Ionis Provides Improved 2017 Guidance Following Strong Financial Performance

August 8, 2017

Conference Call Webcast Tuesday, August 8, 11:30 a.m. ET at www.ionispharma.com

CARLSBAD, Calif., Aug. 8, 2017 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) today reported improved financial results with an operating loss of $1.7 million and operating income of $12.3 million for the three and six months ended June 30, 2017, respectively, compared to an operating loss of $48.9 million and $103.6 million for the same periods last year, all on a GAAP basis. Ionis also reported pro forma operating income of $19.6 million and $54.5 million for the three and six months ended June 30, 2017, respectively, compared to a pro forma operating loss of $29.7 million and $64.2 million for the same periods in 2016. Ionis' second quarter was the Company's fourth consecutive quarter of pro forma operating income and pro forma net income. Additionally, the Company ended the second quarter with over $855 million in cash. Based on Ionis' strong financial performance during the first half of 2017, the Company is revising upward its original pro forma operating income and cash guidance for 2017. Ionis is projecting to end the year with pro forma operating income in the mid $50 million range and a year end cash balance of more than $950 million.

"The U.S. launch of SPINRAZA continued to demonstrate sustained growth as the positive trends in the table below illustrate, resulting in second quarter sales of over $200 million. In the U.S., payers are now covering SPINRAZA broadly. In addition, launch momentum outside the U.S. continues to build," said B. Lynne Parshall, chief operating officer of Ionis Pharmaceuticals. "In June, SPINRAZA was approved in the EU with sales already in Germany and the Nordics, and additional country rollouts planned through 2018. In addition, SPINRAZA has been approved in Japan and Canada, and is under review in several other key countries with additional filings planned in 2017.

"In July, working closely with us, Akcea filed for marketing authorization for volanesorsen in the EU and is on track to file in the U.S. and Canada in September. Also in July, Akcea completed its IPO in which it raised more than $190 million, including the $25 million we invested and the $50 million Novartis AG invested. The IPO was an important step in our strategy to maximize the value of our broad pipeline. As an independent, public company of which we own nearly 70%, we believe Akcea is well-positioned to create substantial value for both Akcea and Ionis shareholders. Importantly, we can stay focused on continuing to advance our pipeline of novel, best-in-class drugs while participating significantly in the value Akcea is creating through our equity ownership and sublicensing revenue and royalties on Akcea's drugs.

"We and our partner, GSK, are preparing to file for regulatory approval for inotersen in the U.S. and EU by the end of 2017 following our report of positive top-line results from the Phase 3 NEURO-TTR study in May. GSK has an option to license inotersen following a review of the data from the NEURO-TTR study and prior to regulatory submissions.

"With regulatory plans on track for volanesorsen and inotersen, we anticipate both drugs could be on the market next year. With the strong launch and potential for growth in SPINRAZA sales, as well as volanesorsen and inotersen moving towards commercialization, we believe we are on the verge of becoming a multi-product, profitable, commercial company, delivering innovative medicines to patients in need," concluded Ms. Parshall.

	Q1:17*	**Q2:17****
SPINRAZA Sales	• $47M	• $203M
Current Approvals	• U.S.	• U.S., EU, Canada, Japan
U.S. Administration Sites	• 88	• 145
U.S. Site Start Submission Forms	• 203	• 233
U.S. Insurance Coverage	• 100 commercial plans • 65 Medicaid plans	• 80% of commercially insured patients • 65% of Medicaid patients • Most cover all SMA types
Patients in EAP	• 353 in total of which 306 in EU	• 600 in total of which 460 in EU
Current Filings	• EU, Canada, Japan	• Australia, Brazil, Switzerland, Israel, South Korea

*As of April 21, 2017

**As of July 14, 2017

Financial Results

"As a result of our strong financial performance in the first half of 2017, including our increasing SPINRAZA royalty revenue, we are revising upward our 2017 guidance. We expect to end 2017 with pro forma operating income in the mid $50 million range and more than $950 million in cash. Our revised guidance is substantially improved over our original guidance of break even at the operating line on a pro forma basis and year end cash of more than $825 million. Because we have several large potential payments in the second half of 2017, we are being particularly conservative with our guidance this year," said Elizabeth L. Hougen, chief financial officer of Ionis Pharmaceuticals.

"We reported pro forma operating income of $54 million and pro forma net income of $34 million for the first half of this year. Our results were driven by the more than $210 million of revenue we earned in the first half of this year, including the $28 million of commercial revenue from SPINRAZA royalties we added to our substantial base of R&D revenue. As expected, our operating expenses increased for the first half of 2017 compared to 2016 primarily due to higher commercialization expenses as Akcea continues to prepare to launch volanesorsen globally in 2018 and from fees we owe under our in-licensing agreements related to SPINRAZA. We received over $380 million from our partners in the first half of 2017 to end the quarter with a cash balance of more than $855 million, not including the proceeds from Akcea's IPO and the EU approval milestone payment for SPINRAZA, both of which we received in July 2017," concluded Ms. Hougen.

