
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): February 28, 2017

IONIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125

(Commission File No.)

33-0336973

(IRS Employer Identification No.)

2855 Gazelle Court
Carlsbad, CA 92010

(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: **(760) 931-9200**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 2.02 Results of Operations and Financial Condition.

On February 28, 2017, Ionis Pharmaceuticals, Inc. (the “Company”) issued a press release announcing the Company’s financial results for the quarter and fiscal year ended December 31, 2016. In addition to disclosing results that are determined in accordance with Generally Accepted Accounting Principles (GAAP), the Company also discloses pro forma or non-GAAP results of operations, which are adjusted from GAAP to exclude non-cash compensation related to stock awards. The Company is presenting pro forma information excluding non-cash compensation because the Company believes it is useful for investors in assessing the Company’s operating results compared to the prior year. A copy of the release is furnished with this report as an exhibit pursuant to “Item 2.02. Results of Operations and Financial Condition” of Form 8-K in accordance with SEC Release Nos. 33-8216 and 34-47583.

The information in this Current Report on Form 8-K and the Exhibit attached hereto shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934 (the “Exchange Act”) or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, regardless of any general incorporation language in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated February 28, 2017.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

IONIS PHARMACEUTICALS, INC.

Dated: February 28, 2017

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL
Chief Operating Officer

[99.1](#) Press Release dated February 28, 2017.



IONIS' 2016 FINANCIAL RESULTS OUTPERFORM FINANCIAL GUIDANCE

Conference Call Webcast Tuesday, February 28, 11:30 a.m. ET at www.ionispharma.com

CARLSBAD, Calif., February 28, 2017 – Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today reported that it outperformed its financial guidance by ending 2016 with pro forma operating income of \$25.8 million and \$665.2 million in cash, cash equivalents and short-term investments. The Company also reported a GAAP loss from operations of \$46.3 million.

“2016 was a year of significant accomplishments for Ionis, culminating in the U.S. approval of SPINRAZA, in record time and with a very broad label. The approval of SPINRAZA is a testament to the efficacy, safety and tolerability that SPINRAZA demonstrated in multiple clinical studies in multiple SMA patient populations. We are pleased with Biogen’s early launch efforts in the U.S. and their actions directed to making SPINRAZA available to patients around the world as soon as possible,” said B. Lynne Parshall, chief operating officer of Ionis Pharmaceuticals.

“In 2016, we reported positive clinical data from 11 studies with six drugs. We also continued to advance over 36 drugs in development, including our Phase 3 drugs, volanesorsen and IONIS-TTR_{Rx}, which will complete pivotal trials shortly. We also added five new drugs to our pipeline, including our first Generation 2.5 LICA drug and our first oral locally acting drug for gastrointestinal autoimmune diseases.

“In the first week of 2017, we and our subsidiary, Akcea, initiated a collaboration with Novartis to develop and co-commercialize AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx} for patients with cardiovascular disease. Our partner for our Factor XI program, Bayer, is advancing IONIS-FXI_{Rx} and is expanding the program by initiating development of the LICA follow-on, IONIS-FXI-L_{Rx}. In addition, our broad strategic collaborations with Biogen and AstraZeneca continue to be productive. We believe our constellation of partnerships demonstrate the potential of our antisense drugs to address a wide variety of diseases with both large and small patient populations.

“In 2017, we expect to be breakeven or profitable at the operating line on a pro forma basis, driven in part by revenue from SPINRAZA. Biogen anticipates EU approval mid-year and has filed for regulatory authorization in Japan, Canada and Australia, and is planning to file additional applications in other countries this year. Approval in additional markets could broaden access to SPINRAZA and further bolster our revenues. We and Akcea expect to report Phase 3 data in March from the APPROACH study of volanesorsen in patients with familial chylomicronemia syndrome. Together with Akcea, we are preparing the regulatory submissions and plan to file for marketing authorization in the U.S., EU and Canada this year, provided the Phase 3 data are positive. Akcea has also made progress in preparing to launch volanesorsen. In the second quarter, we plan to report Phase 3 data from the NEURO-TTR study with IONIS-TTR_{Rx} in patients with familial amyloid polyneuropathy. We and our partner, GSK, are preparing to file an NDA before year end if the Phase 3 data are positive. While progress in these late-stage programs represents key visible catalysts for the year, we also plan to provide updates from our large and diverse pipeline throughout the year.

“We believe we have the key elements in place to achieve sustained, long-term financial growth. We have multiple drivers of revenue; a partnership strategy that leverages partner resources; a mature, broad and rapidly advancing clinical pipeline; and an innovative, more efficient drug discovery platform that enables us to continue developing new drugs with the potential for significant commercial opportunity in both rare and more prevalent diseases. We are now closer to achieving our goal of becoming a profitable, multi-product company delivering innovative medicines to patients with serious diseases,” concluded Ms. Parshall.

