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): **May 4, 2016**

IONIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction of Incorporation)

000-19125	**33-0336973**
(Commission File No.)	(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))

Item 2.02. Results of Operations and Financial Condition.

On May 4, 2016, Ionis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended March 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 May 4, 2016.

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: May 4, 2016

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL
Chief Operating Officer

INDEX TO EXHIBITS

99.1	Press Release dated May 4, 2016.

Exhibit 99.1

IONIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR FIRST QUARTER 2016

- *Conference Call Webcast Wednesday, May 4, 10:30 a.m. ET at **www.ionispharma.com***

CARLSBAD, Calif., May 4, 2016 – Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today reported its financial results for the first quarter were in line with the company's expectations.

"2016 is off to a strong start. Target enrollment is complete in four Phase 3 studies across nusinersen, IONIS-TTR_{Rx} and volanesorsen. These important new drugs are now one step closer to potentially reaching the market and being available to patients. We are actively engaged in NDA preparations for all three of these drugs in anticipation of Phase 3 data from each in the first half of next year," said B. Lynne Parshall, chief operating officer of Ionis Pharmaceuticals. "We are pleased to have chosen a new commercial partner for Kynamro. We believe Kastle Therapeutics has the rare disease expertise, financial resources and initiative to expand the market potential for Kynamro. Already Kastle has begun to identify new patients to bring onto Kynamro therapy in the United States, and it is initiating activities to pursue marketing approval in other countries."

"Just last month at the AAN meeting, we provided an update on our Phase 2 open-label study with a data cut-off of January 26, 2016 in infants with SMA treated with nusinersen. The infants in this study are continuing to improve. At the AAN meeting, we reported that we had no deaths or events of permanent ventilation since late 2014. All of the continuing infants are over two years old and several have passed their third birthday. We are especially encouraged by continued improvements in motor function in these infants, as evidenced by both continued increases in muscle function scores and achievement of developmental milestones that infants with Type 1 SMA are never expected to achieve, including sitting, standing and even walking. These data give us further confidence in our two Phase 3 studies in infants and children with SMA, from which we expect to have data in the first half of 2017. We continue to work closely with our partner, Biogen, who is preparing to bring this drug to the market for infants and children with SMA," continued Ms. Parshall.

"Also at the AAN meeting, we and our collaborators presented more than a dozen presentations and posters highlighting our broad neurological disease pipeline, which is focused on treating diseases that have been largely untreatable using other therapeutic modalities. Over the last several years, we have substantially expanded the reach of our technology to address a large number of disease targets in the central nervous system," said Ms. Parshall. "We continue to increase the value of our pipeline and technology by expanding the use of our antisense technology into new disease areas, new targets, new tissues and new mechanisms. We hope that you will join us in July for our R&D day during which we will be discussing our broad, innovative pipeline and the groundbreaking work we are doing to continue to broaden the application of our technology," concluded Ms. Parshall.

Financial Results

"We finished the first quarter of 2016 with a pro forma net operating loss of $35 million and more than $700 million in cash. On a GAAP basis, our operating loss was $55 million. In the first quarter, we earned $37 million of revenue including more than $15 million in milestone payments, the majority of which were related to the progression of our Phase 3 program for nusinersen. As nusinersen and our other partnered programs advance, we have the opportunity to earn significant revenue this year. We are eligible to earn up to $95 million in upfront and milestone payments from Kastle, $15 million of which we will recognize in the second quarter. We will receive a ten percent common equity position in Kastle's parent company. Starting in 2017, we are also entitled to royalties that average in the mid to low teens on global sales of Kynamro. Additionally, our financial projections include numerous significant milestone payments in the second half of this year, including a $55 million milestone payment from Bayer related to advancing IONIS-FXI$_{Rx}$, compared to 2015 when our revenue was more evenly spread throughout the year. We also have the opportunity to earn a $25 million milestone payment for advancing the first drug under our cardiometabolic collaboration with AstraZeneca and a $10 million milestone payment for advancing the first drug under our J&J collaboration. We also have numerous opportunities during the remainder of 2016 to earn meaningful milestone payments as we advance research programs and drugs under our Biogen collaborations," said Elizabeth L. Hougen, chief financial officer of Ionis Pharmaceuticals.

"Our pro forma operating expenses for the first quarter were $71 million, a significant portion of which were associated with the five Phase 3 studies and three open-label extension studies related to these Phase 3 studies, we are conducting. In addition, Akcea continues to build its infrastructure and conduct the pre-commercialization activities necessary to launch volanesorsen. We are doing all of this while managing our expenses prudently. On a GAAP basis, our operating expenses were $92 million," continued Ms. Hougen.

