Filed Pursuant to Rule 424(b)(7)
Registration No. 333-217422

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Unit(2)	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee(3)
Common stock, par value $0.001 per share	1,631,435	$42.09	$68,658,942	$7,958

(1) Pursuant to Rule 416 under the Securities Act of 1933, as amended, or Securities Act, the shares of common stock being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares of common stock being registered hereunder as a result of stock splits, stock dividends or similar transactions.

(2) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457 promulgated under the Securities Act. The offering price per share and the aggregate offering price are based upon the average of the high and low prices of the registrant's shares of common stock as reported on The NASDAQ Global Select Market on April 18, 2017.

(3) The registration fee is calculated and being paid pursuant to Rule 457(r) under the Securities Act, and relates to the registration statement on Form S-3 (File No. 333-217422) filed by the Registrant on April 21, 2017.

PROSPECTUS SUPPLEMENT
(To Prospectus dated April 21, 2017)

1,631,435 Shares of Common Stock

This prospectus supplement relates to the disposition from time to time of up to 1,631,435 shares of common stock that are held or beneficially owned by the selling stockholder named in this prospectus supplement. We are not selling any shares of common stock under this prospectus supplement and will not receive any of the proceeds from the sale of shares of common stock by the selling stockholder.

The selling stockholder identified in this prospectus supplement, or its permitted transferees or other successors-in-interest that may be identified in amendments to this prospectus supplement, may offer the shares of common stock from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices, or at privately negotiated prices. We provide more information about how the selling stockholder may sell its shares of common stock in the section entitled "Plan of Distribution" beginning on page 10 of this prospectus supplement. We will not be paying any underwriting discounts or commissions in connection with any offering of shares of common stock under this prospectus supplement and the accompanying prospectus.

Our shares of common stock are listed on The NASDAQ Global Select Market under the symbol "IONS." On April 20, 2017, the last reported sale price of our shares of common stock on The NASDAQ Global Select Market was $42.91.

Investing in our shares of common stock involves a high degree of risk. You should review carefully the risks and uncertainties incorporated by reference herein under the heading "Risk Factors" on page 6 of this prospectus supplement, and under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is April 21, 2017.

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Prospectus Supplement

Prospectus

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that Ionis Pharmaceuticals, Inc. filed with the Securities and Exchange Commission, or SEC, using the "shelf" registration process. Under this process, among other transactions, the selling stockholder may from time to time, in one or more offerings, sell the shares of common stock described in this prospectus supplement.

This prospectus supplement describes the terms of the offerings by the selling stockholder and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The accompanying prospectus, dated April 21, 2017, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to this prospectus supplement and the accompanying prospectus combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in the accompanying prospectus — the statement in the document having the later date modifies or supersedes the earlier statement. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference, in their entirety before making an investment decision.

Neither we nor the selling stockholder have authorized anyone to provide you with information other than the information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. This document may only be used where it is legal to sell these securities. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate as of any date other than its respective date, regardless of when this prospectus supplement and the accompanying prospectus is delivered, or when any sale of our shares of common stock occurs. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus supplement, the accompanying prospectus and the information incorporated herein by reference include trademarks, service marks and trade names owned by us or others. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement and the accompanying prospectus are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary may not contain all of the information that may be important to you. You should read the entire prospectus supplement and the accompanying prospectus, including the risks of investing in our shares of common stock incorporated by reference herein under the heading "Risk Factors" and under similar headings in the other documents that are incorporated by reference into this prospectus, as well as the financial statements and related notes, pro forma financial information, and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

Ionis Pharmaceuticals, Inc.

