Ionis Reports Fourth Quarter and Full Year 2017 Financial Results

February 27, 2018

SPINRAZA launch one of the most successful in rare disease history
FY 2017 GAAP operating income of $25M; FY 2017 pro forma operating income of $111M
2017 year-end cash over $1B
Mid-2018 launches planned for inotersen and volanesorsen
Conference call and webcast today, February 27, 2018, at 11:30 a.m. Eastern Time

CARLSBAD, Calif., Feb. 27, 2018 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) today reported its financial results for the fourth quarter and full year 2017 and highlighted recent progress in advancing its business and drug pipeline.

"In 2017, our accomplishments were remarkable. The historic launch of SPINRAZA and the acceptance of our regulatory filings for inotersen and volanesorsen, which set up potential launches of these two drugs in 2018, combined with our strong financial performance, demonstrate our ability to execute across all areas of our business. We also advanced our pipeline of novel drugs with positive data readouts from 11 clinical studies, including five with our LICA drugs, and introduced eight new drugs to the pipeline, further highlighting the broad capabilities and potential of our antisense technology platform," said Stanley T. Crooke, M.D., Ph.D., chairman of the board and chief executive officer.

"Looking ahead, we believe 2018 could be an important turning point for Ionis. Most important will be the launch of inotersen and volanesorsen, if approved. We also expect to report data from at least six Phase 2 studies, initiate at least five Phase 2 programs and report data from multiple proof-of-concept clinical studies. These important events build on our recent momentum, solidifying Ionis as a multi-product, commercial company delivering innovative antisense medicines to patients in need," continued Crooke. "As we advance our pipeline of antisense drugs and achieve important milestones in our collaborations, we expect to continue to provide substantial value to our shareholders and the patients we serve."

Financial Results and Highlights

- *Revenues for 2017 increased by more than 45%*
  - For the fourth quarter and full year 2017, revenue was $172 million and $508 million, compared to $160 million and $347 million for the same periods in 2016.
  - Commercial revenue for 2017 was $113 million from SPINRAZA royalties and $9 million from other licensing and royalty payments. R&D revenue for 2017 was $386 million and increased by nearly 20% from 2016.
- *Operating income for 2017 increased by more than 150%, driven by strong revenues and reflecting prudent expense management*
  - GAAP operating income was $25 million for 2017, compared to a GAAP operating loss of $46 million for the same period in 2016. Pro forma operating income was $111 million for 2017, compared to $26 million for the same period in 2016.
  - Operating expenses increased at a much slower rate than revenue with the increase primarily due to higher SG&A expenses as Ionis prepares to commercialize volanesorsen and inotersen this year.
- *Substantial cash position enabled pipeline progress*
  - As of December 31, 2017, Ionis had cash, cash equivalents and short-term investments of more than $1 billion compared to $665 million at December 31, 2016.
  - During 2017 Ionis received over $580 million in partner payments. Additionally, Ionis' cash balance at December 31, 2017 included proceeds from Akcea's 2017 IPO and Novartis' strategic investment in Akcea.

"2017 was our first year of commercial revenue in which we earned $113 million in SPINRAZA royalties. It was also our sixth consecutive year of revenue growth, driven by our focus on high-value, innovative drugs like SPINRAZA and multiple other exciting programs in our pipeline," said Elizabeth L. Hougen, chief financial officer of Ionis. "Our goal is to be a multi-product, sustainably profitable company. Consistent with this goal, we project 2018 will be our third consecutive year of pro forma operating profitability even as we prepare to launch two new drugs. For 2018, we are projecting R&D expenses of $360 million to $390 million and SG&A expenses of $180 million to $210 million both on a pro forma basis. We project that we will end 2018 with more than $800 million in cash."

