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): October 10, 2018

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))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (Section 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (Section 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 1.01 Entry into a Material Definitive Agreement.

On October 10, 2018, Ionis Pharmaceuticals, Inc. (the "Company") issued a press release announcing that the Company has entered into an exclusive, worldwide collaboration agreement with Roche for the development of IONIS-FB-L_{Rx}.

A copy of this press release is attached as Exhibit 99.1 to this Current Report and incorporated herein by reference.

Item 8.01 Other Events.

On October 5, 2018, the Company and Akcea Therapeutics, Inc., an affiliate of the Company, announced that the U.S. Food and Drug Administration (FDA) has approved TEGSEDI™ (inotersen) for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. TEGSEDI is now approved in the U.S., the European Union and Canada.

A copy of the press release is attached as Exhibit 99.2 to this Current Report and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1	Press Release dated October 10, 2018.
99.2	Press Release dated October 5, 2018.

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: October 10, 2018

By: /s/ Patrick R. O'Neil

PATRICK R. O'NEIL
Senior Vice President, Legal, General Counsel and Chief Compliance Officer

Exhibit 99.1

Ionis Enters New Collaboration with Partner to Develop IONIS-FB-L_{Rx} for Complement-Mediated Diseases

Transaction valued at up to $760 million, including $75 million upfront payment, plus royalties up to 20%

Planned Phase 2 program to begin in early 2019

CARLSBAD, Calif., October 10, 2018 – Ionis Pharmaceuticals, Inc (NASDAQ: IONS) today announced a new collaboration with Roche to develop IONIS-FB-L_{Rx} for the treatment of complement-mediated diseases. This collaboration will leverage Ionis' leadership in RNA-targeted therapeutics to develop IONIS-FB-L_{Rx} targeting Factor B (FB) for a broad range of diseases. The first indication the two companies will pursue is the treatment of patients with Geographic Atrophy (GA), the advanced stage of dry age-related macular degeneration (AMD). A Phase 2 study in patients with GA is planned to begin in early 2019.

"Ionis is committed to bringing new therapies to patients living with unmet medical needs. The collaboration is designed to maximize both the potential benefit to patients and the likelihood of success, while optimizing our commercial participation in IONIS-FB-L_{Rx}. This new agreement builds upon our productive relationship with Roche on IONIS-HTT_{Rx} (RG6042), an antisense drug for the treatment of people with Huntington's disease," said Brett P. Monia, chief operating officer at Ionis. "Our antisense technology is the first to demonstrate robust, dose-dependent and sustained reduction of FB in a clinical study. We believe that we have found the right partner whose experience in retinal disease drug development and commercialization will enhance our efforts to effectively develop IONIS-FB-L_{Rx} for patients who currently have no adequate treatment options."

IONIS-FB-L_{Rx}, an antisense drug using Ionis' advanced **LI**gand **C**onjugated **A**ntisense (LICA) technology, reduces the production of FB, a key protein in the complement innate immune system. FB is predominately produced in the liver and circulates throughout the vascular system, including vessels in the eye and kidney. This complement protein plays a pivotal role in an innate immunogenic cascade that, when overactivated, has been associated with the development of several complement-mediated diseases, including dry AMD.

In a Phase 1 study in 54 healthy volunteers IONIS-FB-L_{Rx} reduced plasma FB and was safe and well tolerated.

Under this new collaboration with Roche, Ionis will receive a $75 million upfront payment. In addition, Ionis is eligible to receive up to $684 million in development, regulatory and sales milestone payments and license fees. Ionis also has the potential to receive tiered royalties that range from the high teens to twenty percent on sales from the product when commercialized. Ionis is responsible for conducting a Phase 2 study in patients with dry AMD and exploring the drug in a rare severe renal indication. Roche has the option to license IONIS-FB-L_{Rx} at the completion of the studies. Upon licensing, Roche will be responsible for all global development and commercialization activities.