Overview

We are leaders in discovering and developing RNA-targeted therapeutics. We have created an efficient and broadly applicable drug discovery platform. Using this platform, we have developed a large, diverse and advanced pipeline of potentially first-in-class and/or best-in-class drugs that we believe can provide high value for patients with significant unmet medical needs. In this way, we believe we are fundamentally changing medicine with the goal to transform the lives of those suffering from severe, often life-threatening, diseases. The recent U.S. approval of SPINRAZA for pediatric and adult patients with spinal muscular atrophy, or SMA, highlights our progress toward this goal. Our pipeline also contains two near-term potentially transformative medicines for two different severe and rare diseases, each with significant commercial potential. We plan to file for marketing authorization in the U.S., Europe and Canada in 2017 for volanesorsen to treat familial chylomicronemia, or FCS. We also plan to report data from our Phase 3 study of IONIS-TTR_{Rx} in patients with familial amyloid polyneuropathy, or FAP, in the second quarter of 2017.

With FDA approval in December 2016, SPINRAZA™ (nusinersen) injection became the first and only approved drug to treat pediatric and adult patients with SMA. SMA is a leading genetic cause of death in infants and toddlers that is marked by progressive, debilitating muscle weakness. We and Biogen conducted a broad, innovative clinical development program that moved SPINRAZA from its first dose in humans in 2011 to its first regulatory approval five years later. We conducted two sham-controlled Phase 3 studies, one in babies with infantile-onset SMA called ENDEAR and one in children with later-onset SMA called CHERISH. Both of these studies achieved statistically significant improvements in their primary endpoints and the drug demonstrated a favorable safety profile. Biogen has filed for marketing authorization in the EU, Japan, Australia and Canada, and plans to file in other countries this year. The European Medicines Agency, or EMA, is reviewing the SPINRAZA marketing application under accelerated assessment. Biogen estimates that there are approximately 20,000 patients with SMA in the U.S., EU and Japan, with a large percentage in the United States.

Akcea Therapeutics, Inc. is our wholly owned subsidiary focused on developing and commercializing volanesorsen and three other clinical-stage drugs for serious cardiometabolic diseases caused by lipid disorders, AKCEA-APO(a)-L_{Rx}, AKCEA- AKCEA-APOCIII-L_{Rx} and ANGPTL3-L_{Rx}. Each of these four drugs could potentially treat multiple patient populations. Moving these drugs into a company that we own allows us to retain substantial value from them and ensures Ionis' core focus remains on innovation. Akcea is assembling the global infrastructure to continue developing the drugs in its pipeline, to commercialize them with a focus on lipid specialists as the primary call point and to provide the specialized patient and physician support required to address rare disease patient populations.

We and Akcea are developing volanesorsen to treat two severe and rare, genetically defined diseases, FCS and familial partial lipodystrophy, or FPL. FCS and FPL are orphan diseases characterized by severely high triglyceride levels that result in severe, daily symptoms and a high risk of life-threatening pancreatitis. Volanesorsen acts to reduce triglyceride levels by inhibiting the production of ApoC-III, a protein that is a key regulator of triglyceride clearance. The clinical development program for volanesorsen consists of three Phase 3 studies called APPROACH, BROADEN and COMPASS. We have completed the COMPASS and APPROACH studies. We plan to file for marketing authorization in the U.S., Europe and Canada in 2017. The BROADEN study is in patients with FPL. The study is currently enrolling patients and we plan to have data from this study in 2019. We estimate that FCS and FPL each affect 3,000 to 5,000 patients globally. If approved, we plan to commercialize volanesorsen for both FCS and FPL through Akcea.

IONIS-TTR$_{Rx}$ is potentially a first-in-class and best-in-class drug for the treatment of all forms of transthyretin, or TTR, amyloidosis, a debilitating, progressive, fatal disease in which patients experience a progressive buildup of amyloid plaque deposits in tissues throughout the body, including peripheral nerves, heart, intestinal tract, kidney and bladder. IONIS-TTR$_{Rx}$ is given as one subcutaneous injection, once a week. We are evaluating IONIS-TTR$_{Rx}$ in an ongoing Phase 3 study, NEURO-TTR, in patients with FAP. More than half of these patients also have TTR amyloid cardiomyopathy. As part of our Phase 3 study, we are evaluating cardiomyopathy in this subset of patients by cardiac imaging and biomarkers which will provide data on cardiovascular endpoints. Together the polyneuropathy and cardiomyopathy forms of TTR amyloidosis represent a large commercial opportunity for IONIS-TTR$_{Rx}$. We plan to have data from the NEURO-TTR study in the second quarter of 2017. We and GSK, our partner for IONIS-TTR$_{Rx}$, are preparing to file for marketing authorization if these data are positive. In our open-label extension study, we have observed substantial TTR reductions in patients with FAP. In a Phase 2 open-label, investigator-initiated study, Dr. Merrill Benson, professor of pathology and lab medicine and molecular genetics at Indiana University School of Medicine, observed sustained reductions in TTR and evidence of disease stabilization in patients with the cardiomyopathy form of TTR amyloidosis. GSK is preparing to commercialize IONIS-TTR$_{Rx}$.

