Akcea and Ionis Receive Positive EU CHMP Opinion for TEGSEDI

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CAMBRIDGE, Mass. and CARLSBAD, Calif., June 01, 2018 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ:AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ:IONS), announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending approval of TEGSEDI™ (inotersen) for the treatment of Stage 1 or Stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis (hATTR). Click here to read the EMA's press release.

The positive opinion will now be referred to the European Commission (EC), which grants marketing authorization for medicines in the European Union, as well as to European Economic Area members Iceland, Liechtenstein and Norway. TEGSEDI is also under regulatory review for marketing approval in the United States and Canada.

"Today's positive CHMP opinion is an important step toward making TEGSEDI available to people with this systemic, progressive and fatal hereditary disease that relentlessly deprives them of their independence and dignity," said Paula Soteropoulos, chief executive officer at Akcea Therapeutics. "We are now anticipating approval in Europe shortly and we are ready to launch TEGSEDI to bring this new treatment to people with hATTR amyloidosis."

"For people with hATTR amyloidosis and their families, effective treatment can mean the difference between working or not working, independence or the need for constant care," said Teresa Coelho, M.D., neurologist and neurophysiologist at Santo António Hospital, Porto, Portugal. "The benefit demonstrated by TEGSEDI in the Phase 3 NEURO-TTR trial on both measures of quality of life and neurological disease progression provides hope for patients and their families that they may be able to maintain greater independence from their disease by alleviating debilitating symptoms while preserving their ability to perform daily activities."

The positive CHMP opinion for the TEGSEDI Marketing Authorization Application (MAA) is based on results from the Phase 3 NEURO-TTR study and the Open Label Extension study in patients with hATTR amyloidosis with symptoms of polyneuropathy. Results from the NEURO-TTR 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.

Treatment with TEGSEDI was associated with substantial reductions in the levels of the transthyretin (TTR) protein. The abnormal formation and aggregation of TTR protein results in TTR amyloid deposits, which is the underlying cause of hATTR amyloidosis. Risk of thrombocytopenia and glomerulonephritis were identified during the study. Enhanced monitoring was implemented and proven effective during the study to support early detection and management of these issues. The most frequently observed adverse events were associated with injection site reactions.

"This positive CHMP opinion moves Ionis one step closer to becoming a multi-product sustainably profitable company delivering life-changing drugs to patients. Our antisense technology platform continues to deliver many important scientific and medical advances that should support continuing growth," said Brett P. Monia, Ph.D., chief operating officer at Ionis Pharmaceuticals. "We remain highly committed to bringing TEGSEDI and other drugs from our pipeline to patients."

ABOUT TEGSEDI ™ (INOTERSEN)

TEGSEDI ™ (inotersen) is an antisense drug designed to reduce the production of transthyretin, or TTR protein, to treat ATTR amyloidosis, a systemic, progressive and fatal disease. TEGSEDI is currently under regulatory review in the US, EU and Canada. The U.S. Food and Drug Administration has granted TEGSEDI Orphan Drug Designation and Fast Track Status, and the European Medicines Agency has granted TEGSEDI Orphan Drug Designation.

The submission is based on the NEURO-TTR study which was a Phase 3 randomized (2:1), double-blind, placebo-controlled, international study in 172 patients with polyneuropathy due to hATTR amyloidosis. The 15-month study measured the effects of TEGSEDI on neurological dysfunction and on quality-of-life by measuring the change from baseline in the modified Neuropathy Impairment Score +7 (mNIS+7) and in the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QOL-DN) total score. Risk of thrombocytopenia and glomerulonephritis were identified during the study. Enhanced monitoring was implemented and proven effective during the study to support early detection and management of these issues. The most frequently observed adverse events were associated with injection site reactions.

The NEURO-TTR open label extension (OLE) study is ongoing for patients who completed the NEURO-TTR study. Results from the OLE study have shown that patients treated with TEGSEDI in the NEURO-TTR study who enrolled in the OLE continued to show benefit at the 12-month cut off of the OLE. Furthermore, patients who were treated with placebo in the NEURO-TTR study who enrolled in the OLE also demonstrated evidence of benefit in the OLE at the 12 month cut off of the OLE. No new safety concerns were identified in the OLE. The TEGSEDI expanded access program (EAP) has been initiated for eligible patients in the U.S. Click here for more information on the TEGSEDI EAP.

ABOUT HEREDITARY TRANSTHYRETIN (hATTR) AMYLOIDOSIS

hATTR amyloidosis is a progressive, systemic and fatal hereditary 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. 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. People with hATTR amyloidosis often present with a mixed phenotype and experience overlapping symptoms of polyneuropathy and cardiomyopathy. People with hATTR with symptoms of polyneuropathy are classified into 3 stages: Stage 1 patients do not require assistance with ambulation, Stage 2 patients do require assistance with ambulation and Stage 3 patients are bound to wheelchair.

Ultimately, hATTR amyloidosis results in death within three to fifteen years of symptom onset. Therapeutic options for the treatment of patients with hATTR amyloidosis are limited and there are currently no disease-modifying drugs approved for the disease. There are an estimated 50,000 patients with hATTR amyloidosis worldwide. Additional information on hATTR amyloidosis, including a full list of organizations supporting the hATTR amyloidosis community worldwide, is available at www.hattrchangethecourse.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 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 under regulatory review in the U.S., EU and Canada for the treatment of people with hereditary transthyretin amyloidosis, or hATTR. WAYLIVRA is under regulatory review in the U.S., EU and Canada 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, 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 40 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. TEGSEDI ™ (inotersen) and WAYLIVRA ™ (volanesorsen) are two antisense drugs that Ionis discovered and successfully advanced through Phase 3 studies. TEGSEDI is under regulatory review for marketing approval in the U.S., EU and Canada for the treatment of patients with hereditary ATTR amyloidosis, or hATTR. WAYLIVRA is under regulatory review for marketing approval in the U.S., EU, and Canada for the treatment of patients with familial chylomicronemia syndrome, or FCS. WAYLIVRA is also in a Phase 3 study in patients with familial partial lipodystrophy, or FPL. Akcea Therapeutics, an affiliate of Ionis focused on developing and commercializing drugs to treat patients with serious and rare diseases, will commercialize TEGSEDI and WAYLIVRA, if approved. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

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, WAYLIVRA 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. "Ionis", "Akcea," "Company," "Companies" "we," "our," and "us" refers to Ionis Pharmaceuticals and/or Akcea Therapeutics.

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