About AMD

Age-related macular degeneration, or AMD is the most common cause of blindness in the elderly population that can progress through a succession of stages from early to late. Late stages of AMD are classified as “wet” or “dry,” with approximately 90 percent of U.S. cases diagnosed as “dry.” Dry AMD is the leading cause of blindness in the U.S. and developed countries. This disease is expected to affect up to 3 million people in the U.S. and 196 million people worldwide by 2020.[1] Geographic Atrophy (GA) is a late stage manifestation of dry AMD resulting from a progressive loss of retinal pigment epithelial (RPE) cells, photoreceptor cells and choriocapillaries in the central retina. Patients with GA experience trouble with facial recognition, decreased reading speeds and difficulty driving at night, and ultimately, blindness.[2] It is estimated that more than 5 million people worldwide suffer from GA, a disease with no approved therapies.[3]

About Ionis Pharmaceuticals, Inc.

As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, proprietary antisense technology platform with the potential to treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs – such as children and adults with spinal muscular atrophy (SMA). We created SPINRAZA® (nusinersen)* and are proud to have brought new hope to the SMA community by developing the first and only approved treatment for this disease.

Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 drugs with the potential to treat patients with cardiovascular disease, rare diseases, neurological diseases, infectious diseases and cancer. We created TEGSEDI™ (inotersen) the world’s first RNA-targeted therapeutic approved for the treatment of polyneuropathy of hereditary transthyretin (TTR) amyloidosis (ATTR) in adult patients that our affiliate Akcea Therapeutics is commercializing. Together with Akcea, we are also bringing new medicines to patients with cardiometabolic lipid disorders.

To learn more about Ionis follow us on twitter @ionispharma or visit http://ir.ionispharma.com/.

*Spinraza is marketed by Biogen.

Ionis’ Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' alliance with Roche and the development, activity, therapeutic potential, commercial potential and safety of IONIS-HTT$_{Rx}$ (RG6042) and IONIS-FB-L$_{Rx}$. 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, 2017, and its most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of this and other documents are available from the Company.

In this press release, unless the context requires otherwise, “Ionis,” “Company,” “we,” “our,” and “us” refers to Ionis Pharmaceuticals and its subsidiaries.

Ionis Pharmaceuticals™ is a trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutics™ is a trademark of Akcea Therapeutics, Inc. TEGSEDI™ is a trademark of Akcea Therapeutics, Inc. WAYLIVRA™ is a trademark of Akcea Therapeutics, Inc. SPINRAZA® is a registered trademark of Biogen.

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2. Suness JS, Rubin GS, Broman A, et al. “Low luminance Visual Dysfunction as a Predictor of Subsequent Visual Loss From Geographic Atrophy in Age-Related Macular Degeneration.” Ophthalmology. 115 (2008):1480-1488. / Suness JS, Applegate CA, Bressler NM, et al. “Visual Function Abnormalities and Prognosis in Eyes with Age-Related Geographic Atrophy of the Macula and Good Visual Acuity.” Ophthalmology. 104.10 (1997):1677-1691.
3. Buch H, Vinding T, Nielsen NV et al. “14-year Incidence Progression and Visual Morbidity of Age-related Maculopaty: The Copenhagen City Eye Study.” Ophthalmology.112 (2005):787-798. / Vaz F and Picoto M, “Georgraphic Atrophy” -- http://www.amdbook.org/content/geographic-atrophy-0

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Exhibit 99.2

Akcea and Ionis Receive FDA Approval of TEGSEDI™ (inotersen) for the Treatment of the Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis in Adults

TEGSEDI provides powerful knockdown of TTR protein, delivering significant and sustained benefits in neuropathy and quality of life

TEGSEDI is an effective treatment choice that allows self-administration at a time and place that works for the patient

Conference call and webcast scheduled for today at 5:45pm ET

BOSTON, Mass. and CARLSBAD, Calif., October 5, 2018 (GLOBENEWSWIRE) – Akcea Therapeutics, Inc. (NASDAQ: AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), announced today that the U.S. Food and Drug Administration (FDA) has approved TEGSEDI™ (inotersen) for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. TEGSEDI is now approved in the U.S., European Union and Canada.

