

Ionis provides fourth quarter and full year 2019 financial results

February 26, 2020

2019 revenues nearly doubled to more than \$1.1 billion
Exceeded improved 2019 guidance
2020 guidance reflects investment in strategic priorities
Webcast today, February 26, 2020, at 11:30 a.m. Eastern Time

CARLSBAD, Calif., Feb. 26, 2020 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today reported its financial results for the fourth quarter and full year 2019 and recent business highlights.

"2019 was an exceptional year. We achieved our goals across the business, including advancing four medicines into pivotal studies and growing our Ionis-owned pipeline. We also made significant progress across our broad pipeline, including in our neurological and cardiometabolic disease franchises, and further advanced our antisense technology through investments in new, complementary technologies. Together these achievements position us to deliver on our goal of ten or more new drug applications through 2025," said Brett P. Monia, chief executive officer at Ionis. "This year, our priorities include further growing and advancing our Ionis-owned pipeline, initiating additional Phase 3 studies, reporting clinical proof-of-concept results from six or more studies and further developing our commercial strategy to maximize the value of each medicine in our pipeline."

2019 Financial Results and Highlights

- Nearly doubled 2019 revenues, driven by SPINRAZA's continued blockbuster performance and increasing R&D revenue
 - Commercial revenue from SPINRAZA[®] (nusinersen) royalties increased by more than 20 percent to \$293 million compared to 2018
 - Product sales from TEGSEDI[®] (inotersen) and WAYLIVRA[®] (volanesorsen) were \$42 million
 - R&D revenue more than doubled to \$771 million compared to 2018
- Invested in commercializing TEGSEDI and WAYLIVRA and advanced the pipeline while remaining profitable
 - Operating income and net income significantly improved to \$366 million and \$294 million, respectively, compared to 2018, on a GAAP basis
 - Non-GAAP operating income and net income significantly improved to \$513 million and \$402 million, respectively, compared to 2018
- Increased cash position to \$2.5 billion; further strengthened balance sheet by refinancing a significant portion of the Company's 1 percent convertible debt due in 2021
 - Extended maturity to 2024, achieved 0.125 percent interest rate, and significantly increased conversion price
- Returned value to shareholders by repurchasing 2 million shares of Ionis common stock in late 2019 and early 2020 for \$125 million

2020 Financial Guidance

The Company's full year 2020 financial guidance consists of the following components (on a non-GAAP basis):

Guidance	
Revenue	>\$700 million
Operating Expenses	~\$650 million to \$690 million
Meaningfully Profitable	

"2019 was also an exceptional year financially, with growth in both commercial revenues and R&D revenues. We delivered over \$1 billion in revenue and more than \$400 million in net income. Our revenue nearly doubled compared to 2018, driven primarily by nearly \$400 million in revenue from licensing AKCEA-APO(a)-LR_x and AKCEA-ANGPTL3-LR_x, both of which could address very large patient populations. We achieved our third consecutive year of net income while investing substantially in our pipeline and technology," said Elizabeth L. Hougen, chief financial officer of Ionis. "This year, we expect to be meaningfully profitable. We expect growth in commercial revenues, with another strong year for SPINRAZA combined with growing revenue from TEGSEDI and WAYLIVRA as we expand into new countries. We also expect to achieve important milestones as we advance our medicines in development. Our projected increase in operating expenses reflects our plan to continue investing aggressively in all aspects of our business to generate substantial value, including growing and advancing our Ionis-owned pipeline and further advancing and broadening our technology. With a 2019 year-end cash balance of \$2.5 billion, we have the financial strength to fully execute on these strategic priorities."

All non-GAAP amounts referred to in this press release exclude non-cash compensation expense related to equity awards. Please refer to the reconciliation of non-GAAP and GAAP measures, which is provided later in this release.

Commercial Medicines

- SPINRAZA: a global foundation-of-care for the treatment of spinal muscular atrophy (SMA) patients of all ages
 - Worldwide sales increased to more than \$2 billion in 2019, an approximately 22 percent increase compared to 2018
 - Worldwide patients on treatment increased to over 10,000, including patients in commercial, early access and clinical trial settings
 - In the fourth quarter, patients on treatment outside the U.S. increased by approximately 10 percent, driven by growth from existing and newly launched markets