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

Recent Pipeline and Technology Highlights

- *SPINRAZA for SMA – one of the most successful orphan drug launches in history*

    - SPINRAZA®, commercialized by Biogen, generated 2017 global sales of $884 million
    - Results from the ENDEAR study and CHERISH study, in which people with infantile-onset and later-onset SMA, respectively, were treated with SPINRAZA, were published in *The New England Journal of Medicine*
    - Prestigious 2017 Prix Galien USA Award for Best Biotechnology Product awarded to Ionis and Biogen for SPINRAZA
    - New collaboration with Biogen initiated to discover new antisense drugs with enhanced properties to treat SMA
- *Inotersen for hATTR – potential to transform the lives of people with hATTR*
    - Marketing applications accepted, no FDA Advisory Committee recommended, Priority Review in the U.S. and Accelerated Assessment in the EU
    - Preparations for global launch, planned for mid-2018, progressing
    - Phase 3 NEURO-TTR study met both primary endpoints demonstrating benefit compared to placebo in multiple measures of quality of life and disease severity; 50% of inotersen-treated patients experienced improvement from baseline in quality of life
- *Volanesorsen for FCS and FPL – potential first treatment for people with FCS*
    - Marketing applications accepted in the U.S., EU and Canada with Promising Innovative Medicine designation in the UK and Priority Review in Canada
    - Preparations for global launch for FCS, planned for mid-2018, progressing
    - Phase 3 APPROACH study met primary endpoint of reducing triglyceride levels in people with FCS
- *Pipeline Programs (early and mid-stage) – advancing wholly owned and partnered programs*
    - Positive results from seven Phase 2 studies reported, including:
        - Positive data from Phase 1/2 study of IONIS-STAT3-2.5$_{Rx}$ in combination with AstraZeneca's Imfinzi reported for people with head and neck cancer
        - Robust, dose-dependent reductions of mHTT observed in people with Huntington's disease treated with IONIS-HTT$_{Rx}$
    - Positive clinical data on five LICA drugs reported, demonstrating consistent, positive performance and sustained target reduction with potential for monthly or less frequent dosing
    - Positive results from six Phase 1 studies reported
    - Nine Phase 2 studies and four Phase 1 studies initiated across multiple therapeutic areas to treat people with both broad and rare diseases

"In 2017, we and our partners advanced key programs in all of our therapeutic areas, including cardiometabolic, oncology, neurology, and severe and rare disease. Of the eight new drugs we added to the pipeline, six were drugs that use our more potent LICA technology or Generation 2.5 chemistry, and two were drugs to treat neurodegenerative disorders. We also added to our pipeline our second orally delivered, locally acting drug for a GI autoimmune disease. These achievements demonstrate the success of our wholly owned and partnered programs," said Brett P. Monia, Ph.D., chief operating officer and senior vice president of antisense drug discovery and translational medicine at Ionis Pharmaceuticals. "Looking ahead, we plan to pursue only those partnerships with infrastructure and resources that complement our own. Simultaneously, we plan to continue to build our wholly owned pipeline of drugs to treat patients with rare and serious diseases."

Expected Events Through Mid-2018

- Launch of inotersen for people with hATTR, if approved
- Launch of volanesorsen for people with FCS, if approved
- Report results from five Phase 2 programs, including data from studies with IONIS-HTT$_{Rx}$ in people with Huntington's disease and data from a 6-12 month study with AKCEA-APO(a)-L$_{Rx}$ in people with high Lp(a) and cardiovascular disease
- Initiate up to six Phase 2 or Phase 3 studies and three Phase 1 studies, including the initiation of a clinical study with follow-on LICA drug, IONIS-TTR-L$_{Rx}$

Revenue

Ionis' revenue for the fourth quarter and full year 2017 was $172.3 million and $507.7 million, compared to $160.3 million and $346.6 million for the same periods in 2016. Ionis' revenue in 2017 consisted of the following:

Commercial Revenue:

- $113 million from SPINRAZA royalties; and
- $9 million from other licensing and royalty payments.

R&D Revenue:

- $118 million in milestone payments from Biogen, including $90 million in milestone payments for SPINRAZA, $15 million for validating two undisclosed neurological disease targets and $10 million for initiating a Phase 1/2 study of IONIS-MAPT$_{Rx}$;
- $65 million from Bayer for the license of IONIS-FXI-L$_{Rx}$;
- $48 million from Roche primarily for the license of IONIS-HTT$_{Rx}$;

- $10 million from Janssen for license of IONIS-JBI2-2.5$_{Rx}$ and initiation of Phase 1 study of IONIS-JBI1-2.5$_{Rx}$;
- $115 million from the amortization of upfront fees; and
- $30 million from services Ionis performed for its partners, of which more than half related to manufacturing services.