“TEGSEDI is the first and only RNA-targeting therapeutic that powerfully reduces the production of TTR protein through a once-weekly subcutaneous injection offering patients an effective treatment for people living with polyneuropathy caused by hATTR amyloidosis. We believe this profile will make TEGSEDI an excellent choice for many patients and that it’s self-administration gives the flexibility to treat at a time that works for them which could change the way this progressive and debilitating disease is treated and managed,” said Paula Soteropoulos, chief executive officer at Akcea Therapeutics. “As we execute on our multi-country launch, we are committed to delivering a comprehensive treatment experience for people taking TEGSEDI. Beyond the drug itself, this includes ensuring patients who need this therapy have access to it, offering personalized support programs and enabling patients to administer treatment on their own terms.”

In hATTR amyloidosis, transthyretin (TTR) protein misfolds and accumulates as amyloid deposits throughout the body. TEGSEDI targets the disease at its source by reducing the production of TTR protein. In the NEURO-TTR study, treatment with TEGSEDI produced up to a 79% mean decrease from baseline in serum TTR protein in patients regardless of TTR mutation, sex, age, or race.

“Although the true incidence is not known of hereditary ATTR amyloidosis with polyneuropathy, there is no doubt that it is currently significantly underdiagnosed,” said Isabelle Lousada, founder and chief executive officer of the Amyloidosis Research Consortium. “This approval represents a significant advancement for the patients, families, caregivers and healthcare professionals in the U.S. who need more options for the medical management of this disease. I am now more optimistic than ever that we can increase awareness of this rare disease, support faster diagnosis and provide better treatment.”

The FDA's approval of TEGSEDI was based on results from the Phase 3 NEURO-TTR study in patients with hATTR amyloidosis with symptoms of polyneuropathy. Results from that study demonstrated that patients treated with TEGSEDI experienced significant benefit compared to patients treated with placebo across both co-primary endpoints: the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QoL-DN) and modified Neuropathy Impairment Score +7 (mNIS+7), a measure of neuropathic disease progression.

TEGSEDI is associated with risk of thrombocytopenia and glomerulonephritis. Enhanced monitoring is required to support early detection and management of these identified risks. For TEGSEDI's full prescribing information, including boxed warning, please visit www.TEGSEDI.com and please see Important Safety Information below. TEGSEDI is being marketed with a Risk Evaluation and Mitigation Strategy (REMS).

"hATTR amyloidosis is a fatal disease that affects multiple organs and body systems and robs people of so much – the ability to work, the ability to carry out daily tasks – all the things that make them feel in control of their lives," said Morie Gertz, M.D., hematologist and Chair Emeritus of Internal Medicine at Mayo Clinic. "TEGSEDI has demonstrated a nearly 80% reduction in TTR, which is now a validated approach to treating this disease. The rapid and sustained improvements compared to placebo and reversal in measures of disease seen in a substantial proportion of patients coupled with the independence offered through self injection provide a sense of hope not only to patients, but to their caregivers and families as well."

To assist hATTR amyloidosis patients in gaining access to TEGSEDI, Akcea has created Akcea Connect™, a patient support program made up of dedicated, regionally-based nurse case managers who have a wide range of medical knowledge and experience.This program offers free, private and personalized support to patients and their caregivers and families across the United States. Akcea Connect is now accepting patient enrollment and authorization forms.For more information, please see the contact information for Akcea Connect below.

