Ionis provides third quarter financial results and improved 2019 guidance

November 6, 2019

Year-to-date revenues increased more than 50% to nearly $630 million
Ionis increases 2019 revenue guidance to $1 billion
Ionis significantly improves operating income and net income guidance
Webcast today, November 6, 2019, at 11:30 a.m. Eastern Time

CARLSBAD, Calif., Nov. 6, 2019 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today reported its financial results for the third quarter and year-to-date 2019 and recent business highlights.

"Our commitment to innovation and to advancing our antisense technology has enabled us to produce a broad pipeline of potentially transformational medicines for patients with rare and common diseases. Our commercial medicines, SPINRAZA, TEGSEDI and WAYLIVRA, are important examples of the life-changing potential of our pipeline. In early October, we licensed AKCEA-ANGPTL3-L_{Rx} to Pfizer, which plans to develop it for the millions of people with certain cardiovascular and metabolic diseases. The favorable up-front and back-end economics we achieved with this transaction, coupled with the recent commitments by Novartis, Bayer and GSK to advance our medicines for broad patient populations, reflect the substantial and increasing value of our technology," said Stanley T. Crooke, M.D., Ph.D., chairman of the board and chief executive officer of Ionis. "Our significantly improved financial guidance is a result of the substantial economics we can command for our medicines and technology. As we continue to advance our pipeline and technology, we aim to deliver even greater value to patients and shareholders. In keeping with that goal, our board of directors has authorized a share repurchase program."

Revised 2019 Financial Guidance

The Company's revised full year 2019 financial guidance consists of the following components (on a non-GAAP basis):

	Improved Guidance	Previous Guidance
Total Revenue	~$1 billion	>$725 million
R&D Expenses	unchanged	~$360 million to $390 million
SG&A Expenses	unchanged	~$260 million to $290 million
Operating Income	>$375 million	>$100 million
Net Income	>$300 million	achieve net income
Cash and Short-Term Investments	~$2.2 billion	~$2 billion

"Our strong financial results put us on track to achieve $1 billion in revenue and more than $300 million in net income this year. Our strong financial position is driven by growth in our commercial revenues primarily from SPINRAZA's continued blockbuster performance and substantial R&D revenues from our numerous partnerships, including our recent Pfizer collaboration. Based on these strong results, we are substantially increasing our 2019 revenue, operating income and net income guidance. We plan to deliver these full year results while continuing to invest aggressively in commercializing TEGSEDI and WAYLIVRA and advancing our pipeline and technology. Our ability to achieve these successes while maintaining a strong balance sheet and delivering value to patients and shareholders continues to set us apart from our peers," said Elizabeth L. Hougen, chief financial officer of Ionis.

Year-to-Date 2019 Financial Results and Highlights

- Revenues for the first nine months ended September 30, 2019 increased by more than 50 percent, driven by SPINRAZA's continued blockbuster performance and increasing R&D revenue
  - Commercial revenue from SPINRAZA® (nusinersen) royalties increased by more than 25 percent to $212 million compared to 2018.
  - Product sales from TEGSEDI® (inotersen) and WAYLIVRA® (volanesorsen) were $29 million.
  - R&D revenue increased by more than 65 percent to $377 million compared to 2018.
- On track to achieve the fourth consecutive year of operating income and third consecutive year of net income, both on a non-GAAP basis
  - Operating income and net income significantly improved to $105 million and $110 million, respectively, compared to 2018, on a GAAP basis.
  - Non-GAAP operating income increased by more than 8-fold compared to 2018.
  - Non-GAAP net income increased by more than 4-fold compared to 2018.
- Maintained substantial cash position of $2.2 billion for the third quarter
- Ionis' board of directors approved an initial share repurchase program of up to $125 million. The company may consider additional share repurchases in the future as part of the company's overall capital allocation strategy.

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.

"With Phase 3 programs for AKCEA-APO(a)-L_{Rx} and AKCEA-TTR-L_{Rx} expected to begin soon, we are on track to achieve our goal of advancing four late-stage medicines into Phase 3 development this year. These programs, together with our medicines for Huntington's disease and SOD1-ALS, represent significant commercial opportunities. We had multiple new medicines enter development, including our medicine targeting LRRK2 for the treatment of people with Parkinson's disease. We also added multiple wholly owned programs to our already broad pipeline," said Brett P. Monia, chief operating officer at Ionis. "We are looking forward to numerous upcoming data events through the middle of next year, including Phase 2 data for AKCEA-ANGPTL3-L_{Rx} and AKCEA-APOCIII-L_{Rx}. We are also excited to report data from our aerosol-delivered medicine for cystic fibrosis, which has

the potential to broaden the reach of our technology to treat diseases of the lung."

