Gemphire Announces Interim LDL-C Lowering Data from COBALT-1 Phase 2b Clinical Trial

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Gemcabene 600 mg Decreased Mean LDL-C by 28% on Top of Maximum Statin Lipid-Lowering Therapy in HoFH Patients

LIVONIA, Mich., Jan. 30, 2017 (GLOBE NEWSWIRE) -- Gemphire Therapeutics Inc. (NASDAQ:GEMP) today announced interim data on the LDL-C primary endpoint from the ongoing open label COBALT-1 trial. COBALT-1 is investigating gemcabene in homozygous familial hypercholesterolemia (HoFH) patients diagnosed by genetic confirmation or a clinical diagnosis to assess the efficacy, safety, and tolerability of multiple rising doses of gemcabene in patients with HoFH who are on maximally tolerated lipid lowering therapies. Conventional therapies such as statins and ezetimibe are the most commonly used drugs for HoFH, reducing LDL-C 15% to 25% in this very high-risk patient population.

Interim results on two genetically confirmed HoFH patients through 8 weeks of treatment (4 weeks on 300 mg of gemcabene followed by 4 weeks on 600 mg of gemcabene) are reported herein. Both subjects were on a background of high intensity statin therapy (atorvastatin 80 mg or rosuvastatin 40 mg), and one subject was also on ezetimibe before receiving gemcabene. Gemcabene lowered mean LDL-C by 23% and 28% at doses of 300 mg and 600 mg, respectively. Adverse events (AEs) have been mild to moderate in intensity across all doses of gemcabene; there have been no serious AEs or withdrawals due to AEs in the COBALT-1 study.

"We are encouraged by the COBALT-1 Phase 2b interim results in HoFH patients of 28% mean LDL-C lowering at our target commercial gemcabene dose of 600 mg, which suggests gemcabene may offer a new treatment option for these patients," said Mina Sooch, President and CEO of Gemphire Therapeutics. “The reduction in both patients is consistent with the goals of the trial and compares favorably with the LDL-C reductions reported in Phase 2 trials with other therapies recently approved to treat HoFH patients. We believe the interim clinical data supports gemcabene’s proposed novel mechanism, which is complementary to existing lipid lowering therapies. We look forward to sharing the top-line results in June 2017.”

COBALT-1 is designed to evaluate the LDL-C lowering effect of gemcabene in up to 8 HoFH patients, which is similar in size to the 3 to 8 patient Phase 2 proof-of-concept trials for recently approved therapies Repatha®, Juxtapid®, and KYNAMRO®. Patients enrolled in COBALT-1 are sequentially administered once daily 300 mg, 600 mg and then 900 mg oral doses of gemcabene escalated every 4 weeks for a total of 12 weeks. At screening, adult male or female patients are required to maintain a stable low-fat, low-cholesterol diet in combination with a pre-existing, regulatory-approved, lipid-lowering therapy (i.e., statins, monoclonal antibodies to PCSK9, cholesterol‑absorption inhibitors, bile acid sequestrants, nicotinic acid, or any combination thereof) at a stable dose for at least 4 weeks prior to treatment. Patients are excluded from the study if they are undergoing apheresis or taking mipomersen or lomitapide. All enrolled patients are genetically tested for confirmation of HoFH. The primary endpoint is mean percent change in LDL-C from baseline at 4, 8, and 12 weeks. Secondary endpoints include mean percent change in hsCRP, apoB, non-HDL-C, TG, VLDL-C and total cholesterol from baseline. Safety is being assessed by AE monitoring, clinical laboratory assessments, ECGs, physical examinations and vital sign assessments. Interim results by patient are summarized in the table below.

COBALT-1 Interim Data Results

Patient Gender	HoFH Entry Criteria	Maximal Lipid-Lowering Therapies	Baseline LDL-C mg/dL	% Change From Baseline, Gemcabene 300 mg/day (4 weeks)	%Change From Baseline, Gemcabene 600 mg/day (4 weeks)

1	Male	Genotype (Compound Heterozygous)	Rosuvastatin 40mg	138	-28.7	%	-32.4	%
2	Male	Genotype (Compound Heterozygous)	Atorvastatin 80mg Ezetimibe 10mg	195	-18.3	%	-22.9	%

“The interim data announced today are consistent with the add-on LDL-C efficacy of gemcabene that has been demonstrated through the Phase 1 and Phase 2 clinical program to date,” said Lee Golden, MD, CMO of Gemphire Therapeutics. “HoFH patients have the greatest risk for developing atherosclerosis over their lifetime, and often do not reach LDL-C reduction goals despite aggressive treatment with multiple therapies. Gemcabene has demonstrated no drug-drug interactions with high dose statin therapy and has the potential to offer an important novel mechanism for these high-risk patients who are generally on a background of high intensity statin therapy. COBALT-1 is similar in design to the Phase 2 trials of several other recently approved HoFH drugs, and should provide the efficacy, safety and tolerability data to move forward into a small, single Phase 3 registration trial in HoFH.”