- o In the fourth quarter, U.S. patient growth was driven by pediatric and adult SMA patients, with adults accounting for more than 50 percent of new patient starts
 - o Biogen initiated the Phase 2/3 DEVOTE study evaluating the safety and potential to achieve increased efficacy with a higher dose of SPINRAZA in SMA patients of all ages, including adults
- TEGSEDI: launched in multiple markets for the treatment of hereditary transthyretin amyloidosis (hATTR) with polyneuropathy in adult patients
 - o Revenue increased for each quarter during 2019, driven by growth in patients on treatment
 - o Total units shipped to U.S. patients increased by 17 percent in the fourth quarter
 - o Commercially available in more than ten countries
 - o Launching in Brazil through PTC Therapeutics
 - o Launching in additional EU countries this year
- WAYLIVRA: launched in the EU as the only approved treatment for adults with genetically confirmed familial chylomicronemia syndrome (FCS) at high risk for pancreatitis
 - o Commercial patients on therapy in Germany
 - o Patient enrollment underway in France through the Temporary Authorization for Use (ATU)
 - o Launching in additional EU countries this year
 - o Potential approval in Brazil by the end of this year through PTC Therapeutics
 - o Goal to refile for marketing authorization in the U.S. this year

Neurological Disease Franchise

- Ionis-owned programs:
 - o Initiated the Phase 3 NEURO-TTTransform study of AKCEA-TTR-L_{Rx} for the treatment of hATTR polyneuropathy
 - o Advanced two new Ionis-owned neurological disease medicines into development:
 - ION716 for the treatment of Prion disease
 - ION283 for the treatment of Lafora disease
 - o ION373, for the treatment of Alexander disease, granted orphan drug designation by the European Medicines Agency (EMA)
- Partnered programs:
 - o More than \$55 million for licensing and advancing IONIS-MAPT_{Rx} for the treatment of Alzheimer's disease
 - o \$10 million for advancing the Phase 1/2 study of IONIS-C9_{Rx} for the treatment of C9ORF72-related ALS
 - o \$10 million for advancing ION581 into development for the treatment of Angelman syndrome
 - o \$30 million for advancing four new neurological disease programs toward development

Cardiometabolic Disease Franchise

- Ionis-owned programs:
 - o Initiated the Phase 3 CARDIO-TTTransform cardiovascular outcomes study of AKCEA-TTR-L_{Rx} in patients with hereditary and wild-type ATTR cardiomyopathy
 - o AKCEA-APOCIII-L_{Rx} achieved its primary efficacy endpoint and demonstrated a favorable safety and tolerability profile in a Phase 2 proof-of-concept study
- Partnered programs:
 - o Novartis began enrolling patients in the Phase 3 HORIZON cardiovascular outcomes study of AKCEA-APO(a)-L_{Rx} in patients with established cardiovascular disease
 - o AKCEA-ANGPTL3-L_{Rx} achieved its primary efficacy endpoint and demonstrated a favorable safety and tolerability profile in a Phase 2 proof-of-concept study
 - o Received \$250 million from Pfizer upon closing of the license agreement for the development and commercialization of AKCEA-ANGPTL3-L_{Rx} for the treatment of patients with certain cardiovascular and metabolic diseases

Key 2020 Catalysts

- Initiate a Phase 3 study of AKCEA-APOCIII-L_{Rx} in patients with FCS
- Report clinical proof-of-concept results from six or more studies, including IONIS-GHR-L_{Rx}, IONIS-PKK-L_{Rx}, IONIS-ENaC-2.5_{Rx} and an orally delivered medicine
 - o Reported positive topline results for AKCEA-APOCIII-L_{Rx} and AKCEA-ANGPTL3-L_{Rx} in January 2020
- Initiate ten or more Phase 2 studies
- Advance five or more new medicines into development

Revenue

Ionis' revenue increased by more than 85 percent in 2019 compared to the same period in 2018 and was comprised of the following (amounts in

millions):

	Three months ended, Year ended			
	December 31,		December 31,	
	2019	2018	2019	2018
Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$81	\$70	\$293	\$238
Product sales, net	13	2	42	2
Licensing and royalty revenue	6	1	17	15
Total commercial revenue	100	73	352	255
R&D Revenue:				
Amortization from upfront payments	46	33	146	125
Milestone payments	51	38	115	83
License fees	292	38	490	102
Other services	5	10	20	35
Total R&D revenue	394	119	771	345
Total revenue	\$494	\$192	\$1,123	\$600

Operating Expenses

Operating expenses increased for the year ended December 31, 2019, compared to the same period in 2018 principally due to Ionis' investment in the global launch of TEGSEDI, the EU launch of WAYLIVRA and advancing medicines in the Company's pipeline.

Loss on Early Retirement of Debt

In December 2019, Ionis refinanced a significant portion of its 1% convertible senior notes due 2021 (1% Notes) for new 0.125% convertible senior notes due 2024 (0.125% Notes). Ionis significantly reduced its interest rate, extended the maturity to December 2024 and increased the conversion price. As a result of the early refinance of the 1% Notes, Ionis recognized a \$22 million non-cash loss in 2019.

Income Tax Expense (Benefit)

Ionis' income tax expense in 2019 was primarily because the Company generated U.S. federal and state taxable income in 2019. The tax benefit in 2018 was due to a one-time non-cash tax benefit recognized in 2018 related the Company's deferred income tax assets.

