



IONIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR FIRST QUARTER 2017

Profitable First Quarter with Operating Income of \$14 Million and Net Income of \$3 Million

First Full Quarter of Commercial Revenues from SPINRAZA

Conference Call Webcast Tuesday, May 9, 11:30 a.m. ET at www.ionispharma.com

CARLSBAD, Calif., May 9, 2017 – Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today reported significantly improved financial results over the same period last year with operating income of \$14 million and net income of \$3 million, both on a GAAP basis. The Company's pro forma results were also improved over the same period last year. Ionis ended the first quarter with more than \$860 million in cash, cash equivalents and short-term investments and is on track to meet its financial guidance for the year.

"SPINRAZA's launch is off to a strong start with sales in the first quarter of over \$47 million. As of April 21st, more than 165 insurance plans, including commercial and Medicaid plans, have approved individual uses of SPINRAZA. Importantly, Biogen estimates that 75% of commercially insured SMA patients in the U.S. are covered under a plan with an established policy for SPINRAZA and half of those patients are under a policy with broad access. Additionally, Biogen has had success in streamlining access to SPINRAZA at SMA treatment centers, and patient access is expanding further as non-SMA centers are also treating SMA patients. Further, we believe the positive data presented at AAN from the CHERISH study in patients with later-onset SMA and from the NURTURE study in pre-symptomatic infants demonstrate the benefit of treatment across SMA populations," said B. Lynne Parshall, chief operating officer of Ionis Pharmaceuticals. "We anticipate the European Commission's approval decision for SPINRAZA shortly following the recent CHMP positive opinion with a recommendation for a broad indication. Biogen also expects regulatory approvals in Canada and Japan this year and plans to initiate filings in additional countries this year. We are looking forward to seeing growth in SPINRAZA sales as the launch progresses.

"We and Akcea reported positive results from the Phase 3 APPROACH study of volanesorsen in March. With these positive data in hand, we are well along in preparing to file for regulatory approval in the U.S., EU and Canada in the third quarter. In addition, Akcea is making substantial progress in their preparations to launch volanesorsen in 2018. The Akcea team has also continued to make progress in advancing the rest of their pipeline. In January, Akcea formed a collaboration with Novartis to develop and commercialize AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx}. Novartis will be responsible for globally developing and commercializing each drug, including conducting and paying for the cardiovascular outcome study for each drug when the Phase 2b study for that drug is complete, and Novartis exercises its option to license the drug. Akcea plans to co-commercialize any drug Novartis licenses through the specialized sales force it is building to commercialize volanesorsen. Recently, Akcea initiated the Phase 2b study of AKCEA-APO(a)-L_{Rx} to determine the dose and regimen for the planned Phase 3 outcome study. Later this year, Akcea also plans to initiate a Phase 2b study of AKCEA-APOCIII-L_{Rx} in preparation for the planned Phase 3 outcome study.

"This quarter, we plan to report data from our Phase 3 NEURO-TTR study of IONIS-TTR_{Rx} in patients with familial amyloid polyneuropathy. We and our partner, GSK, are preparing to file for marketing approval before year-end. With the SPINRAZA launch gaining momentum, volanesorsen moving toward the market, Phase 3 data for IONIS-TTR_{Rx} imminent, and a large and growing pipeline supported by our efficient technology platform, we believe we have the elements in place to achieve sustained, long-term financial growth," concluded Ms. Parshall.

Financial Results

"We continued the momentum from 2016 into the first quarter of this year by achieving operating income and net income on both a GAAP and pro forma basis. These strong financial results were driven by more than \$110 million of revenue we earned in the first quarter. Importantly, we added more than \$5 million of commercial revenue from SPINRAZA royalties to our substantial base of R&D revenue, which included \$66 million from the expansion of our Bayer relationship. Consistent with our expectations, our operating expenses were relatively flat year over year. During the remainder of 2017, we expect our SG&A expenses to increase as Akcea continues to prepare to launch volanesorsen globally in 2018. However, we expect our R&D expenses to decrease over the year as we conclude our Phase 3 programs. We received more than \$290 million from our partners in the first quarter to end the quarter with a cash balance of more than \$860 million," said Elizabeth L. Hougen, chief financial officer of Ionis Pharmaceuticals.

"We are on track to meet our 2017 guidance of being breakeven or profitable at the operating line on a pro forma basis and a year-end cash balance of over \$825 million. We are encouraged by SPINRAZA sales in the first quarter of 2017 and we look forward to continued growth in commercial revenue from SPINRAZA royalties as the launch progresses and SPINRAZA is approved in additional countries," 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 months ended March 31, 2017 was \$110.3 million, compared to \$36.9 million for the same period in 2016. Ionis' revenue in the first quarter of 2017 consisted of the following:

Commercial Revenue:

- \$5.2 million from SPINRAZA royalties; and
- \$3.6 million from other licensing and royalty payments.

