Gemphire Therapeutics Announces Initiation of its First NASH Proof-of-Concept Clinical Trial and its Differentiated NASH Program

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Phase 2a trial will investigate gemcabene in Familial Partial Lipodystrophy (FPL) – a rare genetic disease with characteristic presentation of cardiovascular disease and NASH

Gemcabene has a differentiated profile based on its clean safety profile and ability to improve cardio-protective dyslipidemia markers

NASH program expected to be Phase 2b ready by year-end 2018

LIVONIA, Mich., Dec. 21, 2017 (GLOBE NEWSWIRE) -- Gemphire Therapeutics Inc. (NASDAQ:GEMP), a clinical-stage biopharmaceutical company focused on developing and commercializing therapies for cardiometabolic disorders, including dyslipidemia and nonalcoholic steatohepatitis (NASH), today announced the launch of a clinical program to develop gemcabene as a treatment for NASH/nonalcoholic fatty liver disease (NAFLD). The company has an open Investigational New Drug (IND) application for gemcabene in NASH. The program is beginning with a Phase 2a proof-of-concept (POC) clinical trial in adults with FPL, a rare genetic disorder and orphan disease characterized by an abnormal distribution of fatty (adipose) tissue, which can lead to a variety of metabolic abnormalities including NASH.

“We are very pleased to initiate this clinical trial as the first step in our plan to develop gemcabene as a highly differentiated treatment for NASH,” said Dr. Steven Gullans, Interim CEO of Gemphire. “As the only compound in development that targets the triple threat of LDL-C, inflammation and triglycerides (TG) – addressing the full spectrum of dyslipidemia– we believe gemcabene has potential to be highly effective in this adult population, which is burdened by multiple cardiometabolic risk factors. With the strong preclinical data and scientific rationale for gemcabene in NASH based on its novel mechanism of action, we believe there may be significant potential for gemcabene to demonstrate effects on established measures of NASH that are also present and evaluable in FPL patients. In addition, Gemphire plans to launch a second Phase 2a POC trial in NASH early in 2018. Our goal is that together these trials will pave the way for confirmatory trials in a broader NASH population.”

FPL is an ideal patient population to demonstrate POC in adult NASH

FPL is a rare genetic disorder and orphan disease characterized by an abnormal distribution of fatty (adipose) tissue. As the body is unable to store fat correctly, a buildup can occur around all vital organs and in the blood (hypertriglyceridemia). FPL can also cause an abnormal buildup of fats in the liver (hepatic steatosis), which can result in an enlarged liver (hepatomegaly) and abnormal liver function. FPL can lead to loss of metabolic control and a variety of metabolic abnormalities, including diabetes, cardiovascular disease, hypertriglyceridemia and NASH.

“Treatment of FPL is typically directed towards the specific symptoms present in each individual. FPL patients are also a high-risk orphan population since currently available medications do not effectively manage their cardiometabolic comorbidities. Many patients are statin intolerant and use polypharmacy for their diabetes and lipid abnormalities with inadequate results,” said Elif Oral, MD, Associate Professor of Medicine, Department of Internal Medicine, University of Michigan Medical Center and Primary Investigator of this study.

"Individuals living with FPL face great medical complications that currently have no FDA approved treatment. Many struggle with very high triglycerides and traditional therapies are not tolerated or effective. Lipodystrophy United is encouraged by this potential treatment and excited to support the research," said Andra Stratton, President & Co-Founder of Lipodystrophy United, an organization with the mission to provide an interactive community, facilitate support and education for anyone affected by this rare disease (https://www.lipodystrophyunited.org.)

“Gemcabene’s mechanism of action is uniquely suited toward treatment of NASH given that it has demonstrated both

cardio-protective and liver protective qualities in prior studies," said Lee Golden, MD, CMO of Gemphire Therapeutics. "There are currently no FDA-approved therapies for NASH and we believe that gemcabene will be a safe and effective treatment to meet the significant unmet needs in this population. We will study this compound in this unique group of patients with the hope of learning more about the drug and also learning more about disease mechanisms."

