Akcea and Ionis Announce Filing of New Drug Submission for Volanesorsen to Health Canada

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Health Canada grants priority review for volanesorsen NDS filing

Volanesorsen could be the first approved treatment for patients with FCS

CAMBRIDGE, Mass. and CARLSBAD, Calif., Sept. 12, 2017 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ:AKCA), an affiliate of Ionis Pharmaceuticals, Inc. (NASDAQ:IONS) focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders, and Ionis, today announced the filing of a New Drug Submission (NDS) to Health Canada for volanesorsen, an investigational medicine for the treatment of familial chylomicronemia syndrome (FCS). Health Canada has also granted priority review for the volanesorsen NDS. Priority review provides for the "fast-tracking" of eligible regulatory filings in Canada intended for the treatment, prevention or diagnosis of serious, life-threatening or severely debilitating diseases or conditions.

"We are pleased to have completed our third global regulatory filing for volanesorsen. This is a tremendous achievement for Akcea and Ionis, and I would like to express my thanks to all those who helped us get to this place. We are also pleased that Health Canada has granted priority review for the volanesorsen NDS for the treatment of FCS in Canada, which could accelerate access to this important new medicine for Canadians suffering with FCS," said Paula Soteropolous, president and chief executive officer of Akcea. "With regulatory filings for marketing authorization for volanesorsen submitted in the U.S., EU and now Canada, we are on track for a potential global commercial launch of volanesorsen in 2018."

FCS is a severe, rare disorder characterized by extremely high levels of triglycerides, symptoms such as abdominal pain that affect daily living, and the risk of recurrent, potentially fatal, acute pancreatitis. People with FCS are unable to effectively metabolize large, triglyceride-rich lipid particles called chylomicrons due to a deficiency in lipoprotein lipase, an enzyme that helps to break down triglycerides. There is no effective therapy available.

"Patients with FCS have triglyceride levels that can reach 20 to 30 times those of healthy individuals. This predisposes them to episodes of acute pancreatitis, which is potentially fatal," said Dr. Robert Hegele, distinguished professor of medicine and biochemistry, Western University and the director of Lipid Genetics Clinic and staff endocrinologist at the London Health Sciences Centre. "Today, there is no effective therapy for FCS patients, so I'm encouraged that we are now very close to having, for the first time, a therapeutic option for FCS patients that can substantially reduce triglycerides to levels that markedly reduce the risk for pancreatitis and could relieve some of the other symptoms that FCS patients live with on a daily basis."

"We are encouraged that Health Canada has granted priority status to volanesorsen, thereby recognizing the serious, severely debilitating nature of FCS and the potential role this new therapy could play," says Durhane Wong-Rieger, president of the Canadian Organization of Rare Disorders and chair of the Canadian Heart Patient Alliance. "I have met several individuals with FCS, and have heard many of their stories of intense pain, their utter lack of control in preventing an attack and their fear of the inevitable consequences of their disease."

ABOUT THE VOLANESORSEN CLINICAL PROGRAM

The submission of volanesorsen for the treatment of FCS is based on data from the Phase 3 APPROACH and COMPASS studies. The pivotal APPROACH study, a one-year, randomized, placebo-controlled study in 66 patients with FCS (average baseline triglycerides of 2,209 mg/dL, or 25.0 mmol/L), achieved its primary endpoint of reduction in triglycerides at three months, with a 77% mean reduction in triglycerides, which translated into a 1,712 mg/dL (19.3 mmol/L) mean absolute triglyceride reduction in volanesorsen-treated patients. The treatment difference is 94% compared to an 18% increase for placebo. In addition, in the APPROACH study, treatment with volanesorsen was associated with a statistically significant reduced rate of on-study pancreatitis attacks in the group of patients who had multiple pancreatitis events during the 5 years prior to screening and reduced abdominal pain in patients reporting pain during the screening period.

The COMPASS study, a six-month randomized placebo-controlled study in 113 patients with very high triglycerides (>500 mg/dL), also achieved its primary endpoint of reduction in triglycerides at three months, with a 71% mean reduction in triglycerides. In the COMPASS study, treatment with volanesorsen was associated with a statistically significant reduction in on-study pancreatitis attacks.