Ionis’ 2017 goals and a list of corporate and drug development highlights can be found at the end of this press release prior to the financial tables.

Financial Results

“2016 was marked by continued progress, highlighted by the approval of SPINRAZA. We earned substantial license fees and milestone payments from our many achievements, which led us to significantly improve upon our revenue, pro forma net operating loss and cash guidance for 2016. In 2016, we generated \$347 million of revenue, an increase of 45 percent compared to our guidance of \$240 million. Importantly, we were able to achieve all of our 2016 accomplishments with only a nominal increase in our expenses over 2015. We ended 2016 with a GAAP loss from operations of \$46 million, which included \$72 million in non-cash compensation expense related to equity awards resulting in pro forma operating income of \$26 million. In addition, we reported GAAP and pro forma net income for the third and fourth quarters. During the year, we received more than \$190 million from our partners and ended the year with \$665 million in cash, exceeding our year-end cash guidance by \$65 million. This cash balance does not include more than \$100 million that we earned in 2016 and received payment for in 2017,” said Elizabeth L. Hougen, chief financial officer of Ionis Pharmaceuticals.

“We are pleased to add commercial revenue from SPINRAZA to our already significant revenue from partnerships. Over the past five years, we have consistently increased our revenue, reflecting the successes of our partnered programs and drugs. This R&D revenue provides a base of revenue that funds most of our pro forma operating expenses. While in any year the specific sources of our R&D revenue change, the consistent growth in revenue we have achieved over the last five years supports the sustainability of this component of our operating model. In 2017, we expect to continue to have a strong R&D revenue base that funds most of our pro forma operating expenses. To that revenue base, we are adding commercial revenue from SPINRAZA royalties. This revenue is nearly all profit to us, in other words we have only a nominal amount of corresponding expense associated with it. For 2017, we expect our operating expenses to be essentially flat compared to 2016; however, the composition of our expenses will change to reflect the evolution of our business. We plan to continue to increase our commercial spending for volanesorsen as our subsidiary, Akcea, prepares to launch volanesorsen globally in 2018. These increases will be offset by a decrease in our R&D expenses, reflecting the fact that our current Phase 3 programs are coming to a close. Because of the efficiency of our technology, we can advance our earlier stage drugs and add new drugs to our pipeline while still decreasing our research and development expenses. The combination of a solid base of R&D revenue, SPINRAZA commercial revenue and prudent spending, support our projection that we will be breakeven or profitable at the operating line on a pro forma basis for 2017. As we have more visibility on SPINRAZA sales, we will provide more detailed guidance. Already in 2017, we have generated more than \$250 million in cash from our partnered programs. As such, we are projecting a year-end cash balance of over \$825 million,” 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 GAAP to pro forma measures, which is provided later in this release.

Revenue

Ionis' revenue for the three and twelve months ended December 31, 2016 was \$160.3 million and \$346.6 million, compared to \$51.6 million and \$283.7 million for the same periods in 2015. Ionis' revenue in 2016 consisted of the following:

- \$170 million from Biogen for FDA approval, licensing and advancing the Phase 3 program for SPINRAZA;
- \$53 million from AstraZeneca for advancing and licensing IONIS-KRAS-2.5_{Rx} and selecting IONIS-AZ4-2.5-L_{Rx} to move into development;
- \$15 million from Janssen for licensing IONIS-JBI1-2.5_{Rx} and validating an undisclosed target to treat patients with a gastrointestinal autoimmune disease;
- \$15 million from Kastle Therapeutics for acquiring Kynamro;
- \$8 million from Biogen for advancing IONIS-SOD1_{Rx}, IONIS-BIIB4_{Rx} and IONIS-BIIB6_{Rx};
- \$61 million from the amortization of upfront fees; and
- \$25 million primarily from its partners for the manufacturing services Ionis performed.

In comparison, Ionis' revenue in 2015 included \$115.7 million in milestone payments from partnered programs, \$91.2 million in connection with Bayer's exclusive license of IONIS-FXI_{Rx}, \$56.2 million from the amortization of upfront fees and \$20.6 million primarily from the manufacturing services Ionis performed for its partners.