Recent Business Highlights

- SPINRAZA – global foundation-of-care for the treatment of patients of all ages with spinal muscular atrophy (SMA)
  - Worldwide sales of SPINRAZA in the first nine months of 2019 increased by nearly 25 percent to over $1.5 billion compared to last year.
  - Patients on SPINRAZA treatment increased by approximately 11 percent compared to last quarter to approximately 9,300 patients across global commercial, clinical and expanded access settings.
  - Biogen plans to initiate 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.
  - Biogen presented new long-term follow up data from NURTURE and SHINE, adding to the body of evidence underscoring SPINRAZA's durable efficacy and established safety profile across a broad range of SMA patients.
    - NURTURE: Data from pre-symptomatic infants treated for up to nearly four years demonstrating consistent safety and unprecedented motor milestone achievement compared to natural history were published online in *Neuromuscular Disorders*.
    - SHINE: Data demonstrating continuing improvement or stabilization in one or more measures of motor function in patients with later-onset SMA treated with SPINRAZA for up to nearly six years were presented at the annual Congress of the European Pediatric Neurology Society.
- TEGSEDI – launched in multiple markets for the treatment of polyneuropathy of hereditary transthyretin amyloidosis (hATTR) in adult patients
  - Approved in Brazil and preparing to launch through PTC Therapeutics
  - First commercial patients treated in the United Kingdom following acceptance by the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC)
  - Successfully completed pricing negotiations in Germany
  - Launched in Sweden and Austria following successful completion of reimbursement negotiations
  - Preparing to launch in additional EU countries
- WAYLIVRA – launched in the EU for the treatment of adults with genetically confirmed familial chylomicronemia syndrome (FCS) at high risk for pancreatitis
  - First commercial patients treated in Germany, and a reimbursed early access program (ATU) launched in France
  - Preparing to launch in additional EU countries
  - Published results from Phase 3 APPROACH study in patients with FCS in *The New England Journal of Medicine (NEJM)*
  - Reported top-line results from the BROADEN study of WAYLIVRA in patients with familial partial lipodystrophy (FPL), which met the primary endpoint and a key secondary endpoint
- Biogen Collaboration – Developing robust pipeline of medicines for the treatment of neurological diseases
  - Dosed the first patient in a Phase 1/2 study targeting LRRK2 for the treatment of people with Parkinson's disease
  - Advanced multiple programs, with eight programs now in development
- Ionis and Akcea generated $250 million when Pfizer licensed AKCEA-ANGPTL3-L_{Rx} to treat patients with certain cardiovascular and metabolic diseases.
  - The companies are eligible to receive up to $1.3 billion in milestone payments plus tiered double-digit royalties on worldwide net sales.
  - Ionis' 50 percent portion of the $250 million license fee is expected to be settled in Akcea common stock, demonstrating Ionis' confidence in the future of Akcea.
- Ionis earned a $25 million license fee from GSK to develop and commercialize Ionis' program for the treatment of people with chronic hepatitis B virus infection.
- Ionis generated $10 million from Bayer to advance IONIS-FXI-L_{Rx} for the treatment of people with clotting disorders.
- Akcea and Ionis presented data from the Phase 1/2 study of AKCEA-TTR-L_{Rx} in healthy volunteers demonstrating >90 percent target reduction and a positive safety profile at the European ATTR Amyloidosis meeting and at the Heart Failure Society of America.
- Roche expanded enrollment in the GENERATION HD1 Phase 3 study of IONIS-HTT_{Rx} (RG6042) in patients with Huntington's disease (HD).
- Ionis initiated a Phase 2 study of IONIS-FB-L_{Rx} in patients with IgA nephropathy, the second disease indication under its collaboration with Roche to develop the medicine for complement-mediated diseases.

Key Upcoming Events

- Ionis and GSK plan to report data from the HBV clinical program at the AASLD Liver Meeting in November 2019.
- Ionis and Akcea plan to initiate the Phase 3 program for AKCEA-TTR-L_{Rx} in the fourth quarter of 2019.
- Novartis plans to begin enrolling patients in the Phase 3 HORIZON cardiovascular outcomes study of AKCEA-APO(a)-L_{Rx}.
- Akcea and Ionis plan to report top line results from Phase 2 studies of AKCEA-ANGPTL3-L_{Rx} and AKCEA-APOCIII-L_{Rx} in

early 2020.

- Ionis plans to report data from healthy volunteers evaluated in a Phase 1 study of IONIS-ENaC-2.5$_{Rx}$, an aerosol-delivered medicine in development for the treatment of people with cystic fibrosis.
- Roche plans to present data from the open-label extension portion of the Phase 1/2 study of IONIS-HTT$_{Rx}$ (RG6042) and natural history study in patients with Huntington's disease.

