

## **Gemphire to Present New COBALT-1 Clinical Data at the 2017 FH Global Summit**

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COBALT-1 results show significant LDL-C lowering for FH patients, including a mean reduction in LDL-C of 39% in the HeFH population

Gemcabene demonstrates novel mechanism to significantly lower LDL-C in FH patients with non-functioning (deficient) LDL receptors

Gemcabene 600 mg demonstrated a median reduction of 33% in inflammatory biomarker hsCRP

Gemcabene demonstrated significant LDL-C lowering on top of PCSK9 inhibitors

LIVONIA, Mich., Sept. 25, 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 NASH, announced the presentation today of their open-label Phase 2b COBALT-1 clinical data at the 2017 FH Global Summit, taking place in Miami, Florida from September 24-25, 2017. As previously announced, COBALT-1 achieved its primary endpoint, showing a statistically significant reduction in LDL cholesterol (LDL-C) in gemcabene-treated patients, compared to baseline at 12 weeks ( $p=0.0035$ ). The additional data being presented today show that gemcabene is efficacious in both Homozygous Familial Hypercholesterolemia (HoFH) and Heterozygous Familial Hypercholesterolemia (HeFH) patients.

### **COBALT-1 results demonstrate LDL-C lowering benefit for a broad FH population**

“The positive COBALT-1 data underscore the benefits that gemcabene can bring to a broad FH population,” said Dr. Steven Gullans, Interim CEO of Gemphire Therapeutics. “The results show that gemcabene is efficacious, and very importantly, it is also safe and well-tolerated, even when used on top of the highest prescribed doses of cholesterol lowering medications, including statins. The types of patients enrolled in this study reflect a subgroup of very high-risk Familial Hypercholesterolemic (FH) patients who comprise a market of approximately one million patients in the U.S. We look forward to sharing these data with the FDA and EMA in our planned end of Phase 2 meetings and to advancing gemcabene into Phase 3 trials in FH in 2018.”

“FH is associated with a markedly elevated risk of coronary heart disease, stroke, and peripheral vascular disease. Although a number of lipid-lowering treatments are available, achievement of target LDL-C level remains a challenge for these patients,” said Dr. Joshua Knowles Chief Medical Advisor for the FH Foundation. “We are very encouraged to see the positive results that have been achieved with gemcabene presented today at the 2017 FH Global Summit.”

COBALT-1 was designed to enroll patients clinically or genetically diagnosed with HoFH, who were on a variety of background lipid lowering therapies including the highest doses of the highest intensity statins and/or ezetimibe and/or PCSK9 inhibitors. Eight subjects (5 male and 3 female, all Caucasian, average age 53 years) were enrolled at sites in the US, Canada and Israel. Genetic analysis of the patients subsequently confirmed that 3 of them had no LDL receptor activity, the most severe form of HoFH, and that 5 had the more common HeFH. The trial, therefore, enrolled a broader FH population than originally planned.

Patients were administered oral gemcabene once daily, with dosage escalating from 300 mg to 600 mg and then 900 mg every 4 weeks, for a total duration of 12 weeks. On various baseline aggressive lipid lower therapies, the eight FH subjects had a mean baseline LDL-C level of 351 mg/dl prior to add-on gemcabene treatment. Treatment with gemcabene 600 mg, the Company’s target commercial dose, resulted in an absolute reduction of 93 mg/dL for the overall population and 92 mg/dL and 94 mg/dL for the HoFH and HeFH subjects, respectively. The results for the primary endpoint of mean percent change in LDL-C from baseline at each dose and related time point are presented below.

## Primary Endpoint: Change in LDL-C mg/dL Levels by Dose of Gemcabene

	300 mg, week 4	600 mg, week 8	900 mg, week 12
Overall population (n=8)	-25% p=0.0063	-30% p=0.0047	-29% P=0.0035
HeFH (n=5)	-34% p< 0.0001	-39% p< 0.0001	-40% p< 0.0001
HoFH (n=3)	-10% p=0.3601	-15% p=0.1920	-12% p=0.2912

As shown the table below, gemcabene impacted multiple secondary endpoints, showing reductions from baseline in total cholesterol (TC), triglycerides (TG), non-HDL, apoB, apoE, high sensitivity C-Reaction Protein (hsCRP), and other relevant biomarkers. Importantly, gemcabene 600 mg showed a 33% reduction in hsCRP.

## Secondary Endpoints For Overall Population

Baseline Level (SD)	Mean Change by Dose of Gemcabene (% Change from Baseline)					
	300 mg, week 4	600 mg, week 8	900 mg, week 12	300 mg, week 4	600 mg, week 8	900 mg, week 12
<b>Total Cholesterol (mg/dL)</b> 425.4 (167.1)	-21.3	% -24.6	% -24.6	%	%	%
<b>Non-HDL-C (mg/dL)</b> 379.9 (177.3)	-23.8	% -27.2	% -26.5	%	%	%
<b>ApoB (mg/dL)</b> 221.3 (97.3)	-18.8	% -24.8	% -22.4	%	%	%
<b>ApoE (mg/dL)</b> 6.7 (1.7)	-19.5	% -23.0	% -19.2	%	%	%
<b>ApoC-III (mg/dL)</b> 10.6 (4.1)	-7.8	% -9.7	% -6.5	%	%	%
<b>VLDL-C (mg/dL)</b> 28.7 (12.5)	-13.5	% -8.4	% -7.2	%	%	%
<b>Triglycerides (mg/dL)</b> 143.6 (62.7)	-12.6	% -9.01	% -7.2	%	%	%
<b>HDL-C (mg/dL)</b> 45.4 (18.7)	-11.89	% -13.3	% -12.9	%	%	%
<b>hsCRP* (mg/L)</b> 3.75	38.7	% -33.3	% -45.3	%	%	%

\*Two subjects had acute events that were associated with elevation in hsCRP during the first dosing period and resolved prior to week 8.