Phase 2a POC clinical trial will measure NASH-related endpoints in FPL

The primary objective of this phase 2a study is to assess the efficacy and safety of two dosing regimens of gemcabene in up to eight FPL patients with elevated TG and NAFLD. At entry, patients must have a fasting TG value ≥ 250 mg/dL and quantifiable steatosis (stage 2 or 3) while on a stable, low-fat, low-cholesterol diet. Patients will be randomized to two treatment groups, to receive either gemcabene 300 mg once daily for 24 weeks or gemcabene 300 mg once daily for 12 weeks immediately followed by gemcabene 600 mg once daily for a further 12 weeks.

The trial's primary endpoint is the reduction in TG after 12 weeks of treatment. Secondary endpoints will include measures of liver fat (MRI-PDFF) and NAS (histology) at 24 weeks. Patients who are considered responders (i.e., defined as TG lowering > 30% at Week 12) will be offered the opportunity for long-term therapy with gemcabene in a separate open-label extension study. Gemphire anticipates top line results from the trial in the second half of 2018.

"We are very excited to initiate our NASH clinical program and to collaborate with Dr. Oral, who is a leading physician in the diagnosis and management of patients suffering from FPL," said Lee Golden, MD, Chief Medical Officer, Gemphire Therapeutics. "This is the first part of our program in NASH and we expect that these results will not only provide important insights into how gemcabene may benefit patients with FPL and NASH, but also for the broader patient population with NASH."

Novel Mechanism of Action in NASH: Gemcabene has both liver- and cardio-protective properties

Gemphire's decision to move forward with development of gemcabene in NASH is based on the strong mechanistic rationale for the compound to target the pathology of the disease. It has the potential to add complementary mechanisms that lower both TG (fat) and inflammation, which are believed to prevent the progression of liver fibrosis, particularly for diabetic and obese patients, who represent a large portion of the NASH population. It has been shown that obesity and diabetes can reduce a patient's ability to remove atherogenic lipids, fat causing particles, from the blood, and NASH patients have been shown to have a particularly high burden of disease causing fat particles. Historical preclinical and clinical studies have shown significant lowering in plasma of atherogenic particles, TG and CRP (a measure of inflammation) in subjects given oral, once-daily gemcabene. Additionally in an animal model of NASH, gemcabene has demonstrated the ability to reduce the extent of inflammation, hepatocyte (liver cell) ballooning and fibrosis. Gemcabene has also demonstrated a doubling of mean increase in glucose disposal rate compared to placebo suggesting potential effects on insulin sensitivity. The impact that gemcabene has been shown to have on abnormalities in NASH patients and the efficacy it has demonstrated in preclinical models support the evaluation of the potential utility of gemcabene in a disorder characterized by excess fat accumulation and inflammation of the liver.

Gemcabene's clean safety profile confers an important competitive advantage in NASH/NALFD

Gemphire has compiled a comprehensive data set on gemcabene from more than 950 subjects across 20 completed trials. The drug has been shown to be well tolerated and has not shown any liver toxicities at doses between 150 to 900 mg for up to 12 weeks. Gemcabene has also shown a low likelihood for drug-drug interactions, particularly with statins that are widely used in diabetic and dyslipidemic patients, underlying conditions associated with NASH.

About NAFLD/NASH

NASH is a severe disease of the liver caused by inflammation and a buildup of fat in the organ. In the United States, NASH affects up to approximately 2-5% of the adult population. An additional 10-30% of Americans have fat in their liver, but no inflammation or liver damage, a condition called NAFLD or "fatty liver." The underlying cause of NASH is

unclear, but it most often occurs in persons who are middle-aged and overweight or obese. Many patients with NASH have elevated serum lipids, diabetes or pre-diabetes. Progression of NAFLD/NASH can lead to liver cirrhosis, fibrosis, hepatocellular carcinoma, liver failure and liver-related death. Liver transplantation is currently the only treatment for advanced cirrhosis with liver failure. At this time, there are no approved treatments by the FDA for NAFLD/NASH.