In addition to our Phase 3 programs, we have a pipeline of drugs with the potential to be first-in-class and/or best-in-class drugs to treat patients with diseases that have inadequate treatment options. We are addressing a broad spectrum of diseases from common diseases affecting millions, such as cardiovascular disease, clotting disorders, Alzheimer's and Parkinson's disease, to rare diseases, such as amyotrophic lateral sclerosis and Huntington's disease. Our pipeline has over a dozen drugs in Phase 2 development, many of which we believe have the potential to be significant commercial opportunities. In particular, IONIS-FXI$_{Rx}$ and AKCEA-APO(a)-L$_{Rx}$ represent the value we have created. IONIS-FXI$_{Rx}$ is the first antithrombotic in development that has shown it can decrease the risk of blood vessel obstruction caused by a blood clot without increasing bleeding risk. Given the unique profile of IONIS-FXI$_{Rx}$, we believe that IONIS-FXI$_{Rx}$ has the potential to be an important therapy for the many patients who need an antithrombotic but cannot take currently available therapies due to the high risk of bleeding. AKCEA-APO(a)-L$_{Rx}$ is the first and only drug in clinical development designed to selectively and robustly lower Lp(a), a key driver of cardiovascular disease. We believe that addressing Lp(a) is the next important horizon in lipid-focused cardiovascular disease treatment.

The depth of our knowledge and expertise with antisense technology, together with our strong financial position, provides us the flexibility to determine the optimal development and commercialization strategy to maximize the near- and longer-term value of our drugs. We have distinct partnering strategies that we employ based on the specific drug, therapeutic area and expertise and resources our potential partners may bring to the collaboration. For some drugs, we may choose to develop and commercialize them through wholly owned subsidiaries like Akcea. In general, these are drugs, such as volanesorsen, that we have the internal expertise to advance, that have a clear development path with manageable costs and that have the potential for initial rare disease indications. For other drugs, we may form partnerships that enable us to leverage our partner's global expertise and resources needed to support large commercial opportunities, as we did with Bayer and Novartis.

We have established alliances with a cadre of leading global pharmaceutical companies that are working alongside us in developing our drugs, advancing our technology and preparing to commercialize our products. Our partners bring substantial resources and expertise that augment and build upon our internal capabilities. We have strategic partnerships with Biogen and AstraZeneca through which we can broadly expand our drug discovery efforts to new disease targets in specific therapeutic areas for which our partners can provide expertise, tools and resources to complement our drug discovery efforts. We also have partnerships with Bayer, GSK, Janssen, Novartis and Roche. Each of these companies brings significant expertise and global resources to develop and potentially commercialize the drugs under each partnership. Most recently, in January 2017, we and Akcea initiated a collaboration with Novartis to develop and commercialize AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$. As a leader in the cardiovascular disease space, Novartis brings significant resources and expertise that should support the development and commercialization of these two drugs for significant high-risk patient populations. The collaboration with Novartis should enable us to accelerate the development of these drugs for broader patient populations as Novartis plans to conduct a cardiovascular outcomes study for each of these drugs. In addition, Akcea has the right to co-commercialize these drugs using its specialized sales force focused on lipid specialists in select markets. We also form early stage research and development partnerships that allow us to expand the application of our technology to new therapeutic areas. For example, we established a collaboration with Janssen, which brings together our RNA-targeted technology platform and Janssen's expertise in autoimmune disorders and therapeutic formulation to discover and develop antisense drugs to treat autoimmune disorders in the gastrointestinal, or GI, tract. Lastly, we also work with a consortium of companies that can exploit our drugs and technologies outside our primary areas of focus. We refer to these companies as satellite companies.