Ionis' 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 and twelve months ended December 31, 2016 on a GAAP basis were \$119.2 million and \$392.9 million, respectively, and on a pro forma basis were \$104.0 million and \$320.8 million, respectively. This is compared to GAAP operating expenses of \$114.5 million and \$359.5 million and pro forma operating expenses of \$97.1 million and \$300.2 million for the same periods in 2015. The increase in operating expenses was primarily due to Phase 3 programs for SPINRAZA, IONIS-TTR_{Rx} and volanesorsen that Ionis conducted in 2016. The Company completed target enrollment in four of the Phase 3 studies at the end of 2015, and as a result, these studies were in their most expensive stage during 2016. In addition, Akcea continued to build a global organization and prepare for the launch of volanesorsen. In addition, Ionis' operating expenses for 2016 on a GAAP basis increased due to an increase in non-cash compensation expense related to equity awards that resulted from an increase in the exercise price of the stock options the Company has granted over the past several years.

Loss on Retirement of Debt

In December 2016, Ionis refinanced a majority of its 2¾% convertible senior notes due 2019 (2¾% Notes). In the refinancing, Ionis reduced the interest rate to 1% by issuing an additional \$185.5 million of its 1% convertible senior notes due 2021 (1% Notes). Ionis also significantly reduced the potential dilution from its convertible notes and extended the maturity to November 2021. As a result of the early repurchase of the 2¾% Notes, Ionis recognized a \$4.0 million non-cash loss.

Income Tax Expense

Ionis recognized income tax expense of \$2.9 million for the year ended December 31, 2016 compared to \$0.4 million in 2015. Ionis' tax expense increased in 2016 compared to 2015 primarily due to an increase in taxable income resulting from Ionis' strong financial performance in 2016.

Net Income (Loss)

Ionis reported net income of \$25.9 million and a net loss of \$86.6 million for the three and twelve months ended December 31, 2016 on a GAAP basis, respectively, compared to a net loss of \$71.4 million and \$88.3 million for the same periods in 2015. Ionis recorded pro forma net income of \$41.0 million for the three months ended December 31, 2016 compared to a pro forma net loss of \$54.0 million for the same period in 2015. For the twelve months ended December 31, 2016, the Company had a pro forma net loss of \$14.4 million compared to a pro forma net loss of \$29.0 million in 2015. Basic and diluted net income per share for the three months ended December 31, 2016 on a GAAP basis was \$0.21. Basic and diluted net loss per share for the twelve months ended December 31, 2016 was \$0.72. This is compared to a basic and diluted net loss of \$0.59 and \$0.74 per share for the three and twelve months ended December 31, 2015, respectively.

Balance Sheet

As of December 31, 2016, Ionis had cash, cash equivalents and short-term investments of \$665.2 million compared to \$779.2 million at December 31, 2015. Ionis' cash balance decreased in 2016 primarily due to spending to support the Company's ongoing Phase 3 programs. Ionis' cash balance at the end of 2016 did not include \$107 million the Company earned in the fourth quarter of 2016 and received in 2017. Since the end of 2016, Ionis has generated more than \$250 million primarily from its Novartis and Bayer partnerships. Ionis' working capital was \$664.1 million at December 31, 2016 compared to \$688.1 million at December 31, 2015.

Conference Call

At 11:30 a.m. Eastern Time today, February 28, 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 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, 2015, 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 release, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" refers to Ionis Pharmaceuticals and its subsidiaries.

Ionis PharmaceuticalsTM is a trademark of Ionis Pharmaceuticals, Inc. Akcea TherapeuticsTM is a trademark of Ionis Pharmaceuticals, Inc. SPINRAZATM is a trademark of Biogen.

Ionis Pharmaceuticals' Corporate Goals for 2017

In 2017, Ionis plans to achieve the following objectives:

- Support Biogen in expanding access to SPINRAZA
 - o Assist Biogen with regulatory approval in the EU and filings in multiple countries outside the U.S., including Japan, Australia and Canada
- Advance volanesorsen and IONIS-TTR_{Rx} toward the market
 - o File regulatory submissions for volanesorsen with Akcea, if Phase 3 study is positive
 - o File regulatory submissions for IONIS-TTR_{Rx} with GSK, if Phase 3 study is positive
 - o Build out U.S. and EU commercial infrastructure and prepare for commercial launch of volanesorsen through Akcea
 - o Assist GSK in preparing for commercial launch of IONIS-TTR_{Rx}
- Advance the pipeline
 - o Report clinical data on multiple drugs, including:
 - § Phase 3 data for volanesorsen in patients with familial chylomicronemia syndrome (FCS)
 - § Phase 3 data for IONIS-TTR_{Rx} in patients with transthyretin (TTR) familial amyloid polyneuropathy (FAP)
 - o Advance volanesorsen Phase 3 study in patients with familial partial lipodystrophy (FPL)
 - o Initiate multiple clinical studies
 - o Advance multiple LICA and Generation 2.5 drugs in development
- Broaden the pipeline by adding three to five new drugs into development
- Continue to advance antisense technology
- Achieve break-even or profitability on the operating line on a pro forma basis