"Our first quarter financial results were in line with our expectations and we are on track to meet our 2016 guidance of a pro forma NOL in the low $60 million range and a year-end cash balance in excess of $600 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 pro forma and GAAP measures, which is provided later in this release.

Revenue

Ionis' revenue for the three months ended March 31, 2016 was $36.9 million, compared to $62.6 million for the same period in 2015. Ionis' revenue in the first quarter of 2016 included the following:

- $12.5 million from Biogen for advancing the Phase 3 program for nusinersen and advancing IONIS-BIIB4$_{Rx}$;
- $1.5 million from GSK for advancing IONIS-HBV-L$_{Rx}$; and
- $22.9 million primarily from the amortization of upfront fees and 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. The Company's financial projections include numerous significant milestone payments in the second half or this year, compared to 2015 when its revenue was more evenly spread throughout the year.

Operating Expenses

Ionis' operating expenses included costs to support the Company's ongoing Phase 3 studies for nusinersen, IONIS-TTR$_{Rx}$ and volanesorsen. In addition, Akcea continued to build its operations in preparation for the commercial launch of volanesorsen. As such, Ionis' pro forma operating expenses were $71.4 million for the three months ended March 31, 2016, and increased compared to $58.6 million for the same period in 2015. On a GAAP basis, Ionis' operating expenses for the three months ended March 31, 2016 were $91.5 million, compared to $71.9 million for the same period in 2015. Ionis' operating expenses on a GAAP basis included non-cash compensation expense related to equity awards, which increased because the average fair value of unvested stock options has risen due to the increase in the exercise price of the stock options the Company has granted over the past several years.

Net Loss

Ionis reported a net loss of $62.9 million for the three months ended March 31, 2016, compared to a net loss of $16.7 million for the same period in 2015. Basic and diluted net loss per share for the three months ended March 31, 2016 was $0.52 compared to $0.14 for the same period in 2015. Ionis' net loss increased for the three months ended March 31, 2016 compared to the same period in 2015 primarily due to variations in the timing of revenue from milestone payments and to a lesser extent, an increase in operating expenses primarily associated with the Company's Phase 3 studies.

Balance Sheet

As of March 31, 2016, Ionis had cash, cash equivalents and short-term investments of $703.8 million compared to $779.2 million at December 31, 2015. Ionis' cash balance decreased in 2016 primarily due to spending to support the Company's ongoing Phase 3 programs for nusinersen, IONIS-TTR$_{Rx}$ and volanesorsen. Ionis' working capital was $639.4 million at March 31, 2016 compared to $688.1 million at December 31, 2015.

Conference Call

At 10:30 a.m. Eastern Time today, May 4, 2016, 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 a dozen drugs in mid- to late-stage development. 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; IONIS-TTR$_{Rx}$, a drug Ionis is developing with GSK to treat patients with all forms of TTR amyloidosis; and nusinersen, a drug Ionis is developing with Biogen to treat infants and children with spinal muscular atrophy. 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 Pharmaceuticals, and the therapeutic and commercial potential of Ionis' technologies and products in development, including nusinersen, 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, 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' Contacts:

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Ionis Pharmaceuticals' Corporate and Drug Development Highlights

(Q1 2016 and subsequent activities)

