

## Ionis and Akcea Partner to Commercialize Inotersen for hATTR

March 15, 2018

**Ionis licenses to Akcea worldwide rights to inotersen and IONIS-TTR-L Rx  
Collaboration advances commercial readiness for planned mid-2018 inotersen launch, positioning Akcea to successfully  
launch two drugs for significant rare diseases this year  
Ionis Chief Business Officer Sarah Boyce will join Akcea as President and Board member  
Companies to host conference call today, March 15th at 8:30 a.m. Eastern Time**

CARLSBAD, Calif. and CAMBRIDGE, Mass., March 15, 2018 /PRNewswire/ -- Ionis Pharmaceuticals (NASDAQ: IONS) ("Ionis") and Akcea Therapeutics, Inc. (NASDAQ: AKCA) ("Akcea"), an affiliate of Ionis, today announced an exclusive, worldwide license by Ionis to Akcea for inotersen and AKCEA-TTR-L<sub>Rx</sub>, formerly IONIS-TTR-L<sub>Rx</sub>, in a transaction potentially worth up to approximately \$1.7 billion to Ionis plus profit sharing payments.



This transaction strengthens the companies' ability to successfully launch inotersen upon approval by leveraging the commercial preparations carried out by Ionis along with Akcea's commercial infrastructure and capabilities. The newly combined Akcea team is preparing to launch inotersen in the U.S. and EU following planned approvals in mid-2018 to treat people with hereditary transthyretin amyloidosis, or hATTR, a systemic, progressive and fatal disease.

The companies are also developing AKCEA-TTR-L<sub>Rx</sub> for hereditary and wild-type forms of ATTR. AKCEA-TTR-L<sub>Rx</sub> is planned to enter clinical development in 2018.

"This collaboration reflects our ever-increasing confidence in the value of inotersen and exemplifies our strategy to use commercial affiliates to commercialize our drugs, keeping the core of Ionis focused on innovation and our antisense pipeline. This collaboration will allow the combined Ionis-Akcea team to rapidly deliver inotersen to the patients who desperately need this treatment," said Stanley T. Crooke, M.D., Ph.D., chief executive officer and chairman of Ionis. "Our partnering discussions resulted in a number of options and we decided this partnership with Akcea will maximize the commercial value of inotersen and our TTR franchise. The potential to add commercial revenue from both inotersen and volanesorsen to our growing Spinraza<sup>®</sup> royalties helps us achieve our goal of being a multiproduct, profitable company."

"This collaboration is transformational for Akcea," said Paula Soteropoulos, chief executive officer of Akcea Therapeutics. "Adding two potentially life-changing therapies, inotersen and AKCEA-TTR-L<sub>Rx</sub>, expands our pipeline of drugs to treat people with serious and under-served rare diseases. Inotersen's launch will benefit from Akcea's patient-centric approach and our focus, dedication and expertise. Through our launch preparations for volanesorsen, we have rapidly expanded our capabilities and team to become a unique and leading presence in rare diseases. This commercial build-up, combined with our highly accomplished team, allows us to accelerate readiness for the upcoming inotersen launch. Further, it increases our options to scale our business given the expansion of our call points and sales force as we work with this new physician community."

As part of the collaboration, the inotersen commercial team is joining Akcea, enabling a seamless and rapid transition in the ongoing launch preparations for inotersen. Sarah Boyce, currently Ionis' chief business officer, will join Akcea as president and take a seat on the Akcea board of directors upon closing. Ms. Boyce, who has been leading the inotersen launch, will bring to Akcea extensive, global experience in the life sciences industry where she established organizations from inception and built high performing teams.

"The strength and experience of the joint inotersen and volanesorsen teams, and Akcea's global capabilities, further enhance our potential to maximize inotersen's benefit to people with hATTR," said Ms. Boyce. "We are confident inotersen can provide hope for people with hATTR by giving them greater freedom and control over their disease. In its pivotal study, inotersen treatment provided significant benefit in measures of disease progression and improved quality of life in the majority of people with hATTR, while offering simple and quick administration as a once-weekly subcutaneous injection. We are committed to bringing this important drug to those suffering from this devastating and fatal disease."