Through our partnerships, we have created a broad and sustaining base of potential research and development, or R&D, revenue in the form of license fees, upfront payments and milestone payments while spending prudently to advance our pipeline and technology. Our R&D revenue has consistently grown year over year since 2011. In 2016, we earned more than $345 million in R&D revenue. Moreover, we have the potential to earn nearly $13 billion in future milestone payments and licensing fees from our current partnerships. We also have the potential to share in the future commercial success of our inventions and drugs resulting from our partnerships through earn out or royalty arrangements. With the approval of SPINRAZA in the U.S., we are adding commercial revenue from SPINRAZA royalties to our existing R&D revenue base. Looking forward, we have the potential to increase our commercial revenue from SPINRAZA royalties if Biogen achieves marking authorization in additional countries. We also have the potential to further increase our commercial revenue with volanesorsen product sales and IONIS-TTR$_{Rx}$ royalties. We believe we have the key elements in place to achieve sustained long-term financial growth, including multiple drivers of revenue; a mature, broad and rapidly-advancing clinical pipeline; a partnership strategy that leverages our partner resources; and an innovative drug technology that we continue to deploy across a range of therapeutic areas to address both rare and large patient populations.

Corporate Information

We incorporated in California in 1989 and in January 1991 we changed our state of incorporation to Delaware. In December 2015, we changed our name to Ionis Pharmaceuticals, Inc. from Isis Pharmaceuticals, Inc. Our principal executive offices are located at 2855 Gazelle Court, Carlsbad, CA 92010. Our telephone number is (760) 931-9200. Our website address is *www.ionispharma.com*. Information contained in, or accessible through, our website does not constitute a part of this prospectus supplement or the accompanying prospectus.

THE OFFERING

The selling stockholder named in this prospectus supplement may offer and sell up to 1,631,435 of our shares of common stock. Shares of common stock that may be offered in this offering will be fully paid and non-assessable. We will not receive any of the proceeds of sales by the selling stockholder of any of the shares of common stock covered by this prospectus supplement. Throughout this prospectus supplement, when we refer to the selling stockholder, we are referring to the selling stockholder named herein and, as applicable, any donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus supplement from the selling stockholder as a gift, pledge, or other non-sale related transfer that may be identified in a prospectus supplement.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading “Risk Factors” contained in our annual report on Form 10-K filed with the Securities and Exchange Commission on March 1, 2017, and incorporated by reference in this prospectus supplement and the accompanying prospectus, as the same may be amended, supplemented or superseded by the risks and uncertainties described under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein by reference contain forward-looking statements regarding our business, the business of Akcea Therapeutics, Inc., a subsidiary of Ionis Pharmaceuticals, and the therapeutic and commercial potential of SPINRAZA (nusinersen), volanesorsen and IONIS-TTR$_{Rx}$ and other of our drugs in development. Any statement describing our 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. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors known by us at the times the statements are made. As a result, you are cautioned not to rely on these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section entitled "Risk Factors", as well as in our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q filed with the SEC.

We claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 for all forward-looking statements.

USE OF PROCEEDS

We will not receive any of the proceeds from sale of shares of common stock by the selling stockholder pursuant to this prospectus supplement and the accompanying prospectus.

SELLING STOCKHOLDER

This prospectus supplement relates to the resale of up to an aggregate of 1,631,435 shares of common stock held by or beneficially owned by the selling stockholder listed or otherwise identified in the table below. These shares were initially acquired from us in connection with an exclusive, worldwide option and collaboration agreement with Novartis Pharma AG and were issued in reliance on the exemption from the registration requirements of the Securities Act set forth in Section 4(2) thereof and the rules and regulations promulgated thereunder.