Gemcabene's mechanism of action and safety profile are highly differentiated from other clinical candidates

Gemphire's product candidate gemcabene is a first-in-class, once-daily, oral therapy that may be suitable for patients who are unable to achieve normal levels of LDL-C or triglycerides with currently approved therapies, primarily statins. Gemcabene's mechanism of action (MOA) is designed to enhance the clearance of very low-density lipoproteins (VLDLs) in the plasma and inhibition of the production of cholesterol and triglycerides in the liver. The combined effect of these mechanisms has been clinically observed to result in a reduction of plasma non-HDL-C, VLDL-C, LDL-C, apolipoprotein B and triglycerides. In addition, gemcabene has been shown to markedly lower C-reactive protein in humans and improve insulin sensitization. Gemcabene's MOA is liver-directed involving downregulation of hepatic apolipoprotein C-III (apoC-III) mRNA expression and decrease of plasma apoC-III levels. Gemcabene has also been shown to reduce liver sulfatase-2 mRNA levels, known to be elevated in diabetic and obese patients. Elevated sulfatase-2 is thought to reduce the effectiveness of the liver VLDL-remnant receptor (also known as Syndecan-1), that normally plays a role in removing triglyceride containing particles from the plasma. Gemcabene also reduces acetyl-CoA carboxylase (ACC1) and CCR2/CCR5 receptor mRNA levels, markers involved in the progression of NASH/NAFLD. Gemcabene has demonstrated POC efficacy for NASH in the rodent STAM™ model developed at SMC Laboratories in Tokyo, Japan. Gemcabene has been tested as monotherapy and in combination with statins and other drugs in 956 subjects across 20 Phase 1 and Phase 2 clinical trials. Given this profile of efficacy across multiple pathological pathways, as well as evidence of safety and tolerability, particularly when used as an add-on to many other therapeutic drugs, gemcabene has attributes that support studies in humans for NASH.

About Gemphire

Gemphire is a clinical-stage biopharmaceutical company that is committed to helping patients with cardiometabolic disorders, including dyslipidemia and NASH. The Company is focused on providing new treatment options for cardiometabolic diseases through its complementary, convenient, cost-effective product candidate gemcabene as add-on to the standard of care, especially statins, that will benefit patients, physicians, and payors. Previously Gemphire successfully completed two Phase 2b clinical trials for homozygous familial hypercholesterolemia (HoFH) and heterozygous familial hypercholesterolemia (HeFH)/atherosclerotic cardiovascular disease (ASCVD), and also initiated a Phase 2b clinical trial for severe hypertriglyceridemia (SHTG) under NCT02722408, NCT02634151, and NCT02944383. A fourth planned trial in NASH is expected to initiate by year end 2017. Please visit www.gemphire.com for more information.

Forward Looking Statements

Any statements in this press release about Gemphire's future expectations, plans and prospects, including statements about Gemphire's financial prospects, future operations and sufficiency of funds for future operations, clinical development of Gemphire's product candidate, expectations regarding future clinical trials, regulatory submissions and meetings and future expectations and plans and prospects for Gemphire, expectations regarding operating expenses and cash used in operations, and other statements containing the words "believes," "anticipates," "estimates," "expects," "intends," "plans," "predicts," "projects," "targets," "may," "potential," "will," "would," "could," "should," "continue," "scheduled" and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the success and timing of Gemphire's regulatory submissions and pre-clinical and clinical trials; regulatory requirements or developments; changes to Gemphire's clinical trial designs and regulatory pathways; changes in Gemphire's capital resource requirements; Gemphire's ability to obtain additional financing; Gemphire's ability to successfully market and distribute its product candidate, if approved; Gemphire's ability to obtain and maintain its intellectual property protection; and other factors discussed in the "Risk Factors" section of Gemphire's Annual Report on Form 10-K for the year ended December 31, 2016, Gemphire's

Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 and in other filings Gemphire makes with the SEC from time to time. In addition, the forward-looking statements included in this press release represent Gemphire's views as of the date hereof. Gemphire anticipates that subsequent events and developments will cause Gemphire's views to change. However, while Gemphire may elect to update these forward-looking statements at some point in the future, Gemphire specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Gemphire's views as of any date subsequent to the date hereof.

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