"hATTR amyloidosis is a devastating disease that takes so much from patients. Akcea is ready to help patients take something back," said Sarah Boyce, president of Akcea Therapeutics. "We understand that managing a rare disease goes beyond providing a new medicine and our highly skilled team is fully prepared to provide an effective, safe and comprehensive treatment experience. Our industry-leading patient support program, Akcea Connect, is poised to help patients through every stage of their TEGSEDI treatment journey, and we are well advanced in discussions with leading payers to facilitate access. We are excited and ready to execute on our launch plans and bring TEGSEDI to patients."

" The U.S. approval of TEGSEDI represents another important addition to the expanding Ionis commercial pipeline, a product of 30 years of innovation. We are thrilled to see our efforts result in an important new medicine for people with polyneuropathy caused by hATTR amyloidosis," said Brett P. Monia, Ph.D., chief operating officer of Ionis Pharmaceuticals. "We are confident that the experienced team at Akcea will deliver on the promise of TEGSEDI. We are grateful to all of the patients and physicians who participated in the TEGSEDI clinical program and who made this landmark approval possible."

In April, Akcea licensed the worldwide rights to commercialize TEGSEDI from Ionis. Based on the U.S. approval of TEGSEDI, Ionis will receive a $50 million milestone payment that may be made in Akcea common stock or cash. Commercial profits and losses from TEGSEDI will be split 60 percent to Ionis and 40 percent to Akcea.

CONFERENCE CALL

Akcea and Ionis will hold a live webcast today, October 5 at 5:45pm Eastern Time to discuss today's announcement. Interested parties may listen to the call by dialing (855) 237-2439, passcode 8380957, or access the webcast at www.akceatx.com or www.ionispharma.com. A webcast replay will be available for a limited time at the same address.

ABOUT TEGSEDI™ (INOTERSEN)

TEGSEDI was approved by the U.S. Food and Drug Administration (FDA) for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. TEGSEDI™ (inotersen), discovered and developed by Ionis Pharmaceuticals, is the world's first and only subcutaneous RNA-targeting drug designed to reduce the production of human transthyretin (TTR) protein. TEGSEDI also received marketing authorization in the European Union and Canada for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis (hATTR).

The approval is based on data from the NEURO-TTR study that was a Phase 3 randomized (2:1), double-blind, placebo-controlled, 15-month, international study in 172 patients with hATTR amyloidosis with symptoms of polyneuropathy. In NEURO-TTR, TEGSEDI demonstrated significant benefit compared to placebo in measures of neuropathy and quality of life as measured by the modified Neuropathy Impairment Score +7 (mNIS+7) and in the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QOL-DN) total score. Patients treated with TEGSEDI experienced similar benefit regardless of subgroups such as age, sex, race, region, Neuropathy Impairment Score (NIS), Val30Met mutation status, and disease stage.

The approval is also based on data from the NEURO-TTR Open Label Extension (OLE) that is an ongoing study for patients who completed the NEURO-TTR study, designed to evaluate the long-term efficacy and safety of TEGSEDI.

For TEGSEDI's full prescribing information, please visit www.TEGSEDI.com.

IMPORTANT SAFETY INFORMATION

TEGSEDI can cause serious side effects including:

Low platelet counts (thrombocytopenia): TEGSEDI may cause the number of platelets in your blood to be reduced. This is a common side effect of TEGSEDI. When your platelet count is too low, your body cannot form clots. You could have serious bleeding that could lead to death. **Call your healthcare provider immediately if you have:**

- Unusual bruising or a rash of tiny reddish-purple spots, often on the lower legs
- Bleeding from skin cuts that does not stop or oozes
- Bleeding from your gums or nose
- Blood in your urine or stools
- Bleeding into the whites of your eyes
- Sudden severe headaches or neck stiffness
- Vomiting or coughing up blood
- Abnormal or heavy periods (menstrual bleeding)

Kidney inflammation (glomerulonephritis): Your kidneys may stop working properly. Glomerulonephritis can lead to severe kidney damage and kidney failure that need dialysis. **Call your healthcare provider immediately if you have:**

- Puffiness or swelling in your face, feet, or hands
- New onset or worsening shortness of breath and coughing
- Blood in your urine or brown urine
- Foamy urine (proteinuria)
- Passed less urine than usual

Because of the risk of serious bleeding caused by low platelet counts and because of the risk of kidney problems, TEGSEDI is available only through a restricted program called the TEGSEDI Risk Evaluation and Mitigation Strategy (REMS) Program. Talk to your healthcare provider about how to enroll in the TEGSEDI REMS Program.