The following table sets forth the name of each selling stockholder, the number and percentage of shares of common stock beneficially owned by each selling stockholder as of March 31, 2017, the maximum number of shares of common stock offered by each selling stockholder pursuant to this prospectus supplement and the number of shares of common stock and percentage of shares of common stock beneficially owned by each selling stockholder after completion of the sale of the maximum number of shares of common stock that may be offered under this prospectus supplement by such selling stockholder. Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our common stock. Generally, a person "beneficially owns" shares of common stock if the person has or shares with others the right to vote those shares of common stock or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days. The percentages in the table below are based on 123,880,559 shares of common stock outstanding as of March 31, 2017. Except as otherwise indicated in the footnotes to the table or in cases where community property laws apply, we believe that each person identified in the table possesses sole voting and investment power over all shares of common stock as beneficially owned by such person.

All information contained in the table below and the footnotes thereto is based upon information provided to us by the selling stockholder, and we have not independently verified this information.

	Beneficial Ownership as of March 31, 2017		Maximum Number of Shares of Common Stock Offered	Beneficial Ownership After the Sale of the Maximum Number of Shares of Common Stock[1][2]	
Selling Stockholder	**Number**	**%**		**Number**	**%**
Novartis Pharma AG Lichtstrasse 35 4002, Basel, Switzerland	1,631,435	1.3%	1,631,435	0	0.0

(1) We do not know when or in what amounts the selling stockholder may offer and sell its shares of common stock. The selling stockholder might sell all, some or none of the shares of common stock offered by this prospectus supplement and, as a result, we cannot estimate the number of shares of common stock that will be held by the selling stockholder after completion of the offering. However, for purposes of this table we have assumed that the selling stockholder will sell the maximum number of shares of common stock offered listed in the table above.

(2) Pursuant to an option and collaboration agreement with us, the selling stockholder has a contractual obligation to purchase an additional $50,000,000 of stock from us or our subsidiary, Akcea, if certain conditions are met. For purposes of this table we have not given effect to this obligation since it is unknown at this time whether the selling stockholder will be obligated to purchase our common stock or Akcea stock.

Additional Relationships and Transactions with the Selling Stockholder

Our subsidiary, Akcea Therapeutics, Inc., and the selling stockholder are parties to an exclusive, worldwide option and collaboration agreement under which Akcea and the selling stockholder are developing and commercializing AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx}.

PLAN OF DISTRIBUTION

We are registering the shares of common stock issued to the selling stockholder to permit the resale of these shares by the selling stockholder from time to time after the date of this prospectus supplement. We will not receive any of the proceeds from the sale by the selling stockholder of the shares of common stock. We will bear all fees and expenses incident to the registration of the shares of common stock on behalf of the selling stockholder but not any underwriting discounts or commissions.

The selling stockholder of the shares of common stock and any of its pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their shares of common stock covered hereby on The NASDAQ Global Select Market or any other stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or negotiated prices. The selling stockholder may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- an underwritten public offering in which one or more underwriters participate;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part, to the extent permitted by law;
- in transactions through broker-dealers that agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- put or call options transactions or through the writing or settlement of standardized or over-the-counter options or other hedging or derivative transactions, whether through an options exchange or otherwise;
- by pledge to secure debts and other obligations;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

To the extent required by law, this prospectus supplement and the accompanying prospectus may be amended or further supplemented from time to time to describe a specific plan of distribution, which amended prospectus or prospectus supplement may include the following information to the extent required by law:

- the terms of the offering;
- the names of any underwriters or agents;
- the purchase price of the shares of common stock;
- any delayed delivery arrangements;
- any underwriting discounts and other items constituting underwriters’ compensation;
- any initial public offering price; and
- any discounts or concessions allowed or re-allowed or paid to dealers.

The selling stockholder may also sell shares of common stock under Rule 144 under the Securities Act, if available, rather than under this prospectus supplement and the accompanying prospectus.