Ionis Pharmaceuticals' Corporate and Drug Development Highlights

(2016 and subsequent activities)

2016 and Recent SPINRAZA Accomplishments:

- Ionis and Biogen achieved FDA approval of SPINRAZA in three months under Priority Review for the treatment of SMA in pediatric and adult patients.
 - Biogen filed for marketing authorization in the EU and was granted Accelerated Assessment.
 - Biogen filed for marketing authorization in Canada, Japan, and Australia.
 - Biogen reported positive data from an end of study analysis of the ENDEAR Phase 3 study in patients with infantile-onset (consistent with type 1) SMA at the British Pediatric Neurology Association annual conference. Ionis previously reported data from an interim analysis of ENDEAR, which along with several other studies, formed the basis for the marketing application for SPINRAZA in the U.S.
 - Ionis and Biogen reported positive data from an interim analysis of the Phase 3 CHERISH study in patients with later-onset (consistent with Type 2) SMA.
 - Ionis and Biogen presented new positive clinical data with SPINRAZA at the World Muscle Society Congress supporting the companies' efforts to rapidly make SPINRAZA available to patients with SMA, including:
 - o Safety results from the interim analysis of the Phase 3 ENDEAR study in patients with infantile-onset (consistent with Type 1) SMA;
 - o Encouraging preliminary results from NURTURE, a Phase 2 open-label study in pre-symptomatic infants; and
 - o A recent analysis of the ongoing Phase 2 open-label study in patients with later-onset SMA.
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- Ionis and Biogen reported positive data from an interim analysis of the ENDEAR Phase 3 study in patients with infantile-onset (consistent with Type 1) SMA. Biogen paid Ionis \$75 million to license the drug.

Corporate Highlights:

- Ionis earned more than \$200 million from Biogen in 2016, including payments related to SPINRAZA.
- Ionis and Akcea formed a strategic collaboration with Novartis to develop and co-commercialize AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx} for the treatment of lipid disorders, for which Ionis and Akcea are eligible to receive \$225 million in near-term payments, including \$100 million Ionis has received and \$75 million Ionis expects to receive in the first quarter of 2017. The transaction has a potential value of up to over \$1 billion.
- Ionis earned \$75 million from Bayer to advance both IONIS-FXI_{Rx} and its LICA follow on, IONIS-FXI-L_{Rx}.
- Ionis sold the global rights to develop and commercialize Kynamro to Kastle Therapeutics and earned a \$15 million upfront payment.
- Ionis and MD Anderson Cancer Center formed a strategic alliance to advance novel cancer therapies.
- Ionis added to its pipeline its first oral locally acting drug for gastrointestinal autoimmune diseases for which Ionis earned a \$10 million license fee from Janssen.
- Ionis advanced IONIS-KRAS-2.5_{Rx} into development and earned \$28 million from AstraZeneca.
- Ionis advanced IONIS-AZ4-2.5-L_{Rx}, its first Generation 2.5 LICA drug, into development and earned \$25 million from AstraZeneca.
- Ionis' CEO, Dr. Stanley Crooke, received two awards, the E. B. Hershberg Award from the American Chemical Society and the Lifetime Achievement Award from the Oligonucleotide Therapeutics Society, recognizing his achievements in the field of oligonucleotide therapeutics.