- Ionis and its collaborators presented more than a dozen posters and presentations at the American Academy of Neurology (AAN) meeting including an update on its ongoing Phase 2 study of nusinersen in infants with SMA as well as overviews on its programs on Huntington's disease, myotonic dystrophy type 1, Alzheimer's disease, Parkinson's disease and spinocerebellar ataxia type 2.
    - Ionis reported positive interim data from an ongoing open-label Phase 2 clinical study with a data cut-off of January 26, 2016, on nusinersen in infants with SMA. The data reported show that there have been no new events in the study since December 2014 with continued increases in median event-free survival, muscle function scores as well as achievement of new developmental milestones. Data showing increases in neuromuscular electrophysiology measurements were also reported.
    - IONIS-HTT_{Rx} was highlighted in an oral presentation as the first HTT-lowering drug to be tested in patients with Huntington's disease (HD). IONIS-HTT_{Rx} is the first drug to enter clinical development designed to directly target the cause of HD.
    - IONIS-DMPK-2.5_{Rx} was highlighted in several oral presentations and posters showing preclinical data that supports the therapeutic potential for IONIS-DMPK-2.5_{Rx} in patients with myotonic dystrophy type 1.
    - Additional presentations included preclinical data on new targets for neurological diseases, including TAU for Alzheimer's disease, LRRK2 for Parkinson's disease and ATXN2 for spinocerebellar ataxia type 2.
- Ionis sold the rights to Kynamro to Kastle Therapeutics.
    - Ionis is eligible to receive up to $95 million, which includes a $15 million up-front payment, a $10 million payment Ionis will earn after three years and up to $70 million in sales related milestone payments.
    - Starting in 2017, Ionis is also eligible to earn royalties that average in the mid to low teens on global sales of Kynamro.
    - Ionis will also receive a 10 percent equity position in Kastle's parent company.
    - Sanofi Genzyme, the specialty care global business unit of Sanofi, will be eligible to receive a three percent royalty on sales of Kynamro and three percent of the cash Ionis receives from Kastle Therapeutics.
- Ionis and its collaborators continued to advance Ionis' pipeline of first-in-class or best-in-class drugs. As a result, Ionis earned more than $15 million in milestone payment in the first quarter of 2016.
    - Ionis continued to advance nusinersen in the ongoing open-label study, SHINE, in infants and children with SMA for which, Ionis earned a $7.5 million milestone payment from Biogen.
    - GSK initiated a Phase 1 study of IONIS-HBV-L_{Rx}, a LICA drug in development to treat patients with hepatitis B virus, for which Ionis earned a $1.5 million milestone payment from GSK.
- The European Medicines Agency granted IONIS-HTT_{Rx} orphan drug designation for the treatment of patients with Huntington's disease.
- A jury found in favor of Merck and Ionis in a patent dispute related to Gilead's HCV medicines, including Sovaldi and Harvoni.
    - The jury upheld all claims from the two patents in the cases, including two methods and eight composition of matter claims. Ionis and Merck are co-inventors on these patents. Ionis will receive 20% of the damages awarded to Merck that exceed the costs Merck incurred to conduct the litigation and Ionis will also receive 20% of all future payments, including 20% of royalties, Merck receives from Gilead.

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

	Three months ended, March 31,	
	2016	2015
Revenue:	(unaudited)	
Research and development revenue under collaborative agreements	$ 35,214	$ 61,892
Licensing and royalty revenue	1,660	691
Total revenue	36,874	62,583
Expenses:		
Research, development and patent expenses	80,964	64,447
General and administrative	10,562	7,466
Total operating expenses	91,526	71,913
Loss from operations	(54,652)	(9,330)
Other income (expense):		
Investment income	1,457	845
Interest expense	(9,490)	(9,021)
Loss before income tax benefit	(62,685)	17,506
Income tax benefit	(232)	789
Net loss	$ (62,917)	$ (16,717)
Basic and diluted net loss per share	$ (0.52)	$ (0.14)
Shares used in computing basic and diluted net loss per share	120,598	118,948

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

	Three months ended, March 31,	
	2016	2015
	(unaudited)	
As reported operating expenses according to GAAP	$ 91,526	$ 71,913
Excluding compensation expense related to equity awards	(20,103)	(13,305)
Pro forma operating expenses	$ 71,423	$ 58,608
As reported income (loss) from operations according to GAAP	$ (54,652)	$ (9,330)
Excluding compensation expense related to equity awards	(20,103)	(13,305)
Pro forma income (loss) from operations	$ (34,549)	$ 3,975
As reported net loss according to GAAP	$ (62,917)	$ (16,717)
Excluding compensation expense related to equity awards	(20,103)	(13,305)
Pro forma net loss	$ (42,814)	$ (3,412)

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)

	March 31, 2016	December 31, 2015
Assets:		
Cash, cash equivalents and short-term investments	$ 703,804	$ 779,183
Investment in Regulus Therapeutics Inc.	19,703	24,792
Other current assets	40,403	33,028
Property, plant and equipment, net	90,365	90,233
Other assets	21,544	20,664
Total assets	$ 875,819	$ 947,900
Liabilities and stockholders' equity:		
Other current liabilities	$ 60,800	$ 81,554
Current portion of deferred contract revenue	63,695	67,322
1% convertible senior notes	345,265	339,847
2 3/4% convertible senior notes	50,190	49,523
Long-term obligations, less current portion	74,623	74,558
Long-term deferred contract revenue	123,084	134,306
Stockholders' equity	158,162	200,790
Total liabilities and stockholders' equity	$ 875,819	$ 947,900

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