Ionis' R&D revenue may fluctuate quarterly based on the nature and timing of payments under agreements with its partners and consists primarily of revenue from the amortization of upfront fees, milestone payments and license fees.

At the beginning of 2018, Ionis adopted the new revenue recognition accounting standard on a retrospective basis, which means that starting with the first quarter, Ionis will begin showing all periods presented using the new standard. The Company does not anticipate that there will be a significant impact to its previously reported revenue. Under the new standard, Ionis' revenue for 2017 will increase by approximately 3%.

Operating Expenses

Operating expenses for the fourth quarter and full year 2017 on a GAAP basis were $174.0 million and $483.1 million, respectively, and on a pro forma basis were $151.7 million and $397.2 million, respectively. This is compared to GAAP operating expenses of $119.2 million and $392.9 million and pro forma operating expenses of $104.0 million and $320.8 million for the same periods in 2016. Operating expenses increased in 2017, compared to 2016, principally due to higher SG&A expenses as Ionis prepares to commercialize volanesorsen and inotersen in 2018. The Company's SG&A expenses also increased in 2017 compared to 2016 because of fees it owes under its in-licensing agreements related to SPINRAZA.

Net Income (Loss)

Ionis reported a net loss of $4.7 million and $17.3 million for the fourth quarter and full year 2017, respectively, compared to net income of $25.9 million and a net loss of $86.6 million for the same periods in 2016, all according to GAAP. On a pro forma basis, Ionis reported net income of $17.7 million and $68.7 million for the fourth quarter and full year 2017, respectively, compared to net income of $41.0 million and a net loss of $14.4 million for the same periods in 2016. Ionis' GAAP and pro forma net loss improved for 2017 compared to 2016 primarily due to the addition of commercial revenue from SPINRAZA royalties and increased R&D revenue.

Additionally, in 2017, Ionis recorded two non-cash, non-recurring items in other expenses, which contributed to the Company's net loss. These two items were the previously capitalized fair value of the potential premium Ionis would have received from Novartis if Akcea had not completed its IPO and the loss the Company recognized on the purchase of its primary R&D facility. In 2016, Ionis recorded a $4.0 million non-cash loss related to the early repurchase of its 2¾ percent convertible senior notes, which contributed to the Company's net loss for 2016.

Net Loss Attributable to Noncontrolling Interest in Akcea Therapeutics, Inc.

Akcea sold shares of its common stock to third parties in its IPO in July 2017. From the closing of the IPO through the end of 2017, Ionis owned 68 percent of Akcea. The shares held by third parties 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 holders 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 fourth quarter and full year 2017 was $7.4 million and $11.3 million, respectively. Ionis also added a corresponding account in its stockholders' equity section on its balance sheet called "Noncontrolling interest in Akcea Therapeutics, Inc."

Net Income (Loss) Attributable to Ionis Common Stockholders

Ionis reported net income attributable to Ionis' common stockholders of $2.7 million for the fourth quarter of 2017, compared to $25.9 million for the same period in 2016. For the full years 2017 and 2016, Ionis reported a net loss attributable to Ionis' common stockholders of $6.0 million and $86.6 million, respectively. For the fourth quarter of 2017, basic and diluted net income per share were $0.02 compared to basic and diluted net income per share of $0.21 for the same period in 2016. For the full year 2017, basic and diluted net income per share were $0.08 compared to basic and diluted net loss per share of $0.72 for the same period in 2016.

Webcast and Conference Call

Today, at 11:30 a.m. Eastern Time, Ionis will conduct a live webcast conference call to discuss this earnings release and related activities. Interested parties may listen to the call by dialing 877-443-5662 or access the webcast at www.ionispharma.com. A webcast replay will be available for a limited time.