Do not use TEGSEDI if you have:

- A platelet count that is low
- Had kidney inflammation (glomerulonephritis) caused by TEGSEDI
- Had an allergic reaction to inotersen or any of the ingredients in TEGSEDI. See the end of the Medication Guide for a complete list of ingredients in TEGSEDI

Before you start TEGSEDI, tell your healthcare provider about all of your health issues, including if you:

- Have or had bleeding problems
- Have or had kidney problems
- Are pregnant or plan to become pregnant. It is not known if TEGSEDI can harm your unborn baby

- Are breastfeeding or plan to breastfeed. It is not known if TEGSEDI can pass into your breast milk or harm your baby. Talk with your healthcare provider about the best way to feed your baby while you are taking TEGSEDI

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your healthcare provider if you take vitamin A or beta-carotene supplements, blood thinners (anticoagulants), or drugs that affect blood clotting.

Required monitoring
Your healthcare provider will test your blood and urine to check your platelet counts and kidney and liver function before you start TEGSEDI. While you are receiving TEGSEDI, you will be monitored closely for symptoms, which includes checking your platelet counts every week (or more frequently as needed), kidney function every 2 weeks, and liver function every 4 months. If your healthcare provider has you stop taking TEGSEDI, you will need to continue to get your blood and urine tested for 8 more weeks after treatment.

TEGSEDI may cause serious side effects, including

Stroke. TEGSEDI may cause a stroke. One person taking TEGSEDI had a stroke, which occurred within 2 days after the first dose. Get emergency help immediately if you have symptoms of stroke, including sudden numbness or weakness, especially on one side of the body; severe headache or neck pain; confusion; problems with vision, speech, or balance; droopy eyelids.

Inflammatory and immune system problems. Some people taking TEGSEDI had serious inflammatory and immune system problems. Symptoms of inflammatory and immune system problems included unexpected change in walking, weakness and spasms in legs, back pain, weight loss, headache, vomiting, and problems with speech.

Liver effects. TEGSEDI may cause liver problems. Your healthcare provider should do laboratory tests to check your liver before you start TEGSEDI and while you are using it. Tell your healthcare provider if you have symptoms that your liver may not be working right, which could include unexpected nausea and vomiting, stomach pain, being not hungry, yellowing of the skin, or having dark urine.

Allergic reactions. TEGSEDI may cause serious allergic reactions. These allergic reactions often occur within 2 hours after injecting TEGSEDI. Get emergency help immediately if you have any symptoms of a serious allergic reaction, including joint pain, chills, redness on palms of hands, muscle pain, chest pain, flushing, tremor or jerking movements, flu-like symptoms, high blood pressure, or difficulty swallowing.

Eye problems (low vitamin A levels). Treatment with TEGSEDI will lower the vitamin A levels in your blood. Your healthcare provider will tell you how much supplemental vitamin A to take every day; only take the amount they tell you to take. Call your healthcare provider if you get eye problems, such as having difficulty seeing at night or in low-lit areas (night blindness).

The most common side effects of TEGSEDI include injection site reactions (such as redness or pain at the injection site), nausea, headache, tiredness, low platelet counts (thrombocytopenia), and fever. These are not all of the possible side effects of TEGSEDI. Talk to your healthcare provider about any side affects you may be experiencing.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see Medication Guide and full Prescribing Information, including boxed WARNING.