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.

Revenue
Ionis' revenue for the three and six months ended June 30, 2017 was $104.2 million and $214.5 million, respectively, compared to $38.5 million and $75.3 million for the same periods in 2016. Ionis' revenue in the first half of 2017 consisted of the following:

Commercial Revenue:

- $27.6 million from SPINRAZA royalties; and
- $4.1 million from other licensing and royalty payments.

R&D Revenue:

- $65.1 million from Bayer primarily for the license of IONIS-FXI-L_{Rx};
- $57.0 million from Biogen, including $50 million for the EU approval of SPINRAZA and $5 million for validating an undisclosed neurological disease target;
- $54.0 million from the amortization of upfront fees; and
- $6.7 million primarily from services Ionis performed for its partners.

Operating Expenses
Ionis' operating expenses for the three and six months ended June 30, 2017 on a GAAP basis were $105.8 million and $202.1 million, respectively, and on a pro forma basis were $84.6 million and $160.0 million, respectively. These amounts compare to GAAP operating expenses of $87.4 million and $178.9 million and pro forma operating expenses of $68.1 million and $139.6 million for the same periods in 2016. Ionis' operating expenses increased year over year principally due to higher SG&A expenses as Akcea prepares to commercialize volanesorsen globally next year and from fees Ionis owes under its in-licensing agreements related to SPINRAZA.

Net Loss
Ionis reported a net loss of $11.2 million and $7.7 million on a GAAP basis for the three and six months ended June 30, 2017, respectively, compared to a net loss of $56.9 million and $119.8 million for the same periods in 2016. Ionis reported pro forma net income of $10.1 million and $34.4 million for the three and six months ended June 30, 2017, respectively, compared to a pro forma net loss of $37.6 million and $80.4 million for the same periods in 2016. For the three and six months ended June 30, 2017, basic and diluted net loss per share was $0.09 and $0.06, respectively. Basic and diluted net loss per share for the same periods in 2016 were $0.47 and $0.99. Ionis' net loss decreased for the six months ended June 30, 2017 compared to the same period in 2016 primarily due to the addition of commercial revenue from SPINRAZA royalties and increased R&D revenue.

Balance Sheet
As of June 30, 2017, Ionis had cash, cash equivalents and short-term investments of $855.7 million compared to $665.2 million at December 31, 2016. Ionis' cash balance increased in 2017 due to the over $380 million in payments the Company received, primarily from Novartis, Bayer and Biogen. Ionis' second quarter cash balance did not include the SPINRAZA EU approval milestone payment or the proceeds from Akcea's IPO and Novartis' strategic investment. Ionis' working capital was $772.6 million at June 30, 2017 compared to $664.1 million at December 31, 2016.

Conference Call

At 11:30 a.m. Eastern Time today, August 8, 2017, 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 at the same address.

ABOUT IONIS PHARMACEUTICALS, INC.
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 the U.S., Europe, Japan and Canada for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Drugs

that have successfully completed Phase 3 studies include inotersen (IONIS-TTR$_{Rx}$), an antisense drug Ionis is developing with GSK to treat patients with hereditary TTR amyloidosis, and volanesorsen, an antisense drug discovered by Ionis and co-developed by Ionis and Akcea Therapeutics to treat patients with either 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. Both inotersen and volanesorsen are progressing toward regulatory filings for marketing authorization. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

IONIS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Ionis Pharmaceuticals' financial position and outlook, Ionis' business, the business of Akcea Therapeutics, Inc., and the therapeutic and commercial potential of Ionis' technologies and products in development, including SPINRAZA, inotersen and volanesorsen. 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' Corporate and Drug Development Highlights

(Q2 2017 and subsequent activities)

Recent SPINRAZA Accomplishments:

- Biogen reported more than $200 million from sales of SPINRAZA in the second quarter.
- The European Commission granted marketing authorization for SPINRAZA for the treatment of 5q SMA in the EU, representing approximately 95% of all SMA cases in the EU.
- SPINRAZA has begun selling in Germany and the Nordics, with additional country rollouts planned through 2018.
- Ionis earned a $50 million milestone payment from Biogen for the approval of SPINRAZA in the EU.
- SPINRAZA was also approved in Japan, for which Ionis is eligible to receive a $40 million milestone payment upon determination of pricing in Japan.
- SPINRAZA was approved in Canada.