If underwriters are used in the sale, the shares of common stock will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. In connection with any such underwritten sale of shares of common stock, underwriters may receive compensation from the selling stockholder, for whom they may act as agents, in the form of discounts, concessions or commissions. If the selling stockholder uses an underwriter or underwriters to effectuate the sale of shares of common stock, we and/or the selling stockholder will execute an underwriting agreement with those underwriters at the time of sale of those shares of common stock. To the extent required by law, the names of the underwriters will be set forth in a supplement to this prospectus or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus, used by the underwriters to sell those securities. The obligations of the underwriters to purchase those shares of common stock will be subject to certain conditions precedent, and unless otherwise specified in a prospectus or a prospectus supplement, the underwriters will be obligated to purchase all the shares of common stock offered by such prospectus or prospectus supplement if any of such shares of common stock are purchased. Any initial public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

Broker-dealers engaged by the selling stockholder may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholder (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440-1.

From time to time, the selling stockholder may pledge, hypothecate or grant a security interest in some or all of the shares of common stock owned by it. The pledgees, secured parties, or persons to whom the shares have been hypothecated will, upon foreclosure, be deemed to be selling stockholders. The number of a selling stockholder’s shares of common stock offered under this prospectus supplement will decrease as and when it takes such actions. The plan of distribution for that selling stockholder’s shares of common stock will otherwise remain unchanged.

In connection with the sale of the shares of common stock or interests therein, the selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares of common stock in the course of hedging the positions they assume. The selling stockholder may also sell the shares of common stock short and deliver these securities to close out its short positions or to return borrowed shares in connection with such short sales, or loan or pledge the shares of common stock to broker-dealers that in turn may sell these securities. The selling stockholder may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus supplement, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus supplement and the accompanying prospectus (as supplemented or amended to reflect such transaction).

The selling stockholder may also sell shares of common stock from time to time through agents. We will name any agent involved in the offer or sale of such shares and will list commissions payable to these agents in a prospectus supplement, if required. These agents will be acting on a best efforts basis to solicit purchases for the period of their appointment, unless we state otherwise in any required prospectus supplement.

The selling stockholder may sell shares of common stock directly to purchasers. In this case, it may not engage underwriters or agents in the offer and sale of such shares.

The selling stockholder may make gifts of shares of common stock covered hereby. Such donees may use this prospectus supplement to resell the shares or, if required by law, we may file a prospectus supplement naming such donees.

The selling stockholder and any broker-dealers or agents that are involved in selling the shares of common stock may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any discounts, commissions or concessions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. A selling stockholder who is an “underwriter” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act and may be subject to certain statutory liabilities of, including but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Securities Exchange Act of 1934, as amended, or the Exchange Act. The selling stockholder has informed us that it is not a registered broker-dealer and does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the shares of common stock. In no event shall any underwriter or broker-dealer receive fees, commissions and markups which, in the aggregate, would exceed eight percent (8%).

We are required to pay certain fees and expenses incurred by us incident to the registration of the shares.

The selling stockholder will be subject to the prospectus delivery requirements of the Securities Act including Rule 172 thereunder unless an exemption therefrom is available.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale shares may not simultaneously engage in market making activities with respect to the shares of common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling stockholder will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of shares of common stock by the selling stockholder or any other person. We will make copies of this prospectus supplement and the accompanying prospectus available to the selling stockholder and have informed the selling stockholder of the need to deliver a copy of this prospectus supplement and the accompanying prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

There can be no assurance that the selling stockholder will sell any or all of the shares of common stock registered pursuant to the registration statement, of which this prospectus supplement and the accompanying prospectus form a part. In addition, there can be no assurances that the selling stockholder will not transfer, devise or gift the shares of common stock by other means not described in this prospectus supplement.

Once sold under the registration statement, of which this prospectus supplement and the accompanying prospectus form a part, the shares of common stock will be freely tradable in the hands of persons other than our affiliates.

LEGAL MATTERS

The validity of the issuance of the common stock offered hereby will be passed upon for us by Patrick R. O'Neil, our Senior Vice President, Legal and General Counsel.

Mr. O'Neil holds or has the right to acquire shares of Ionis' common stock in an aggregate amount that is less than 1% of Ionis' outstanding common stock.