ABOUT IONIS PHARMACEUTICALS

Ionis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Ionis has created a large pipeline of first-in-class or best-in-class drugs, with over three dozen drugs in development. SPINRAZA® (nusinersen) has been approved in global markets for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Drugs that have successfully completed Phase 3 studies include inotersen, an antisense drug Ionis is developing to treat patients with hereditary TTR amyloidosis (hATTR), and volanesorsen, an antisense drug discovered by Ionis and co-developed by Ionis and Akcea Therapeutics to treat patients with familial chylomicronemia syndrome or familial partial lipodystrophy. Akcea, an affiliate of Ionis, is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders. If approved, volanesorsen will be commercialized through Ionis' affiliate, Akcea. Inotersen filings for marketing approval have been submitted in the U.S. and EU. Volanesorsen filings for marketing approval have been submitted in the U.S., EU, and Canada. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

IONIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Ionis' business, financial guidance and the therapeutic and commercial potential of SPINRAZA, inotersen, volanesorsen and Ionis' technologies and products in development, including the business of Akcea Therapeutics, Inc., Ionis' majority 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, 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, 2016, and its most recent quarterly report on Form 10-Q, 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 trademark of Ionis Pharmaceuticals, Inc. SPINRAZA® is a registered trademark of Biogen.

IONIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION
Condensed Consolidated Statements of Operations
(In Thousands, Except Per Share Data)

	Three months ended, December 31,		Year ended, December 31,	
	2017	2016	2017	2016
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$52,073	$ 883	$112,540	$ 883
Licensing and royalty revenue	4,537	150	9,519	19,839
Total commercial revenue	56,610	1,033	122,059	20,722
Research and development revenue under collaborative agreements	115,689	159,316	385,607	325,898
Total revenue	172,299	160,349	507,666	346,620
Expenses:				
Research, development and patent expenses	128,285	101,151	374,644	344,320
Selling, general and administrative	45,707	18,043	108,488	48,616
Total operating expenses	173,992	119,194	483,132	392,936
Income (loss) from operations	(1,693)	41,155	24,534	(46,316)
Other income (expense):				
Investment income	654	1,561	8,179	5,472
Interest expense	(10,787)	(9,934)	(44,752)	(38,795)
Loss on extinguishment of financing liability for leased facility	-	(3,983)	(7,689)	(3,983)
Other expenses	-	-	(3,548)	-
Income (loss) before income tax benefit (expense)	(11,826)	28,799	(23,276)	(83,622)
Income tax benefit (expense)	7,164	(2,934)	5,980	(2,934)
Net income (loss)	(4,662)	25,865	(17,296)	(86,556)
Net loss attributable to noncontrolling interest in Akcea Therapeutics, Inc.	7,406	-	11,326	-
Net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders	$2,744	$25,865	$(5,970)	$(86,556)
Basic net income (loss) per share	$0.02	$0.21	$0.08	$(0.72)
Diluted net income (loss) per share	$0.02	$0.21	$0.08	$(0.72)
Shares used in computing basic net income (loss) per share	124,818	121,340	124,016	120,933

Shares used in computing diluted net income (loss) per share	126,862	123,953	126,098	120,933

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

	Three months ended, December 31,		Year ended, December 31,	
	2017	2016	2017	2016
	(unaudited)			
As reported operating expenses according to GAAP	$173,992	$119,194	$483,132	$392,936
Excluding compensation expense related to equity awards	(22,333)	(15,158)	(85,975)	(72,108)
Pro forma operating expenses	$151,659	$104,036	397,157	$320,828
As reported income (loss) from operations according to GAAP	$(1,693)	$41,155	$24,534	$(46,316)
Excluding compensation expense related to equity awards	(22,333)	(15,158)	(85,975)	(72,108)
Pro forma income (loss) from operations	$20,640	$56,313	$110,509	$25,792
As reported net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP	$2,744	$25,865	$(5,970)	$(86,556)
Excluding compensation expense related to equity awards	(22,333)	(15,158)	(85,975)	(72,108)
Pro forma net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders	$25,077	$41,023	$80,005	$(14,448)

Reconciliation of GAAP to Pro Forma Basis

As illustrated in the Selected Financial Information in this press release, pro forma operating expenses, pro forma income (loss) from operations, and pro forma net income (loss) were adjusted from GAAP to exclude compensation expense related to equity awards, which are non-cash. Ionis has regularly reported non-GAAP measures for operating results as pro forma results. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. Ionis reports these pro forma 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' pro forma results is consistent with how Ionis' management internally evaluates the performance of its operations.