The most common adverse event in the studies was injection site reactions, which were mostly mild. Platelet count reductions were observed in many patients. These platelet declines were not clinically significant in most patients and were generally well managed with monitoring and dose adjustment. Five patients discontinued participation in the APPROACH study due to platelet count reductions, two of which were severe; four patients discontinued due to other nonserious adverse events.

Akcea and Ionis continue to conduct the BROADEN study, a Phase 3 clinical trial in patients with familial partial lipodystrophy (FPL), which continues to enroll, with topline data expected in 2019. Akcea plans to file for marketing authorization for volanesorsen to treat FPL in 2019 if the data from the BROADEN study are positive.

The U.S. and EU regulatory agencies have granted Orphan Drug Designation to volanesorsen for the treatment of patients with FCS. Volanesorsen has also received Orphan Drug Designation in the EU for the treatment of FPL.

ABOUT VOLANESORSEN, FCS AND FPL

Volanesorsen, a product of Ionis' proprietary antisense technology, is in development for two rare metabolic disorders: FCS and FPL. Volanesorsen is designed to reduce the production of ApoC-III, a protein produced in the liver that plays a central role in the regulation of plasma triglycerides and may also affect other metabolic parameters.

FCS is a severe, rare disorder characterized by extremely high levels of triglycerides, daily symptoms such as abdominal pain, and the risk of recurrent, potentially fatal, acute pancreatitis. People with FCS are unable to effectively metabolize large, triglyceride-rich lipid particles called

chylomicrons due to a deficiency in lipoprotein lipase, an enzyme that helps to break down triglycerides. There is no effective therapy available. Additional information on FCS is available at www.fcsfocus.com and through the FCS Foundation at http://www.livingwithfcs.org and the LPLD Alliance at www.lpldalliance.org.

FPL is a severe, rare genetic metabolic disorder characterized by an inability of the body to store fat in normal locations. This results in high levels of triglycerides in the bloodstream, abnormal fat distribution around and within organs, such as the liver and heart, and a range of metabolic abnormalities, including severe insulin resistance. People with FPL are at increased risk of acute pancreatitis in addition to other long-term, progressive manifestations, such as premature cardiomyopathy, atherosclerosis, and liver disease. Additional information on FPL is available through Lipodystrophy United at www.lipodystrophyunited.org.

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 cardiometabolic diseases caused by lipid disorders. Akcea is advancing a mature pipeline of four novel drugs with the potential to treat multiple diseases, including volanesorsen, AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx} and AKCEA-APOCIII-L_{Rx}. All four drugs were discovered and are being co-developed by Ionis, a leader in antisense therapeutics, based on Ionis' proprietary antisense technology. The most advanced drug in its pipeline, volanesorsen, 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 familial partial lipodystrophy, or FPL. Akcea is building the infrastructure to commercialize its drugs globally with a focus on lipid specialists as the primary call point. Akcea is located 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 three dozen drugs in development. SPINRAZA® (nusinersen) has been approved in the U.S., Europe, Japan, Canada and Brazil for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Drugs that have successfully completed Phase 3 studies include inotersen (IONIS-TTR_{Rx}), an antisense drug Ionis is developing to treat patients with TTR amyloidosis, 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 cardiometabolic diseases caused by lipid disorders. If approved, volanesorsen will be commercialized through Ionis' affiliate, Akcea. Volanesorsen filings for marketing approval have been filed in the U.S., EU and Canada. Inotersenis progressing toward regulatory filings for marketing authorization. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

AKCEA FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the business of Akcea Therapeutics, Inc. and the therapeutic and commercial potential of volanesorsen and other products in development. Any statement describing Akcea's 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. 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 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 Akcea. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Akcea's programs are described in additional detail in its final prospectus for its initial public offering and its most recent quarterly report on Form 10-Q, which is on file with the SEC.

IONIS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the business of Akcea Therapeutics, Inc. and the therapeutic and commercial potential of volanesorsen and other products in development. 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, 2016, and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

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

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