Akcea and Ionis announce upcoming data presentations at the 5th European Academy of Neurology Annual Congress

June 26, 2019

Multiple clinical presentations focus on the long-term clinical benefits of treatment with TEGSEDI® (inotersen)

BOSTON and CARLSBAD, Calif., June 26, 2019 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), today announced that data from the NEURO-TTR open-label extension study and the clinical impact of TEGSEDI on patients living with hereditary transthyretin amyloidosis (hATTR) will be presented at the 5th European Academy of Neurology Annual Congress (EAN) in Oslo, Norway, June 29-July 2, 2019.

Ionis Logo

Oral Presentation:

Monday, July 1, 2019

5:15 PM – 5:30 PM UTC

- Long-Term Efficacy and Safety of Inotersen for Hereditary Transthyretin Amyloidosis: NEURO-TTR Open-Label Extension 2-Year by Dr. Thomas Brannagan, Columbia Medical Center (Budapest Room)

Satellite Symposium:

Monday, July 1, 2019

1:00 PM – 2:30 PM UTC

- Navigating the Accurate Diagnosis for Rare Neuropathies (Room Svalbard)

ePoster Presentations:

Sunday, June 30, 2019

12:30 PM – 1:15 PM UTC

- Responsiveness of Neuropathy Symptom and Change (NSC) Score Components in Inotersen Treatment of Hereditary Transthyretin Amyloidosis Polyneuropathy by Dr. P. James B. Dyck, Mayo Clinic (Program #EPO2287)
- Responsiveness of mNIS+7 Components in Inotersen Treatment of Hereditary Transthyretin Amyloidosis Polyneuropathy by Dr. P. James B. Dyck, Mayo Clinic (Program #EPO2286)
- What Patients Want: How Patients with hATTR Amyloidosis Define Meaningful Improvement by Dr. Kimberly Raymond, Optum (Program #EPO2290)
- The Impact of Disease and Treatment on Quality of Life as Assessed by the Norfolk Quality of Life Scale in Hereditary Transthyretin Amyloidosis Relative to Diabetic Neuropathy by Dr. Aaron Yarlas, Optum (Program #EPO2284)
- The Impact of Disease and Treatment on Generic Health-Related Quality of Life in Patients with hATTR Amyloidosis: SF-36v2 Results from a Double-Blind Placebo-Controlled Trial of Inotersen by Dr. Asia Sikora Kessler, Optum & the University of Nebraska Medical Center (Program #EPO2291)

Akcea will have an on-site presence at the meeting at booth #C66 where attendees can learn more about TEGSEDI and hATTR amyloidosis with

polyneuropathy.

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, 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.

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 effects 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, the 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 progresses rapidly and can lead to premature death. The median survival is 4.7 years following diagnosis. 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 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 commercializing TEGSEDI® (inotersen) and advancing a mature pipeline of novel drugs, including WAYLIVRA® (volanesorsen), AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx}, AKCEA-APOCIII-L_{Rx}, and AKCEA-TTR-L_{Rx}, 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 approved in the E.U. 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 Boston, Massachusetts. Additional information about Akcea is available at www.akceatx.com and you can follow us on twitter at @akceatx.

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® (inotersen). 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 Akcea's and Ionis' programs are described in additional detail in Akcea's and Ionis' 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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