

Ionis reports fourth quarter and full year 2020 financial results and recent business achievements

February 24, 2021

Achieved 2020 financial guidance
2021 guidance reflects increased investments in wholly owned pipeline to drive future revenue growth
Webcast today, February 24, 2021, at 9:00 a.m. Eastern Time

CARLSBAD, Calif., Feb. 24, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today reported its financial results for the fourth quarter of 2020 and recent business highlights.



"Last year, we laid out a bold new vision for the Company and took important steps towards our goal of becoming one of the most successful biotechnology companies. Key to our vision is our strategy to maximize the value of our pipeline by commercializing our wholly owned medicines. Our acquisition of Akcea was an important step in building our commercial capabilities while enabling us to further strengthen our organization," said Brett P. Monia, Ph.D., chief executive officer at Ionis. "Last year, we also advanced our late-stage pipeline and expanded the utility of our technology. Looking ahead, we expect data from multiple wholly owned programs in the first half of this year, followed by Phase 3 tofersen data in patients with SOD1-ALS in the second half. These key upcoming catalysts, together with our recent pipeline and technology achievements, position us well to have 12 or more products on the market in 2026. Importantly, we continue to have the financial strength to expand investment in our wholly owned pipeline and commercial capabilities to drive meaningful and increasing value for patients and shareholders."

2020 Summary Financial Results

- Achieved 2020 financial guidance
 - \$729 million in total revenues, with half from marketed products
 - \$640 million of operating expenses on a non-GAAP basis⁽¹⁾ and \$901 million on a GAAP basis, reflecting investments in Ionis' wholly owned pipeline
 - Net income of \$111 million on a non-GAAP basis⁽¹⁾ and a net loss of \$451 million on a GAAP basis
- Strong balance sheet with cash of \$1.9 billion at year-end, enabling increasing investment in advancing the pipeline and technology while also preparing to commercialize the Company's wholly owned medicines

2020 Marketed Products Highlights

- SPINRAZA: a global foundation-of-care for the treatment of spinal muscular atrophy (SMA) patients of all ages
 - \$2 billion in worldwide sales in 2020
 - More than 11,000 patients worldwide were on therapy at the end of the fourth quarter across post-marketing, expanded access and clinical trial settings
 - Enrollment began in the RESPOND study evaluating potential SPINRAZA benefit in SMA patients with a suboptimal clinical response to gene therapy
 - Enrollment began in the pivotal randomized treatment cohort of the DEVOTE study evaluating higher doses of SPINRAZA
- TEGSEDI and WAYLIVRA: transformational medicines approved for the treatment of patients with severe rare diseases

- Product sales increased more than 65 percent in 2020, compared to 2019
- Generated growing revenues as major markets launched in 2020
- Restructured European operations through a distribution agreement with Swedish Orphan Biovitrum AB (Sobi)

Q4 2020 and Recent Pipeline Highlights

- Phase 3 Pipeline: growing pipeline positioned for 12 or more products on the market in 2026
 - Advanced IONIS-APOCIII-L_{Rx} into the Phase 3 BALANCE study in patients with FCS
 - Completed enrollment in the tofersen Phase 3 VALOR study in patients with SOD1-ALS
- Mid-stage Pipeline: broad and advancing pipeline of potential first-in-class and/or best-in-class medicines
 - Advanced and expanded the IONIS-AGT-L_{Rx} development program
 - Reported IONIS-AGT-L_{Rx} positive topline Phase 2 results in patients with hypertension uncontrolled with two or three antihypertensive medications
 - Advanced ION904, the follow-on medicine targeting AGT, into Phase 1 development in healthy volunteers
 - Advanced vupanorsen into Phase 2b development with the initiation of the TRANSLATE-TIMI 70 dose-ranging study in statin-treated patients with dyslipidemia, resulting in a \$75 million payment from Pfizer
 - Advanced ION449 (AZD8233), targeting PCSK9, into Phase 2b development in patients with dyslipidemia and AstraZeneca licensed ION455, a new investigational medicine for the treatment of nonalcoholic steatohepatitis (NASH), resulting in \$50 million from AstraZeneca
 - Unlocked potential new pulmonary disease franchise with positive IONIS-ENAC-2.5_{Rx} data
 - Reported positive healthy volunteer results supporting aerosol antisense medicine delivery to the lung
 - Completed dosing in the Phase 2 study in patients with cystic fibrosis
 - Advanced IONIS-ENAC-2.5_{Rx} into Phase 2 development in patients with chronic obstructive pulmonary disease (COPD)
 - Highlighted IONIS-MAPT_{Rx} (BIIB080) Phase 1/2 study in patients with Alzheimer's disease in which IONIS-MAPT_{Rx} was generally well tolerated and demonstrated durable, time and dose-dependent reductions in CSF tau protein