Under the agreement, Akcea will pay Ionis an upfront licensing fee of \$150 million, payable in shares of common stock priced by reference to a recent trading average. Akcea will have rights to commercialize inotersen and AKCEA-TTR-L<sub>Rx</sub> globally. To support commercialization of inotersen, Ionis will purchase \$200 million of Akcea common stock priced by reference to a recent trading average. Upon closing this transaction, Ionis' ownership in Akcea will increase by 7%, from 68% to 75%, totaling 64,114,545 shares. Regulatory approval of inotersen and AKCEA-TTR-L<sub>Rx</sub> in the U.S. and EU will trigger milestone payments to Ionis of \$50 million and \$40 million, respectively, with additional milestone payments due upon approval of both programs in various other geographies. The license fee and initial milestone payments may be payable in Akcea common stock at fair market value. Commercial profits and losses from inotersen will be split 60% to Ionis and 40% to Akcea until the first commercial sales of AKCEA-TTR-L<sub>Rx</sub>, after which the profits and losses will be shared 50/50. The costs of the development of AKCEA-TTR-L<sub>Rx</sub> and the profits from its commercialization will be shared 50/50. The license for the two drugs also includes various sales milestone payments of up to nearly \$1.3 billion. For this transaction, Ionis was advised by Stifel, Nicolaus & Company, Incorporated and Akcea was advised by Cowen and Company, LLC.

The transaction is subject to customary closing conditions and is expected to close in the second quarter of 2018, assuming satisfaction of certain conditions. Closing conditions include a non-waivable condition requiring the approval of the stock purchase agreement, the license agreement and related agreements and the transaction contemplated thereunder by the affirmative vote of holders representing a majority of the issued and

outstanding shares of common stock other than Ionis and its affiliates, which will exclude a vote of Akcea's directors and officers. Novartis Pharma AG, one of Akcea's largest shareholders, has agreed to vote in favor of the proposal with its shares of common stock, representing approximately 9.4% of the issued and outstanding shares.

#### **Conference Call**

Ionis and Akcea will co-host a live webcast today, Thursday, March 15 at 8:30 a.m. ET to discuss this announcement. Interested parties may listen to the call by dialing 877-443-5662 or access the webcast under the investors section at [www.ionispharma.com](http://www.ionispharma.com) or [www.akceatx.com](http://www.akceatx.com). A webcast replay will be available for a limited time.

#### **ABOUT INOTERSEN**

Inotersen is an antisense drug designed to reduce the production of transthyretin, or TTR protein, to treat TTR amyloidosis (ATTR), a systemic, progressive and fatal disease.

Inotersen is currently under regulatory review for marketing authorization in the U.S. and EU. The U.S. Food and Drug Administration has granted Orphan Drug Designation and Fast Track Status to inotersen for the treatment of patients with polyneuropathy due to hereditary TTR amyloidosis (hATTR), and the European Medicines Agency has granted Orphan Drug Designation to inotersen for the treatment of patients with ATTR.

#### **ABOUT HEREDITARY TRANSTHYRETIN AMYLOIDOSIS (hATTR)**

hATTR is a progressive, systemic, and fatal genetic disease caused by the inappropriate formation and aggregation of TTR amyloid deposits in various tissues and organs throughout the body, including in peripheral nerves, heart, intestinal tract, eyes, kidneys, central nervous system, thyroid and bone marrow. Patients with hATTR often present with a mixed phenotype and experience overlapping symptoms of polyneuropathy and cardiomyopathy. The progressive accumulation of TTR amyloid deposits in these tissues and organs leads to sensory, motor and autonomic dysfunction often having debilitating effects on multiple aspects of a patient's life.

Unfortunately, hATTR is often overlooked in the differential diagnosis and accurate identification is unnecessarily delayed for years. Ultimately, hATTR results in death within three to fifteen years of symptom onset. Therapeutic options for the treatment of patients with hATTR are limited and there are currently no disease-modifying drugs approved for hATTR. There are an estimated 50,000 patients with hATTR worldwide.

#### **ABOUT IONIS PHARMACEUTICALS, INC.**

Ionis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Ionis has created a large pipeline of first-in-class or best-in-class drugs, with over three dozen drugs in development. SPINRAZA® (nusinersen) has been approved in global markets for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Drugs that have successfully completed Phase 3 studies include inotersen, an antisense drug Ionis is developing to treat patients with hereditary TTR amyloidosis (hATTR), and volanesorsen, an antisense drug discovered by Ionis and co-developed by Ionis and Akcea Therapeutics to treat patients with either familial chylomicronemia syndrome or familial partial lipodystrophy. Akcea, an affiliate of Ionis, is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious rare diseases. If approved, inotersen and volanesorsen will be commercialized through Ionis' affiliate, Akcea. Inotersen filings for marketing approval have been submitted in the U.S. and EU. Volanesorsen filings for marketing approval have been submitted in the U.S., EU, and Canada. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at [www.ionispharma.com](http://www.ionispharma.com).