Revenue

Ionis' revenue increased by more than 50 percent for the first nine months of 2019 compared to the same period in 2018 and was comprised of the following (amounts in millions):

	Three months ended September 30,		Nine months ended September 30,	
	2019	2018	2019	2018
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$82	$70	$212	$168
Product sales, net	12	-	29	-
Licensing and royalty revenue	2	13	11	14
Total commercial revenue	96	83	252	182
R&D Revenue:				
Amortization from upfront payments	23	31	100	92
Milestone payments	12	26	64	45
License fees	26	1	198	64
Other services	11	4	15	25
Total R&D revenue	72	62	377	226
Total revenue	$168	$145	$629	$408

In the fourth quarter of 2019, Ionis expects to recognize substantially all of the $250 million upfront payment it generated for Akcea's license of AKCEA-ANGPTL3-L$_{Rx}$ to Pfizer and $10 million from Bayer for advancing IONIS-FXI-L$_{Rx}$.

Operating Expenses

Operating expenses increased for the nine months ended September 30, 2019, compared to the same period in 2018 principally due to Ionis' investment in the global launch of TEGSEDI and the launch of WAYLIVRA in the EU.

Income Tax Expense

Ionis' income tax expense in the nine months of this year was primarily due to Ionis' expectation that it will generate U.S. federal and state taxable income in 2019.

Net Loss Attributable to Noncontrolling Interest in Akcea

At September 30, 2019, Ionis owned approximately 75 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 loss attributable to noncontrolling interest in Akcea" on Ionis' statement of operations. Ionis' net loss attributable to noncontrolling interest in Akcea for the three and nine months ended September 30, 2019 decreased compared to the same periods in 2018 primarily because Akcea had a smaller net loss for the three and nine months ended September 30, 2019 compared to the same periods in 2018 primarily as a result of the $150 million license fee Akcea earned from Novartis when Novartis licensed AKCEA-APO(a)-L$_{Rx}$ in the first quarter of 2019. Upon closing of Pfizer's license of AKCEA-ANGPTL3-L$_{Rx}$, Ionis expects to receive 6.9 million shares of Akcea common stock as payment for the sublicense fee Akcea owes Ionis.

Net Income (Loss) Attributable to Ionis Common Stockholders

The increase in Ionis' net income attributable to Ionis' common stockholders for the three and nine months ended September 30, 2019 compared to the same periods in 2018 was primarily due to an increase in revenue. On a GAAP basis, Ionis reported net income attributable to Ionis' common stockholders for the three months and nine months ended September 30, 2019, compared to net losses for the same periods in 2018. On a non-GAAP basis, Ionis reported higher net income attributable to Ionis' common stockholders for the three and nine months ended September 30, 2019, compared to the same periods in 2018.

Ionis' basic and diluted earnings per share also improved during the three months and nine months ended September 30, 2019, compared to the same periods in 2018.

Balance Sheet

Ionis maintained its strong balance sheet, ending the third quarter of 2019 with cash, cash equivalents and short-term investments of $2.2 billion, compared to $2.1 billion at December 31, 2018. Ionis expects its cash position to increase in the fourth quarter of 2019 when it receives the payments the Company recently generated from Pfizer and Bayer.

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 drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. 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, INC.
SELECTED FINANCIAL INFORMATION
Condensed Consolidated Statements of Operations

(In Millions, Except Per Share Data)

	Three months ended, September 30,		Nine months ended, September 30,	
	2019	2018	2019	2018
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$82	$70	$212	$168
Product sales, net	12	-	29	-
Licensing and royalty revenue	2	13	11	14
Total commercial revenue	96	83	252	182
Research and development revenue under collaborative agreements	72	62	377	226
Total revenue	168	145	629	408
Expenses:				
Cost of products sold	1	-	3	-
Research, development and patent	104	95	317	301
Selling, general and administrative	60	69	204	179
Total operating expenses	165	164	524	480
Income (loss) from operations	3	(19)	105	(72)
Other income (expense):				
Investment income	13	10	39	19
Interest expense	(12)	(11)	(35)	(34)
Income (loss) before income tax benefit (expense)	4	(20)	109	(87)
Income tax benefit (expense)	14	- -	(10)	(1)
Net income (loss)	$18	$(20)	$99	$(88)

Net loss attributable to noncontrolling interest in Akcea Therapeutics, Inc.	8	15	11	42
Net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders	$26	$(5)	$110	$(46)
Basic net income (loss) per share	$0.19	$(0.03)	$0.81	$(0.33)
Diluted net income (loss) per share	$0.18	$(0.03)	$0.79	$(0.33)
Shares used in computing basic net income (loss) per share	141	137	140	131
Shares used in computing diluted net income (loss) per share	143	137	143	131

IONIS PHARMACEUTICALS, INC.