Upcoming 2021 Pipeline Catalysts

Anticipated 2021 Data Readouts⁽²⁾

Program	Phase	Anticipated Indication	H1	H2
IONIS-ENAC-2.5 _{Rx}	2	Cystic fibrosis	•	
IONIS-PKK-L _{Rx}	2	Hereditary angioedema (top-line)	•	
IONIS-GHR-L _{Rx}	2	Acromegaly (top-line)	•	
IONIS-AGT-L _{Rx}	2	Hypertension	•	
Tominersen	OLE/NHS	Huntington's disease		•
IONIS-MAPT _{Rx}	1/2	Alzheimer's disease		•
Vupanorsen	2b	sHTG/CVD risk reduction		•
IONIS-C9 _{Rx}	1/2	C9-ALS		•
Tofersen	3 (VALOR study)	SOD1-ALS		•

Anticipated 2021 Study Initiations⁽²⁾

Program	Phase	Anticipated Indication	H1	H2
ION363	3	FUS-ALS	•	
ION373	2	Alexander disease	•	
IONIS-AGT-L _{Rx}	2b	Resistant hypertension	•	
IONIS-AGT-L _{Rx}	2	Heart failure with reduced ejection fraction	•	
ION224	2b	NASH	•	
Tofersen	3 (ATLAS study)	Presymptomatic SOD1-ALS		•
IONIS-APOCIII-L _{Rx}	3	Second CV indication		•
IONIS-ENAC-2.5 _{Rx}	2	Cystic fibrosis not amenable to CFTR modulators		•

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

2020 Financial Results and 2021 Financial Guidance

"We achieved our 2020 financial guidance, even in the challenging COVID-19 pandemic environment. Moreover, in 2020 we made significant progress toward our goal of creating a stronger, more efficient company focused primarily on advancing our wholly owned medicines to the market. We acquired Akcea enabling us to retain full value from its rich portfolio. We also restructured our European operations. Together, these transactions unlocked substantial cost savings that we plan to reinvest to drive future revenue growth," said Elizabeth L. Hougen, chief financial officer of Ionis. "Our 2021 guidance reflects our new strategy to maximize the value of our wholly owned pipeline, focused primarily on commercializing our rare neurological and cardiometabolic disease programs. Our guidance also reflects the investments we are making in three key areas of our business - advancing and expanding our wholly owned pipeline, building commercial capabilities in support of our rich pipeline and broadening the reach of our technology. We can increase our investments in these areas while only modestly increasing our expenses because of the significant cost savings we realized from acquiring Akcea and restructuring our European operations. Importantly, with nearly \$2 billion of cash at the end of last year, we remain well

capitalized with the substantial financial resources to achieve our goals."

2021 Financial Guidance

Ionis' full year 2021 financial guidance consists of the following components (on a non-GAAP basis)⁽¹⁾:

Guidance	
Revenue	>\$600 million
Operating Expenses ⁽¹⁾	\$675 million to \$725 million
Net Loss ⁽¹⁾	<\$75 million

(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 European Operations" for a breakdown 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.