Recent Corporate and Pipeline Accomplishments:

- Inotersen met both co-primary endpoints with a high degree of statistical significance in the Phase 3 NEURO-TTR study.
- Ionis' Phase 1/2a study of IONIS-HTT$_{Rx}$, which is partnered with Roche, completed enrollment, with data anticipated around year-end 2017 or early 2018. Ionis also announced that it plans to initiate an open-label extension study for IONIS-HTT$_{Rx}$ in the second half of 2017.
- Ionis initiated Phase 1 studies for three LICA drugs, including IONIS-GHR-L$_{Rx}$, IONIS-AGT-L$_{Rx}$ and IONIS-TMPRSS6-L$_{Rx}$.
- IONIS-BIIB7$_{Rx}$ marked the seventh neurological disease program under our Biogen collaboration for neurodegenerative diseases to enter development.
- Ionis entered a collaboration and license agreement with Suzhou Ribo Life Science Co., Ltd. (Ribo) to develop and commercialize RNA-targeted therapeutics in China.
- Ionis advanced two wholly owned drugs in its neurological disease franchise.
- Ionis, in collaboration with Dynacure, published in *Nature Communications* preclinical results evaluating antisense drugs targeting DNM2 for the treatment of centronuclear myopathy.
- Preclinical data demonstrating the potential of IONIS-KRAS-2.5$_{Rx}$ in cancer were published in *Science Translational Medicine.*
- Ionis purchased the buildings that house its research and development activities and its manufacturing suites, which should allow Ionis to realize significant cash and interest expense savings.

Recent Akcea Accomplishments:

- Akcea, working closely with Ionis, filed for marketing authorization for volanesorsen for the treatment of FCS in the EU.
- Akcea raised over $190 million in its initial public offering and the concurrent strategic investment by Novartis.
    - The underwriters for Akcea's IPO exercised their full overallotment option to purchase additional shares.
- Akcea and Ionis published key preclinical findings with angiopoietin-like 3 (ANGPTL3)-targeting drugs and Phase 1/2 clinical study results with AKCEA-ANGPTL3-L$_{Rx}$ in the *New England Journal of Medicine.*

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

	Three months ended June 30,		Six months ended June 30,	
	2017	2016	2017	2016
Revenue:	(unaudited)		(unaudited)	
Commercial revenue:				
SPINRAZA royalties	$22,366	$ -	$27,577	$ -
Licensing and royalty revenue	557	16,015	4,103	17,675
Total commercial revenue	22,923	16,015	31,680	17,675
Research and development revenue under collaborative agreements	81,229	22,455	182,776	57,670
Total revenue	104,152	38,470	214,456	75,345
Expenses:				
Research, development and patent expenses	83,506	77,573	166,144	158,536
Selling, general and administrative	22,317	9,824	35,994	20,386
Total operating expenses	105,823	87,397	202,138	178,922
Income (loss) from operations	(1,671)	(48,927)	12,318	(103,577)
Other income (expense):				
Investment income	2,465	1,466	4,744	2,921
Interest expense	(11,778)	(9,625)	(23,141)	(19,115)
Other expense	-	-	(1,438)	-
Loss before income tax (expense) benefit	(10,984)	(57,086)	(7,517)	(119,771)
Income tax (expense) benefit	(222)	231	(222)	(1)
Net loss	$(11,206)	$(56,855)	$(7,739)	$(119,772)
Basic and diluted net loss per share	$(0.09)	$(0.47)	$(0.06)	$(0.99)
Shares used in computing basic and diluted net loss per share	123,988	120,798	123,428	120,698

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, June 30,		Six months ended, June 30,	
	2017	2016	2017	2016
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$105,823	$87,397	$202,138	$178,922
Excluding compensation expense related to equity awards	(21,258)	(19,260)	(42,170)	(39,364)
Pro forma operating expenses	$84,565	$68,137	$159,968	$139,558
As reported income (loss) from operations according to GAAP	$(1,671)	$(48,927)	$12,318	$(103,577)
Excluding compensation expense related to equity awards	(21,258)	(19,260)	(42,170)	(39,364)
Pro forma income (loss) from operations	$19,587	$(29,667)	$54,488	$(64,213)
As reported net loss according to GAAP	$(11,206)	$(56,855)	$(7,739)	$(119,772)
Excluding compensation expense related to equity awards	(21,258)	(19,260)	(42,170)	(39,364)
Pro forma net income (loss)	$10,052	$(37,595)	$34,431	$(80,408)

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)

	June 30, 2017	December 31, 2016
Assets:		

Cash, cash equivalents and short-term investments	$855,709	$665,223
Contracts receivable	50,615	108,043
Other current assets	58,035	22,252
Property, plant and equipment, net	99,677	92,845
Other assets	26,795	24,104
Total assets	$1,090,831	$912,467
Liabilities and stockholders' equity:		
Other current liabilities	$80,920	$82,504
Current portion of deferred contract revenue	110,840	51,280
1% convertible senior notes	516,539	500,511
Long-term obligations, less current portion	66,118	87,409
Long-term deferred contract revenue	100,843	91,198
Stockholders' equity	215,571	99,565
Total liabilities and stockholders' equity	$1,090,831	$912,467

View original content with multimedia:http://www.prnewswire.com/news-releases/ionis-provides-improved-2017-guidance-following-strong-financial-performance-300500862.html

SOURCE Ionis Pharmaceuticals, Inc.

D. Wade Walke, Ph.D., Vice President, Corporate Communications and Investor Relations, 760-603-2741; Alissa Santa Maria, Assistant Director, Corporate Development, 760-603-2643; Jennifer Capuzelo, Assistant Director, Corporate Communications and Investor Relations, 760-603-2606