SELECTED FINANCIAL INFORMATION
Condensed Consolidating Statement of Operations

(In Millions)

	Nine months ended, September 30, 2019 (unaudited)			
	Ionis	Akcea	Eliminations	Ionis Consolidated
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$$212	$ -	$ -	$212
Product sales, net	-	29	-	29
Licensing and royalty revenue	5	6	-	11
Total commercial revenue	217	35	-	252
Research and development revenue under collaborative agreements	201	176	-	377
Intercompany revenue	97	-	(97)	-
Total revenue	515	211	(97)	629
Expenses:				
Cost of products sold	-	10	(7)	3
Research, development and patent expenses	253	145	(81)	317
Selling, general and administrative	102	102	-	204
Profit/ loss share for TEGSEDI commercialization activities	29	(29)	-	-
Total operating expenses	384	228	(88)	524
Income (loss) from operations	131	(17)	(9)	105
Other income (expense):				
Investment income	35	4	-	39
Interest expense	(35)	-	-	(35)
Income (loss) before income tax expense	131	(13)	(9)	109
Income tax expense	(9)	(1)	-	(10)
Net income (loss)	$122	$(14)	$(9)	$99
Net loss attributable to noncontrolling interest in Akcea Therapeutics, Inc.	-	-	11	11
Net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders	$122	$(14)	$2	$110

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, September 30,		Nine months ended, September 30,	
	2019	2018	2019	2018
	(unaudited)			
As reported research, development and patent expenses according to GAAP	$104	$95	$317	$301
Excluding compensation expense related to equity awards	(24)	(19)	(72)	(57)
Non-GAAP research, development and patent expenses	$80	$76	$245	$244
As reported selling, general and administrative expenses according to GAAP	$60	$69	$204	$179
Excluding compensation expense related to equity awards	-	(16)	(39)	(40)
Non-GAAP selling, general and administrative expenses	$60	$53	$165	$139
As reported operating expenses according to GAAP	$165	$164	$524	$480
Excluding compensation expense related to equity awards	(24)	(35)	(112)	(97)
Non-GAAP operating expenses	$141	$129	$412	$383
As reported income (loss) from operations according to GAAP	$3	$(19)	$105	$(72)
Excluding compensation expense related to equity awards	(24)	(35)	(112)	(97)
Non-GAAP income from operations	$27	$16	$217	$25
As reported net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP	$26	$(5)	$110	$(46)
Excluding compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	(25)	(32)	(104)	(89)
Income tax effect related to compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	12	-	25	-
Non-GAAP net income attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP	$39	$27	$189	$43

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)

	September 30, 2019	December 31, 2018
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$2,221	$2,084
Contracts receivable	49	13
Other current assets	138	111
Property, plant and equipment, net	149	132
Other assets	338	328
Total assets	$2,895	$2,668
Liabilities and stockholders' equity:		
Other current liabilities	$94	$ 120
Current portion of deferred contract revenue	138	160
1% convertible senior notes	596	568
Long-term obligations, less current portion	76	65
Long-term deferred contract revenue	493	567
Total Ionis stockholders' equity	1,336	1,049
Noncontrolling interest in Akcea Therapeutics, Inc.	162	139
Total stockholders' equity	1,498	1,188
Total liabilities and stockholders' equity	$2,895	$2,668

IONIS PHARMACEUTICALS, INC.

Condensed Consolidating Balance Sheet
(In Millions)

	September 30, 2019 (unaudited)			
	Ionis	Akcea	Eliminations	Ionis Consolidated
Assets:				
Cash, cash equivalents and short-term investments	$1,968	$253	$-	$2,221
Contracts receivable	38	11	-	49
Other current assets	124	14	-	138
Property, plant and equipment, net	144	5	-	149
Other assets	959	100	(721)	338
Total assets	$3,233	$383	$(721)	$2,895
Liabilities and stockholders' equity:				
Other current liabilities	$62	$32	$-	$94
Current portion of deferred contract revenue	127	11	-	138
1% convertible senior notes	596	-	-	596
Long-term obligations, less current portion	61	15	-	76
Long-term deferred contract revenue	495	-	(2)	493
Total stockholders' equity before noncontrolling interest	1,892	325	(881)	1,336
Noncontrolling interest in Akcea Therapeutics, Inc.	-	-	162	162
Total stockholders' equity	1,892	325	(719)	1,498
Total liabilities and stockholders' equity	$3,233	$383	$(721)	$2,895

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SOURCE Ionis Pharmaceuticals, Inc.

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