Revenue

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

	Three months ended, Year ended,			
	December 31,		December 31,	
	2020	2019	2020	2019
Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$75	\$81	\$287	\$293
Product sales, net	19	13	70	42
Licensing and royalty revenue	2	6	8	17
Total commercial revenue	96	100	365	352
R&D Revenue:				
Amortization from upfront payments	12	46	80	146
Milestone payments	110	51	183	115
License fees	71	292	86	490
Other services	1	5	15	20
Total R&D revenue	194	394	364	771
Total revenue	\$290	\$494	\$729	\$1,123

Financial Impacts of Akcea Acquisition and Restructured European Operations

In the fourth quarter of 2020, the Company's non-GAAP amounts exclude the following expenses related to the Akcea acquisition and restructured European operations because the costs are not part of its normal ongoing operating activities. Refer to the detailed reconciliation of non-GAAP and GAAP measures, which is provided later in this release. (Amounts in millions):

	Three months ended December 31, 2020
Severance, retention and other expenses	\$31
Non-cash stock-based compensation expense for the acceleration of Akcea equity awards	59
Total expenses included in GAAP operating expenses	\$90
Non-cash adjustment of the valuation allowance for Ionis' federal net deferred tax assets and other tax adjustments related to the Akcea acquisition	312
Total expenses included in GAAP net loss	\$402

As a result of the Akcea acquisition, Ionis and Akcea began reporting their federal taxes on a consolidated basis in the fourth quarter of 2020. The Company recorded a valuation allowance against all Ionis' federal net deferred tax assets in the fourth quarter of 2020, due largely to Akcea's history of losses and the expected impact of this on Ionis' consolidated federal taxable income. The Company now maintains a valuation allowance against all its consolidated federal and state net deferred tax assets.

Operating Expenses

Ionis' operating expenses for the year ended December 31, 2020 increased compared to 2019 driven by the Company's investments in advancing the Phase 3 programs for IONIS-TTR-L_{RX}, IONIS-APOCIII-L_{RX} and other medicines in its wholly owned pipeline. Additionally, the Company incurred approximately \$90 million in costs related to the Akcea acquisition and restructured European operations on a GAAP basis. The costs consisted of \$31 million of severance, retention and other costs and \$59 million of non-cash stock-based compensation expense for the acceleration of Akcea equity awards.

Net Loss Attributable to Noncontrolling Interest in Akcea

Prior to completing its acquisition of Akcea in October 2020, Ionis owned approximately 76 percent of Akcea. The line titled "Net loss attributable to noncontrolling interest in Akcea" on Ionis' statement of operations reflects the portion of Akcea's net income or loss attributable to the other owners of Akcea's common stock. From mid-October 2020 through December 31, 2020, Ionis did not recognize any noncontrolling interest in Akcea on its

statement of operations because it owned 100 percent of Akcea. Beginning in 2021, the Company will no longer have an adjustment for noncontrolling interest in Akcea.

Net Income (Loss) Attributable to Ionis Common Stockholders

Ionis recognized a net loss attributable to Ionis' common stockholders for 2020 compared to net income in 2019 primarily due to higher revenue in 2019, including approximately \$400 million in license fees Ionis earned from Pfizer and Novartis. Also contributing to Ionis' net loss in 2020 was the non-cash adjustment of the valuation allowance Ionis recorded against its federal net deferred tax assets discussed above. Additionally, Ionis' operating expenses increased in 2020 compared to the same period last year as described above.

Balance Sheet

Ionis ended 2020 with cash, cash equivalents and short-term investments of \$1.9 billion, compared to \$2.5 billion at December 31, 2019. In October 2020, Ionis used approximately \$545 million of its cash for the Akcea acquisition.

Webcast

Today, at 9:00 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, including the business of Akcea Therapeutics, Inc., Ionis' wholly owned subsidiary. 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 but not limited to those related to our commercial products and the medicines in our pipeline, and particularly 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, 2019, 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, Year ended,			
	December 31,		December 31,	
	2020	2019	2020	2019
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$75	\$81	\$287	\$293
Product sales, net	19	13	70	42
Licensing and royalty revenue	2	6	8	17
Total commercial revenue	<u>96</u>	<u>100</u>	<u>365</u>	<u>352</u>
Research and development revenue under collaborative agreements	194	394	364	771
Total revenue	<u>290</u>	<u>494</u>	<u>729</u>	<u>1,123</u>
Expenses:				
Cost of products sold	3	1	12	4
Research, development and patent	171	149	535	466
Selling, general and administrative	<u>139</u>	<u>83</u>	<u>354</u>	<u>287</u>