Drug Development and Technology Highlights

- Ionis continued to advance its pipeline of innovative first-in-class or best-in-class drugs, reported positive data from 11 clinical studies with six drugs. These data and clinical advancements represent the broad applicability of Ionis' technology to address unmet medical needs across multiple disease targets.
 - The FDA and EMA granted orphan drug designation to IONIS-HTT_{Rx} for the treatment of patients with Huntington's disease.
 - Akcea launched IN-FOCUS, a research study to assess the impact of familial chylomicronemia syndrome.
 - Akcea published positive clinical data from a Phase 2 study of volanesorsen in patients with high plasma triglyceride levels and type 2 diabetes in *Diabetes Care*.
 - Ionis published a paper in *Nature Biotechnology* on the novel mechanism of action for antisense drugs that significantly expands 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 (2'MOE)-modified antisense oligonucleotides (ASOs) on platelet numbers and function.
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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, | |
|---|-------------------------------------|--------------------|-----------------------------|--------------------|
| | 2016 | 2015 | 2016 | 2015 |
| Revenue: | | | | |
| Research and development revenue under collaborative agreements | \$ 159,316 | \$ 50,891 | \$ 325,898 | \$ 281,360 |
| Licensing and royalty revenue | 1,033 | 679 | 20,722 | 2,343 |
| Total revenue | 160,349 | 51,571 | 346,620 | 283,703 |
| Expenses: | | | | |
| Research, development and patent expenses | 101,151 | 101,330 | 344,320 | 322,292 |
| General and administrative | 18,043 | 13,181 | 48,616 | 37,173 |
| Total operating expenses | 119,194 | 114,511 | 392,936 | 359,465 |
| Income (loss) from operations | 41,155 | (62,940) | (46,316) | (75,762) |
| Other income (expense): | | | | |
| Investment income | 1,548 | 1,355 | 5,416 | 4,302 |
| Interest expense | (9,934) | (9,351) | (38,795) | (36,732) |
| Gain on investments, net | 13 | - | 56 | 75 |
| Gain on investment in Regulus Therapeutics, Inc. | - | - | - | 20,211 |
| Loss on early retirement of debt | (3,983) | - | (3,983) | - |
| Income (loss) before income tax benefit | 28,799 | (70,061) | (83,622) | (87,906) |
| Income tax expense | (2,934) | (372) | (2,934) | (372) |
| Net income (loss) | \$ 25,865 | \$ (71,433) | \$ (86,556) | \$ (88,278) |
| Basic net income (loss) per share | \$ 0.21 | \$ (0.59) | \$ (0.72) | \$ (0.74) |
| Diluted net income (loss) per share | \$ 0.21 | \$ (0.59) | \$ (0.72) | \$ (0.74) |
| Shares used in computing basic net income (loss) per share | 121,340 | 120,189 | 120,933 | 119,719 |
| Shares used in computing diluted net income (loss) per share | 123,953 | 120,189 | 120,933 | 119,719 |

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, | |
|--|-------------------------------------|--------------------|----------------------------|--------------------|
| | 2016 | 2015 | 2016 | 2015 |
| As reported operating expenses according to GAAP | \$ 119,194 | \$ 114,511 | \$ 392,936 | \$ 359,465 |
| Excluding compensation expense related to equity awards | (15,158) | (17,408) | (72,108) | (59,314) |
| Pro forma operating expenses | <u>\$ 104,036</u> | <u>\$ 97,103</u> | <u>\$ 320,828</u> | <u>\$ 300,151</u> |
| As reported income (loss) from operations according to GAAP | \$ 41,155 | \$ (62,940) | \$ (46,316) | \$ (75,762) |
| Excluding compensation expense related to equity awards | (15,158) | (17,408) | (72,108) | (59,314) |
| Pro forma income (loss) from operations | <u>\$ 56,313</u> | <u>\$ (45,532)</u> | <u>\$ 25,792</u> | <u>\$ (16,448)</u> |
| As reported net income (loss) according to GAAP | \$ 25,865 | \$ (71,433) | \$ (86,556) | \$ (88,278) |
| Excluding compensation expense related to equity awards | (15,158) | (17,408) | (72,108) | (59,314) |
| Pro forma net income (loss) | <u>\$ 41,023</u> | <u>\$ (54,025)</u> | <u>\$ (14,448)</u> | <u>\$ (28,964)</u> |

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>December 31,</u> 2016 | <u>December 31,</u> 2015 |
|---|-----------------------------|-----------------------------|
| Assets: | | |
| Cash, cash equivalents and short-term investments | \$ 665,223 | \$ 779,183 |
| Contracts receivable | 108,043 | 11,356 |
| Investment in Regulus Therapeutics Inc. | 2,414 | 24,792 |
| Other current assets | 22,252 | 33,028 |
| Property, plant and equipment, net | 92,845 | 90,233 |
| Other assets | 21,690 | 20,664 |
| Total assets | <u>\$ 912,467</u> | <u>\$ 947,900</u> |
| Liabilities and stockholders' equity: | | |
| Other current liabilities | \$ 82,504 | \$ 81,554 |
| Current portion of deferred contract revenue | 51,280 | 67,322 |
| 1% convertible senior notes | 500,511 | 339,847 |
| 2 3/4% convertible senior notes | 124 | 49,523 |
| Long-term obligations, less current portion | 87,285 | 74,558 |
| Long-term deferred contract revenue | 91,198 | 134,306 |
| Stockholders' equity | 99,565 | 200,790 |
| Total liabilities and stockholders' equity | <u>\$ 912,467</u> | <u>\$ 947,900</u> |

Investor and Media Contact:

D. Wade Walke, Ph.D.
Vice President, Corporate Communications and
Investor Relations
760-603-2741

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