As seen with other HoFH trials, these are difficult patients to recruit given the ultra-orphan population. These trials typically take one year from first patient screened to study completion. In COBALT-1, there are currently 5 patients on treatment at sites in the US, Canada, and Israel, with additional patients in screening. More recently enrolled patients provide a higher entry LDL-C on background therapy with statins, ezetimibe and/or PCSK9 inhibitors. Gemphire expects to complete enrollment of COBALT-1 by the end of February and report top-line results in June 2017 for all enrolled HoFH patients.

“These interim results are really encouraging,” said Evan Stein, MD Director Emeritus of the Metabolic & Atherosclerosis Research Center, in Cincinnati, USA. “HoFH patients have variable severity of LDL receptor functioning based on the many potential underlying genetic variants. Since gemcabene is not thought to act directly via the LDL receptor, I would anticipate a similar reduction in LDL-C across the full spectrum of known HoFH genetic mutations. Despite the many therapies that have been approved so far for HoFH, there remains a significant unmet need for additional safe and effective therapies for these patients. If the results at the end of the study are similar, then gemcabene could be an important new mechanistic and well tolerated oral therapy for HoFH patients.”

In 2014, gemcabene was granted Orphan Drug Designation for HoFH by the US FDA.
Additional information on COBALT-1 trial, including eligibility criteria and site locations, can be found at www.clinicaltrials.gov using the NCT Identifier NCT02722408.

About HoFH
HoFH is a rare genetic disease that is usually caused by mutation in both alleles of the LDL receptor gene responsible for removing LDL from the blood. As a result of having defective or deficient LDL receptor function, HoFH patients exhibit severely high LDL-C levels, are at very high risk of experiencing premature cardiovascular events, such as a heart attack or stroke, and develop premature and progressive atherosclerosis. LDL-C levels in untreated HoFH patients are typically in the range of 500 mg/dL to 1,000 mg/dL, compared to a normal target range of 70 mg/dL to 100 mg/dL. Unless treated, most patients with HoFH do not survive adulthood beyond 30 years of age. There are approximately 300 to 2,000 HoFH patients in the United States and approximately 6,000 to 45,000 patients in the rest of the world, with a prevalence rate of about one in 160,000 to one in one million. Gemphire is proud to be a supporter of the FH Foundation.

Currently approved widely available treatments for patients with HoFH include statins, ezetimibe, other approved LDL-C lowering therapies (such as bile acid sequestrants), injectable PCSK9 inhibitor Repatha®, and in some countries novel drugs mipomersen (KYNAMRO®) or lomitapide (Juxtapid®) which both include boxed warnings for liver toxicity. HoFH patients usually also require LDL apheresis when available. Despite the availability of various treatments which

combined may lower LDL-C 40-45%, many patients are still unable to achieve recommended LDL-C levels.

About Gemcabene

Gemphire's product candidate, gemcabene (CI-1027), 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 is designed to enhance the clearance of very low-density lipoproteins (VLDLs) in the plasma and inhibit the production of cholesterol and triglycerides in the liver. The combined effect for these mechanisms has been clinically observed to result in a reduction of plasma VLDL-C, LDL-C, and triglycerides. In addition, gemcabene has been shown to markedly lower C-reactive protein. Gemcabene is liver-directed and reduces apoC-III mRNA and plasma levels. Gemcabene also reduces acetyl-CoA carboxylase (ACC) and CCR2/CCR5 receptor mRNA levels, which may have applications in non-alcoholic steatohepatitis (NASH)/non-alcoholic fatty liver disease (NAFLD). Gemcabene has demonstrated proof of concept efficacy in the STAM™ model for NASH developed at SMC Laboratories in Tokyo, Japan. Gemcabene has been tested as monotherapy and in combination with statins and other drugs in 895 subjects across 18 Phase 1 and Phase 2 clinical trials and has demonstrated promising evidence of efficacy, safety and tolerability.

About Gemphire

Gemphire is a clinical-stage biopharmaceutical company focused on developing and commercializing therapies for the treatment of dyslipidemia, a serious medical condition that increases the risk of life threatening cardiovascular diseases, and NAFLD/NASH. Gemphire has initiated 3 clinical trials for HoFH, heterozygous familial hypercholesterolemia (HeFH)/atherosclerotic cardiovascular disease (ASCVD), and severe hypertriglyceridemia (SHTG) under NCT02722408, NCT02634151, and NCT02944383, respectively. 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 and future expectations and plans and prospects for Gemphire, 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 Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2016, 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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