit	-	3
Net loss	(\$90)	(\$50)
Net loss attributable to noncontrolling interest in Akcea Therapeutics, Inc.	-	10
Net loss attributable to Ionis Pharmaceuticals, Inc. common stockholders	(\$90)	(\$40)
Basic and diluted net loss per share	(\$0.64)	(\$0.28)
Shares used in computing basic and diluted net loss per share	141	139

*The Company revised its 2020 amounts to reflect the simplified convertible instruments guidance the Company adopted retrospectively on January 1, 2021.

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, March 31,	
	2021	2020
	(as revised*)	
	(unaudited)	
As reported research, development and patent expenses according to GAAP	\$140	\$116
Excluding compensation expense related to equity awards	(26)	(26)
Excluding Akcea acquisition and restructured European operations costs	(3)	-

Non-GAAP research, development and patent expenses	<u>\$111</u>	<u>\$90</u>
As reported selling, general and administrative expenses according to GAAP	\$61	\$75
Excluding compensation expense related to equity awards	(12)	(15)
Excluding Akcea acquisition and restructured European operations costs	(4)	-
Non-GAAP selling, general and administrative expenses	<u>\$45</u>	<u>\$60</u>
As reported operating expenses according to GAAP	\$204	\$194
Excluding compensation expense related to equity awards	(38)	(41)
Excluding Akcea acquisition and restructured European operations costs	(7)	-
Non-GAAP operating expenses	<u>\$159</u>	<u>\$153</u>
As reported loss from operations according to GAAP	(\$92)	(\$61)
Excluding compensation expense related to equity awards	(38)	(41)
Excluding Akcea acquisition and restructured European operations costs	(7)	-
Non-GAAP loss from operations	<u>(\$47)</u>	<u>(\$20)</u>
As reported net loss attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP*	(\$90)	(\$40)
Excluding compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	(38)	(39)
Excluding Akcea acquisition and restructured European operations costs	(7)	-
Income tax effect related to compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	-	8
Non-GAAP net loss attributable to Ionis Pharmaceuticals, Inc. common stockholders*	<u>(\$45)</u>	<u>(\$9)</u>

*The Company revised its 2020 amounts to reflect the simplified convertible instruments guidance the Company adopted retrospectively on January 1, 2021.

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) attributable to Ionis Pharmaceuticals, Inc. common stockholders were adjusted from GAAP to exclude compensation expense related to equity awards and costs related to the Akcea acquisition and restructured European operations and the related tax effects. Compensation expense related to equity awards are non-cash. Costs related to the Akcea acquisition and restructured European operations include: severance costs, retention costs and other costs. 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. Condensed Consolidated Balance Sheets (In Millions)

	March 31, 2021	December 31, 2020
	(as revised*)	
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	\$1,820	\$1,892
Contracts receivable	23	76
Other current assets	146	162
Property, plant and equipment, net	180	181
Other assets	80	79
Total assets	<u>\$2,249</u>	<u>\$2,390</u>
Liabilities and stockholders' equity:		
Other current liabilities	\$126	\$183
Current portion of 1% convertible senior notes, net	62	309
Current portion of deferred contract revenue	107	108
1% convertible senior notes, less current portion	247	-
0.125% convertible senior notes, net	541	540
Long-term obligations, less current portion	83	83
Long-term deferred contract revenue	402	424
Total stockholders' equity	<u>681</u>	<u>743</u>
Total liabilities and stockholders' equity	<u>\$2,249</u>	<u>\$2,390</u>

*The Company revised its 2020 amounts to reflect the simplified convertible instruments guidance the Company adopted retrospectively on January 1, 2021.

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