Total operating expenses	313	233	901	757
Income (loss) from operations	(23)	261	(172)	366
Other income (loss), net	(1)	(23)	2	(19)
Income (loss) before income tax benefit (expense)	(24)	238	(170)	347
Income tax benefit (expense)	(318)	(34)	(317)	(44)
Net income (loss)	(\$342)	\$204	(\$487)	\$303
Net loss (income) attributable to noncontrolling interest in Akcea Therapeutics, Inc.	2	(20)	36	(9)
Net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders	(\$340)	\$184	(\$451)	\$294
Basic net income (loss) per share	(\$2.44)	\$1.31	\$(3.23)	\$2.12
Diluted net income (loss) per share	(\$2.44)	\$1.28	\$(3.23)	\$2.08
Shares used in computing basic net income (loss) per share	140	141	140	140
Shares used in computing diluted net income (loss) per share	140	153	140	143

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, 2020	Year ended, December 31, 2019	2020	2019
	(unaudited)			
As reported operating expenses according to GAAP	\$313	\$233	\$901	\$757
Excluding compensation expense related to equity awards	(36)	(35)	(171)	(147)
Excluding Akcea acquisition and restructured European operations costs	(90)	-	(90)	-
Non-GAAP operating expenses	<u>\$187</u>	<u>\$198</u>	<u>\$640</u>	<u>\$610</u>
As reported income (loss) from operations according to GAAP	(\$23)	\$261	(\$172)	\$366
Excluding compensation expense related to equity awards	(36)	(35)	(171)	(147)
Excluding Akcea acquisition and restructured European operations costs	(90)	-	(90)	-
Non-GAAP income (loss) from operations	<u>\$103</u>	<u>\$296</u>	<u>\$89</u>	<u>\$513</u>
As reported net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP	(\$340)	\$184	(\$451)	\$294
Excluding compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	(36)	(33)	(162)	(139)
Income tax effect related to compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	(16)	5	2	31
Excluding Akcea acquisition and restructured European operations costs	(90)	-	(90)	-
Income tax effect related to the Akcea acquisition and restructured European operations costs	(312)	-	(312)	-
Non-GAAP net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders	<u>\$114</u>	<u>\$212</u>	<u>\$111</u>	<u>\$402</u>

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 shareholders 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, other costs, non-cash stock-based compensation expense for the acceleration of Akcea equity awards and non-cash income tax expense as a result of establishing a valuation allowance for Ionis' federal net deferred tax assets. 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)

December 31, December 31,
2020 2019

Assets:	2020	2019
Cash, cash equivalents and short-term investments	\$1,892	\$2,500
Contracts receivable	76	63
Other current assets	162	158
Property, plant and equipment, net	181	154
Other assets	79	358
Total assets	\$2,390	\$3,233
Liabilities and stockholders' equity:		
Other current liabilities	\$182	\$155
Current portion of deferred contract revenue	108	118
1% convertible senior notes (current in 2020)	293	275
0.125% convertible senior notes	456	435
Long-term obligations, less current portion	84	75
Long-term deferred contract revenue	424	490
Total Ionis stockholders' equity	843	1,471
Noncontrolling interest in Akcea Therapeutics, Inc.	-	214
Total stockholders' equity	\$843	\$1,685
Total liabilities and stockholders' equity	\$2,390	\$3,233

† View original content to download multimedia: <http://www.prnewswire.com/news-releases/ionis-reports-fourth-quarter-and-full-year-2020-financial-results-and-recent-business-achievements-301234146.html>

SOURCE Ionis Pharmaceuticals, Inc.

Ionis Pharmaceuticals Investor Contact: D. Wade Walke, Ph.D., Vice President, Investor Relations, 760-603-2741; Ionis Pharmaceuticals Media Contact: Roslyn Patterson, Vice President, Marketing and Communications, 760-603-2681