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

	December 31, 2017	December 31, 2016
Assets:		
Cash, cash equivalents and short-term investments	$1,022,715	$665,223
Contracts receivable	62,955	108,043
Other current assets	82,314	24,666
Property, plant and equipment, net	121,907	92,845
Other assets	32,133	21,690
Total assets	$1,322,024	$912,467
Liabilities and stockholders' equity:		
Other current liabilities	$118,276	$82,504
Current portion of deferred contract revenue	106,465	51,280
1% convertible senior notes	533,111	500,511
Long-term obligations, less current portion	72,745	87,409
Long-term deferred contract revenue	72,708	91,198
Total Ionis stockholders' equity	330,872	99,565
Noncontrolling interest in Akcea Therapeutics, Inc.	87,847	-
Total stockholders' equity	418,719	99,565
Total liabilities and stockholders' equity	$1,322,024	$912,467

IONIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION

Condensed Consolidating Statement of Operations
(In Thousands)

	Year ended, December 31, 2017			
	Ionis	Akcea	Eliminations	Ionis Consolidated
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$112,540	$-	$-	$112,540
Licensing and royalty revenue	9,519	-	-	9,519
Total commercial revenue	122,059	-	-	122,059
Research and development revenue under collaborative agreements	330,398	55,209	-	385,607
Intercompany revenue	54,407	-	(54,407)	-
Total revenue	506,864	55,209	(54,407)	507,666
Expenses:				
Research, development and patent expenses	302,281	126,890	(54,527)	374,644
Selling, general and administrative	71,507	36,981		108,488
Total operating expenses	373,788	163,871	(54,527)	483,132
Income (loss) from operations	133,076	(108,662)	120	24,534
Other income (expense):				
Investment income	8,097	1,813	(1,731)	8,179
Interest expense	(44,752)	(1,731)	1,731	(44,752)
Loss on extinguishment of financing liability for leased facility	(7,689)	-	-	(7,689)
Other expenses	(3,652)	104	-	(3,548)
Income (loss) before income tax benefit (expense)	85,080	(108,476)	120	(23,276)
Income tax benefit (expense)	7,255	(1,275)	-	5,980
Net income (loss)	92,335	(109,751)	120	(17,296)
Net loss attributable to noncontrolling interest in Akcea Therapeutics, Inc.	-	-	11,326	11,326
Net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders	$92,335	$(109,751)	$11,446	$(5,970)

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

	December 31, 2017			
	Ionis	Akcea	Eliminations	Ionis Consolidated
Assets:				
Cash, cash equivalents and short-term investments	$762,585	$260,130	$-	$1,022,715
Contracts receivable	$57,542	5,413	-	62,955
Receivable from Akcea Therapeutics, Inc.	14,365	-	(14,365)	-

Other current assets	81,012	1,302	-	82,314
Property, plant and equipment, net	121,830	77	-	121,907
Other assets	304,494	1,882	(274,243)	32,133
Total assets	$1,341,828	$268,804	$(288,608)	$1,322,024
Liabilities and stockholders' equity:				
Other current liabilities	$102,367	$30,274	$(14,365)	$118,276
Current portion of deferred contract revenue	55,886	50,579	-	106,465
1% convertible senior notes	533,111	-	-	533,111
Long-term obligations, less current portion	72,733	12	-	72,745
Long-term deferred contract revenue	66,101	8,306	(1,699)	72,708
Total stockholders' equity before noncontrolling interest	511,630	179,633	(360,391)	330,872
Noncontrolling interest in Akcea Therapeutics, Inc.	-	-	87,847	87,847
Total stockholders' equity	511,630	179,633	(272,544)	418,719
Total liabilities and stockholders' equity	$1,341,828	$268,804	$(288,608)	$1,322,024

SPINRAZA 2017 Patient Dynamics

US Patient Dynamics*	**Q1:17**	**Q2:17**	**Q3:17**	**Q4:17**
Total patients	210	710	1,240	1,650
New patient starts	210	500	530	420
Average doses per patient	2.3	2.5	1.8	1.5
% Loading doses	100%	100%	90%	75%
% Maintenance doses	0%	0%	10%	25%
% Free doses	25%	20%	20%	20%

*As announced by Biogen in their Q4:17 earnings call

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