R&D Revenue:

- \$65.5 million from Bayer primarily for the license of IONIS-FXI-L_{Rx};
- \$5.0 million milestone payment from Biogen for validating an undisclosed neurological disease target;
- \$25.3 million from the amortization of upfront fees; and
- \$5.7 million primarily from services Ionis performed for its partners.

Ionis' R&D revenue fluctuates 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.

Operating Expenses

Ionis' operating expenses for the three months ended March 31, 2017 on a GAAP basis were \$96.3 million, and on a pro forma basis were \$75.4 million. These amounts compare to GAAP operating expenses of \$91.5 million and pro forma operating expenses of \$71.4 million for the same period in 2016. Ionis' operating expenses were relatively flat year over year. As the year progresses, Ionis projects that its R&D expenses will decrease as its Phase 3 programs wind down and its SG&A expenses will increase as Akcea continues to prepare to launch volanesorsen. Because of the efficiency of Ionis' technology, even with its projected declining R&D expenses this year, Ionis will continue to advance its earlier stage drugs and add new drugs to its pipeline.

Net Income

Ionis reported net income of \$3.5 million on a GAAP basis for the three months ended March 31, 2017, compared to a net loss of \$62.9 million for the same period in 2016. Ionis reported pro forma net income of \$24.4 million for the three months ended March 31, 2017 compared to a pro forma net loss of \$42.8 million for the same period in 2016. For the three months ended March 31, 2017, basic and diluted net income per share was \$0.03. Basic and diluted net loss per share for the same period in 2016 was \$0.52. Ionis' net income increased for the three months ended March 31, 2017 compared to the same period in 2016 primarily due to increased R&D revenue and the addition of commercial revenue from SPINRAZA royalties.

Balance Sheet

As of March 31, 2017, Ionis had cash, cash equivalents and short-term investments of \$860.3 million compared to \$665.2 million at December 31, 2016. Ionis' cash balance increased in 2017 due to the over \$290 million in payments the Company received primarily from Novartis and Biogen. Ionis' first quarter cash balance did not include the \$75 million payment from Bayer it received in April 2017. Ionis' working capital was \$791.8 million at March 31, 2017 compared to \$664.1 million at December 31, 2016.

Conference Call

At 11:30 a.m. Eastern Time today, May 9, 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) is a drug that has been approved in the U.S. for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. Biogen is responsible for commercialization of SPINRAZA. Drugs currently in Phase 3 development include volanesorsen, a drug Ionis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with either familial chylomicronemia syndrome or familial partial lipodystrophy; and IONIS-TTR_{Rx}, a drug Ionis is developing with GSK to treat patients with TTR amyloidosis.

Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

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., a wholly owned subsidiary of Ionis, and the therapeutics and commercial potential of Ionis' technologies and products in development, including SPINRAZA, IONIS-TTR_{Rx}, 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, which is on file with the SEC. Copies of this and other documents are available from the Company.

In this 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 trademark of Biogen.

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Ionis Pharmaceuticals' Corporate and Drug Development Highlights *(Q1 2017 and subsequent activities)*

Recent SPINRAZA Accomplishments:

- Biogen reported \$47 million from sales of SPINRAZA in the first quarter.
- Biogen received a positive CHMP opinion for SPINRAZA, recommending marketing approval with a broad indication in the EU.
- Ionis and Biogen reported positive data at AAN from the CHERISH and NURTURE studies as well as encore data from the ENDEAR study.
 - CHERISH data from an end of study analysis in non-ambulatory patients with later-onset SMA (consistent with Type 2) demonstrated:
 - A highly statistically significant and clinically meaningful improvement in motor function scores in SPINRAZA-treated patients compared to untreated patients.
 - Attainment of new motor milestones and upper limb motor function consistently in favor of SPINRAZA-treated patients.
 - A favorable safety profile with no discontinuations due to adverse events.
 - Data from an interim analysis of the NURTURE study in pre-symptomatic infants with genetically diagnosed SMA demonstrated that at the time of the interim analysis:
 - All infants were alive without the need for permanent ventilation.
 - Most infants achieved new motor milestones on essentially the same timeline as would be expected of a healthy infant.
 - No infants discontinued or withdrew from the study due to adverse events, and no new safety concerns were identified.