## Gemcabene's Novel Mechanism of Action (MOA) Provides Benefit to Statin Resistant Patients

“The data from COBALT-1 further validate gemcabene’s novel MOA and its ability to be additive to statins and other lipid lowering therapies,” said Dr. Charles Bisgaier, Gemphire’s Chief Scientific Officer and Co-Founder. “Our studies of gemcabene’s MOA suggest it can reduce LDL levels by accelerating the clearance of VLDL remnants, through the VLDL remnant receptor (syndecan-1). In addition, gemcabene appears to decrease apoC-III in liver by lowering mRNA levels which would also facilitate VLDL clearance through the remnant receptor. Furthermore, gemcabene appears to reduce LDL-C by inhibiting triglyceride and cholesterol synthesis thereby reducing liver VLDL production. Hence, gemcabene’s MOA appears to be synergistic with statins because it acts through a different pathway by enhancing VLDL clearance via upregulation of the remnant VLDL receptor whereas statins act by up-regulating the LDL-C receptor.”

Dr. Lee Golden, Gemphire's Chief Medical Officer, stated, "It was very encouraging to see clinically meaningful reductions in LDL-C along with concordant reductions in other important lipid parameters, such as non-HDL and apolipoprotein B, in these patients. Targeting inflammation was recently shown, in the CANTOS study, to improve clinical outcomes in high risk cardiovascular patients, and treatment with gemcabene at 600 mg and 900 mg demonstrated a 33% and 45% reduction in hsCRP, respectively. Given that hsCRP is an accepted marker of inflammation that is associated with an increased risk for cardiovascular events, gemcabene may provide multiple levels of benefit to FH patients."

Three patients in the trial were intolerant to statins and two of these were HeFH patients. The LDL-C reductions in two of these three patients was 50% or higher. One patient was previously on stable lomitapide (Juxtapid®) for 3 years, then washed-out, prior to gemcabene as add-on to the patients' baseline therapy. This individual experienced a 55% reduction in LDL-C. In the most difficult to treat subset of HoFH, patients with no LDL-C receptor activity, gemcabene demonstrated a response in 2 of 3 subjects, with a mean reduction across all 3 subjects of 15% with gemcabene 600 mg.

Safety was assessed by adverse event (AE) monitoring, clinical laboratory assessments, electrocardiograms, physical examinations and vital signs. AEs were mild to moderate in intensity across all doses of gemcabene and consistent with previously reported AEs. The majority of AEs were gastrointestinal. There were no serious AEs or withdrawals due to AEs in the COBAL-1 study. There was no evidence of hepatic or muscle injury in the study, including the 5 patients also taking statins.

"The data from COBAL-1 are very exciting," said John Kastelein, MD, Professor of Medicine, Department of Vascular Medicine, Academic Medical Center/University of Amsterdam, The Netherlands. "Familial hypercholesterolemia patients are at high-risk for having premature cardiovascular events, such as heart attacks and strokes, and gemcabene offers a potentially novel mechanism for physicians to help these patients further reduce their LDL-C. Gemcabene provided a 15% LDL-C reduction in the most difficult HoFH patients to treat, those with a completely defective LDL-C receptor. Safety of new therapies when combined with potent statins and other lipid lowering therapies is very important in FH and other hypercholesterolemic patients, and gemcabene has been well tolerated, without any evidence for drug-drug interactions."

It is estimated that up to 28% of HeFH patients have mixed dyslipidemia. Mixed dyslipidemia refers to a group of patients at high risk for cardiovascular disease that have elevated LDL-C, apolipoprotein B, and triglycerides. Gemphire believes that gemcabene offers a unique value proposition for those patients, based on its demonstrated ability to lower these three biomarkers.

The complete data for COBAL-1 will also be submitted for publication in a peer reviewed journal.

### **About the FH Foundation**

The FH Foundation ([www.thefhfoundation.org](http://www.thefhfoundation.org)) is a patient-centered nonprofit organization dedicated to research, advocacy, and education of Familial Hypercholesterolemia (FH). The Foundation's mission is to raise awareness and save lives by increasing the rate of early diagnosis and encouraging proactive treatment. The annual FH Global Summit convenes global experts within various fields to tackle the most pressing issues facing FH populations today. The [2017 FH Global Summit](#), taking place in Miami, Florida, September 24-25, focuses on the challenges and opportunities of navigating diagnosis, treatment and access across diverse FH populations.

### **Gemcabene's mechanism of action and safety profile are highly differentiated**

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 inhibition of 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 non-HDL-C, VLDL-C, LDL-C, apolipoprotein

B and triglycerides. In addition, gemcabene has been shown to markedly lower C-reactive protein and improve insulin sensitization. Gemcabene is liver-directed and reduces apoC-III mRNA and plasma levels. Gemcabene also reduces acetyl-CoA carboxylase (ACC1) 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 for NASH in the 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 and has demonstrated promising evidence of efficacy, safety and tolerability.

## **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. Gemphire has initiated 3 clinical trials for homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH)/atherosclerotic cardiovascular disease (ASCVD), and severe hypertriglyceridemia (SHTG) under NCT02722408, NCT02634151, and NCT02944383, respectively with a fourth planned trial in NASH to initiate in the fourth quarter of 2017. Please visit [www.gemphire.com](http://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 June 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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