Net (Income) Loss Attributable to Noncontrolling Interest in Akcea

At December 31, 2019, Ionis owned approximately 76 percent of Akcea. The shares of Akcea third parties own represent an interest in Akcea's equity that Ionis does not control. However, because Ionis continues to maintain overall control of Akcea through its voting interest, Ionis reflects the assets, liabilities and results of operations of Akcea in Ionis' consolidated financial statements. Ionis reflects the noncontrolling interest attributable to other owners of Akcea's common stock in a separate line called "Net (income) loss attributable to noncontrolling interest in Akcea" on Ionis' statement of operations. Ionis recognized net income attributable to noncontrolling interest in Akcea in 2019 compared to a net loss in 2018. Ionis had net income attributable to noncontrolling interest in Akcea in 2019 primarily because Akcea earned significant license fee revenue from Novartis and Pfizer in 2019 which led to Akcea having net income for 2019.

Net Income Attributable to Ionis Common Stockholders

Ionis' net income attributable to Ionis' common stockholders and basic and diluted earnings per share increased in 2019 compared to 2018 primarily due to the significant increase in Ionis' revenue. Somewhat offsetting this increase was income tax expense the Company recognized in 2019 compared to a one-time non-cash tax benefit recognized in 2018 related to the Company's deferred income tax assets.

Balance Sheet

Ionis strengthened its balance sheet, ending 2019 with cash, cash equivalents and short-term investments of \$2.5 billion, compared to \$2.1 billion at December 31, 2018.

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.

As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, drug discovery platform called antisense technology that can treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs. We created the first and only approved treatment for children and adults with spinal muscular atrophy as well as the world's first RNA-targeted therapeutic approved for the treatment of polyneuropathy in adults with hereditary transthyretin amyloidosis. Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 novel medicines designed to treat a broad range of diseases including cardiovascular diseases, neurological diseases, infectious diseases, pulmonary diseases and cancer.

To learn more about Ionis visit www.ionispharma.com or follow us on twitter @ionispharma.

*Spinraza is marketed by Biogen.

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' majority-owned affiliate. 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, 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, 2018, 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 TM 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 December 31, 2019		Year ended December 31, 2018	
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$81	\$70	\$293	\$238
Product sales, net	13	2	42	2
Licensing and royalty revenue	6	1	17	15
Total commercial revenue	100	73	352	255
Research and development revenue under collaborative agreements	394	119	771	345
Total revenue	494	192	1,123	600
Expenses:				
Cost of products sold	1	1	4	2
Research, development and patent	149	113	466	414
Selling, general and administrative	83	67	287	245
Total operating expenses	233	181	757	661
Income (loss) from operations	261	11	366	(61)
Other income (expense):				
Investment income	13	11	52	30
Interest expense	(14)	(11)	(49)	(45)
Loss on early retirement of debt	(22)	-	(22)	-
Income (loss) before income tax (expense) benefit	238	11	347	(76)
Income tax (expense) benefit	(34)	292	(44)	291
Net income	\$204	\$303	\$303	\$215
Net (income) loss attributable to noncontrolling interest in Akcea Therapeutics, Inc.	(20)	17	(9)	59
Net income attributable to Ionis Pharmaceuticals, Inc. common stockholders	\$184	\$320	\$294	\$274
Basic net income per share	\$1.31	\$2.32	\$2.12	\$2.09
Diluted net income per share	\$1.28	\$2.21	\$2.08	\$2.07
Shares used in computing basic net income per share	141	138	140	132
Shares used in computing diluted net income per share	153	150	143	134

IONIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION
Condensed Consolidating Statement of Operations
(In Millions)

Year Ended,
December 31, 2019
IonisAkceaEliminationsIonis Consolidated

Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$293	\$-	\$-	\$293
Product sales, net	-	42	-	42
Licensing and royalty revenue	7	10	-	17
Total commercial revenue	300	52	-	352
Research and development revenue under collaborative agreements	334	437	-	771
Intercompany revenue	225	-	(225)	-
Total revenue	859	489	(225)	1,123
Expenses:				
Cost of products sold	2	11	(9)	4
Research, development and patent expenses	379	293	(206)	466
Selling, general and administrative	143	146	(2)	287
Profit/ loss share for TEGSEDI commercialization activities	37	(37)	-	-
Total operating expenses	561	413	(217)	757
Income (loss) from operations	298	76	(8)	366
Other income (expense):				
Investment income	47	5	-	52
Interest expense	(49)	-	-	(49)
Loss on early retirement of debt	(22)	-	-	(22)
Income before income tax expense	274	81	(8)	347
Income tax expense	(41)	(3)	-	(44)
Net income (loss)	<u>\$233</u>	<u>\$78</u>	<u>(\$8)</u>	<u>\$303</u>
Net income attributable to noncontrolling interest in Akcea Therapeutics, Inc.	-	-	(9)	(9)
Net income attributable to Ionis Pharmaceuticals, Inc. common stockholders	<u>\$233</u>	<u>\$78</u>	<u>\$(17)</u>	<u>\$294</u>