Recent Corporate and Pipeline Accomplishments:

- Ionis received more than \$290 million in cash from partners in the first quarter of 2017.
- In April, Ionis received \$75 million from Bayer to advance both IONIS-FXI_{Rx} and its LICA follow on, IONIS-FXI-L_{Rx}.
- GSK initiated Phase 2 studies of IONIS-HBV_{Rx} and the LICA follow on, IONIS-HBV-L_{Rx}.
- Ionis initiated a Phase 1 study of IONIS-AGT-L_{Rx}, a wholly owned generation 2.0+ LICA drug, in patients with treatment resistant hypertension.
- Ionis published papers in *Nature Biotechnology* on the mechanism of action for antisense drugs that significantly expand therapeutic opportunities for the technology.
- Ionis published a paper in *Nucleic Acid Therapeutics* on the analysis of its Integrated Safety Database, which demonstrated no class generic effect of 2'-O-methoxyethyl-modified antisense oligonucleotides on platelet numbers and function.
- Ionis' CEO, Dr. Stanley Crooke, received the E. B. Hershberg Award from the American Chemical Society.

Recent Akcea Accomplishments:

- Ionis and Akcea reported that volanesorsen achieved its primary endpoint in the Phase 3 APPROACH study, demonstrating robust reductions in triglycerides and reduced incidence of pancreatitis attacks and reduced frequency and severity of abdominal pain.
- Ionis and Akcea initiated a strategic collaboration with Novartis worth up to more than \$1 billion plus royalties for the development and commercialization of AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx}.

- Akcea initiated a Phase 2b study of AKCEA-APO(a)-L_{Rx} in patients with elevated Lp(a).
- Akcea filed a registration statement with the intention of completing an initial public offering.
- Top-line data from the Phase 3 APPROACH study of volanesorsen were presented at the 2017 European Atherosclerosis Society congress.
- Akcea published interim data in *Expert Review of Cardiovascular Therapy* from the IN-FOCUS survey that was commissioned to quantify the burden of FCS on patients and the healthcare system.

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

	Three months ended, March 31,	
	2017	2016
	(unaudited)	
Revenue:		
Commercial Revenue:		
SPINRAZA royalties	\$5,211	\$-
Licensing and royalty revenue	3,547	1,660
Total commercial revenue	\$8,758	\$1,660
Research and development revenue under collaborative agreements	101,546	35,214
Total revenue	110,304	36,874
Expenses:		
Research, development and patent	82,638	80,964
Selling, general and administrative	13,677	10,562
Total operating expenses	96,315	91,526
Income (loss) from operations	13,989	(54,652)
Other income (expense):		
Investment income	2,280	1,457
Interest expense	(11,363)	(9,490)
Other expense	(1,438)	-
Income (loss) before income tax expense	3,468	(62,685)
Income tax expense	-	(232)
Net income (loss)	\$3,468	\$(62,917)
Basic net income (loss) per share	\$0.03	\$(0.52)
Shares used in computing basic net income (loss) per share	122,861	120,598
Diluted net income (loss) per share	\$0.03	\$(0.52)
Shares used in computing diluted net income (loss) per share	124,972	120,598

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, March 31,	
	2017	2016
	(unaudited)	
As reported operating expenses according to GAAP	\$96,315	\$91,526
Excluding compensation expense related to equity awards	(20,912)	(20,103)
Pro forma operating expenses	\$75,403	\$71,423
As reported income (loss) from operations according to GAAP	\$13,989	\$(54,652)
Excluding compensation expense related to equity awards	(20,912)	(20,103)
Pro forma income (loss) from operations	\$34,901	\$(34,549)
As reported net income (loss) according to GAAP	\$3,468	\$(62,917)
Excluding compensation expense related to equity awards	(20,912)	(20,103)
Pro forma net income (loss)	\$24,380	\$(42,814)

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)

	<u>March 31,</u> <u>2017</u>	<u>December 31,</u> <u>2016</u>
Assets:		
Cash, cash equivalents and short-term investments	\$860,281	\$665,223
Contracts receivable	69,357	108,043
Other current assets	32,734	22,252
Property, plant and equipment, net	95,439	92,845
Other assets	<u>26,185</u>	<u>24,104</u>
Total assets	<u>\$1,083,996</u>	<u>\$912,467</u>
Liabilities and stockholders' equity:		
Other current liabilities	\$62,430	\$82,504
Current portion of deferred contract revenue	108,150	51,280
1% convertible senior notes	508,411	500,511
Long-term obligations, less current portion	87,440	87,409
Long-term deferred contract revenue	115,759	91,198
Stockholders' equity	<u>201,806</u>	<u>99,565</u>
Total liabilities and stockholders' equity	<u>\$1,083,996</u>	<u>\$912,467</u>

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