ABOUT HEREDITARY TRANSTHYRETIN (hATTR) AMYLOIDOSIS

hATTR amyloidosis is a severe, progressive, and life-threatening disease caused by the abnormal formation of the TTR protein and aggregation of TTR amyloid deposits in various tissues and organs throughout the body, including in peripheral nerves, heart and intestinal tract. The progressive accumulation of TTR amyloid deposits in these organs often leads to intractable peripheral sensorimotor neuropathy, autonomic neuropathy, and/or cardiomyopathy, as well as other disease manifestations. hATTR amyloidosis causes significant morbidity and progressive decline in quality of life, severely impacting activities of daily living. The disease often progress rapidly and can lead to premature death. The median survival is 4.7 years following diagnosis[1]. Additional information on hATTR amyloidosis, including a full list of organizations supporting the hATTR amyloidosis community worldwide, is available at www.hattrchangethecourse.com or by visiting www.hATTRGuide.com.

ABOUT AKCEA CONNECT™
Akcea Therapeutics is committed to ensuring that patients have access to TEGSEDI. Our patient assistance program called AKCEA CONNECT offers assistance to qualified patients at no cost. AKCEA CONNECT offers personalized and dedicated support to patients and their care teams through best-in-class services. The program focuses on sharing KNOWLEDGE, enabling ACCESS and EMPOWERING patients in order to optimize care in rare diseases, improve patient outcomes, and enhance patients' overall experiences. For more information please visit www.AkceaConnect.com or call 1-866-AKCEATX (1-866-252-3289).

ABOUT AKCEA THERAPEUTICS

Akcea Therapeutics, Inc., an affiliate of Ionis Pharmaceuticals, Inc., is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious and rare diseases. Akcea is advancing a mature pipeline of six novel drugs, including TEGSEDI™ (inotersen), WAYLIVRA™ (volanesorsen), AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx}, AKCEA-APOCIII-L_{Rx}, and AKCEA-TTR-L_{Rx}, all with the potential to treat multiple diseases. All six drugs were discovered by and are being co-developed with Ionis, a leader in antisense therapeutics, and are based on Ionis' proprietary antisense technology. TEGSEDI is approved in the U.S., E.U. and Canada. WAYLIVRA is under regulatory review for the treatment of familial chylomicronemia syndrome, or FCS, and is currently in Phase 3 clinical development for the treatment of people with familial partial lipodystrophy, or FPL. Akcea is building the infrastructure to commercialize its drugs globally. Akcea is a global company headquartered in Cambridge, Massachusetts. Additional information about Akcea is available at www.akceatx.com.

ABOUT IONIS PHARMACEUTICALS

As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, proprietary antisense technology platform with the potential to treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs – such as children and adults with spinal muscular atrophy (SMA). We created SPINRAZA® (nusinersen)* and are proud to have brought new hope to the SMA community by developing the first and only approved treatment for this disease.

Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 drugs with the potential to treat patients with cardiovascular disease, rare diseases, neurological diseases, infectious diseases and cancer. We created TEGSEDI™ (inotersen) the world's first RNA-targeted therapeutic approved for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin (TTR) amyloidosis (ATTR) that our affiliate Akcea Therapeutics is commercializing. Together with Akcea, we are also bringing new medicines to patients with cardiometabolic lipid disorders.

To learn more about Ionis follow us on twitter @ionispharma or visit http://ir.ionispharma.com/.

*Spinraza is marketed by Biogen.

AKCEA'S AND IONIS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the business of Akcea Therapeutics, Inc. and Ionis Pharmaceuticals, Inc. and the therapeutic and commercial potential of TEGSEDI™ Any statement describing Akcea's or Ionis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of TEGSEDI or other of Akcea's or Ionis' 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. Akcea's and 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 Akcea's and Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Akcea and Ionis. 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 quarterly reports on Form 10-Q and annual reports on Form 10-K, which are on 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.

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1. Swiecicki PL, et al. Amyloid. 2015;22(2):123-31;