IONIS PHARMACEUTICALS, INC.
Reconciliation of GAAP to Non-GAAP Basis:
Condensed Consolidated Operating Expenses, Income (Loss) From Operations, and Net Income
(In Millions)

	Three months ended, December 31, 2019		Year ended, December 31, 2018	
	2019	2018	2019	2018
	(unaudited)			
As reported research, development and patent expenses according to GAAP	\$149	\$113	\$466	\$415
Excluding compensation expense related to equity awards	(23)	(18)	(95)	(77)
Non-GAAP research, development and patent expenses	<u>\$126</u>	<u>\$95</u>	<u>\$371</u>	<u>\$338</u>
As reported selling, general and administrative expenses according to GAAP	\$83	\$67	\$287	\$245
Excluding compensation expense related to equity awards	(12)	(15)	(51)	(55)
Non-GAAP selling, general and administrative expenses	<u>\$71</u>	<u>\$52</u>	<u>\$236</u>	<u>\$190</u>
As reported operating expenses according to GAAP	\$233	\$181	\$757	\$661
Excluding compensation expense related to equity awards	(35)	(34)	(147)	(131)
Non-GAAP operating expenses	<u>\$198</u>	<u>\$147</u>	<u>\$610</u>	<u>\$530</u>
As reported income (loss) from operations according to GAAP	\$261	\$11	\$366	\$(61)
Excluding compensation expense related to equity awards	(35)	(34)	(147)	(131)
Non-GAAP income from operations	<u>\$296</u>	<u>\$45</u>	<u>\$513</u>	<u>\$70</u>
As reported net income attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP	\$184	\$320	\$294	\$274
Excluding compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	(33)	(31)	(139)	(120)
Income tax effect related to compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	5	21	31	21
Non-GAAP net income attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP	<u>\$212</u>	<u>\$330</u>	<u>\$402</u>	<u>\$373</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 the related tax effect. Compensation expense related to equity awards are non-cash. 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, 2019	December 31, 2018
Assets:		
Cash, cash equivalents and short-term investments	\$2,500	\$2,084
Contracts receivable	63	13
Other current assets	158	111
Property, plant and equipment, net	154	132
Other assets	358	328
Total assets	<u>\$3,233</u>	<u>\$2,668</u>
Liabilities and stockholders' equity:		
Other current liabilities	\$155	\$ 120
Current portion of deferred contract revenue	118	160
1% convertible senior notes	275	568
0.125% convertible senior notes	435	-
Long-term obligations, less current portion	75	65
Long-term deferred contract revenue	490	567
Total Ionis stockholders' equity	1,471	1,049
Noncontrolling interest in Akcea Therapeutics, Inc.	214	139
Total stockholders' equity	<u>1,685</u>	<u>1,188</u>
Total liabilities and stockholders' equity	<u>\$3,233</u>	<u>\$2,668</u>

IONIS PHARMACEUTICALS, INC.
Condensed Consolidating Balance Sheet
(In Millions)

	December 31, 2019			
	Ionis Akcea		Eliminations	Ionis Consolidated
Assets:				
Cash, cash equivalents and short-term investments	\$2,036	\$464	\$-	\$2,500
Contracts receivable	53	10	-	63
Other current assets	138	23	(3)	158
Property, plant and equipment, net	149	5	-	154
Other assets	1,105	97	(844)	358
Total assets	<u>\$3,481</u>	<u>\$599</u>	<u>(\$847)</u>	<u>\$3,233</u>
Liabilities and stockholders' equity:				
Other current liabilities	\$118	\$40	\$(3)	\$155
Current portion of deferred contract revenue	116	2	-	118
1% convertible senior notes	275	-	-	275
0.125% convertible senior notes	435	-	-	435
Long-term obligations, less current portion	61	14	-	75
Long-term deferred contract revenue	492	-	(2)	490
Total stockholders' equity before noncontrolling interest	1,984	543	(1,056)	1,471
Noncontrolling interest in Akcea Therapeutics, Inc.	-	-	214	214
Total stockholders' equity	<u>1,984</u>	<u>543</u>	<u>(842)</u>	<u>1,685</u>
Total liabilities and stockholders' equity	<u>\$3,481</u>	<u>\$599</u>	<u>(\$847)</u>	<u>\$3,233</u>

SOURCE Ionis Pharmaceuticals, Inc.

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