#### **ABOUT AKCEA THERAPEUTICS**

Akcea Therapeutics, an affiliate of Ionis Pharmaceuticals, Inc., is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious rare diseases. Akcea is advancing a mature pipeline of four novel drugs, including volanesorsen, AKCEA-APO(a)-LR<sub>x</sub>, AKCEA-ANGPTL3-LR<sub>x</sub> and AKCEA-APOCIII-LR<sub>x</sub>. All four drugs were discovered by and are being co-developed with Ionis, a leader in antisense therapeutics, and are based on Ionis' proprietary antisense technology. Volanesorsen is under regulatory review in the U.S., EU and Canada for the treatment of familial chylomicronemia syndrome, or FCS. Akcea is building the infrastructure to commercialize its drugs globally. Akcea is located in Cambridge, Massachusetts. Additional information about Akcea is available at [www.akceatx.com](http://www.akceatx.com).

#### **IONIS' AND AKCEA'S FORWARD-LOOKING STATEMENT**

This press release includes forward-looking statements regarding the recently announced transaction between Ionis and Akcea, Ionis' and Akcea's business and the therapeutic and commercial potential of inotersen, IONIS-TTR-LR<sub>x</sub> and other products in development. Any statement describing Ionis' or Akcea's goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of inotersen, volanesorsen or other of Ionis' or Akcea's drugs in development 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' and Akcea's 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' and Akcea's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis and Akcea. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' and Akcea's programs are described in additional detail in Ionis' and Akcea's annual reports on Form 10-K for the year ended December 31, 2017, which are on file with the SEC, and Akcea's preliminary proxy statement with respect to the transaction, which it intends to file with the SEC. Copies of these and other documents are available from each company.

In this press release, unless the context requires otherwise, "Ionis", "Akcea," "Company," "Companies" "we," "our," and "us" refers to Ionis Pharmaceuticals and/or Akcea Therapeutics.

Ionis Pharmaceuticals™ is a trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutics™ is a trademark of Ionis Pharmaceuticals, Inc.

#### **IMPORTANT INFORMATION FOR INVESTORS AND SECURITY HOLDERS**

This communication may be deemed to be solicitation material in respect of the proposed transaction of Akcea and Ionis. In connection with the proposed transaction, Akcea intends to file relevant materials with the SEC, including a preliminary proxy statement on Schedule 14A. Following the filing of a definitive proxy statement with the SEC, Akcea will mail the definitive proxy statement and a proxy card to each stockholder entitled to vote at the special meeting relating to the proposed transaction. INVESTORS AND SECURITY HOLDERS OF AKCEA ARE URGED TO READ THESE MATERIALS (INCLUDING ANY AMENDMENTS OR SUPPLEMENTS THERETO) AND ANY OTHER RELEVANT DOCUMENTS IN CONNECTION

WITH THE PROPOSED TRANSACTION THAT AKCEA WILL FILE WITH THE SEC WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT AKCEA AND THE PROPOSED TRANSACTION. The preliminary proxy statement, the definitive proxy statement and other relevant materials in connection with the proposed transaction (when they become available), and any other documents filed by Akcea with the SEC, may be obtained free of charge at the SEC's website at [www.sec.gov](http://www.sec.gov). In addition, investors and security holders may obtain free copies of the documents filed with the SEC or by sending a request to Investor Relations at Akcea Therapeutics, Inc., 55 Cambridge Parkway, Suite 100, Cambridge, Massachusetts 02142.

Akcea and its directors and executive officers may be deemed to be participants in the solicitation of proxies from Akcea's stockholders with respect to the proposed transaction. Information regarding the identity of the potential participants, and their direct or indirect interests in the transaction, by security holdings or otherwise, including Ionis, will be set forth in the proxy statement and other materials to be filed with the SEC in connection with the proposed transaction.



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*A subsidiary of Ionis Pharmaceuticals, Inc.*

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SOURCE Ionis Pharmaceuticals, Inc.; Akcea Therapeutics

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