Esperion Announces Publication in the Journal of the American Medical Association of Bempedoic Acid Phase 3 Study 2 Results

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– Study 2 Demonstrated that Bempedoic Acid Significantly Lowered LDL-Cholesterol and Reduced hsCRP –
– Over 52-Weeks, Overall Adverse Events in the Bempedoic Acid Treatment Arm were Comparable to Placebo –
– Bempedoic Acid is being developed as an Oral, Once-daily ATP Citrate Lyase (ACL) Inhibitor that Reduces Cholesterol –
– Research by Anne C. Goldberg, MD, FACP, FAHA, FNLA published in the Journal of the American Medical Association –

ANN ARBOR, Mich., Nov. 12, 2019 (GLOBE NEWSWIRE) -- Esperion (NASDAQ: ESPR) is pleased to announce that the results from the 779 patient, 52 week, Phase 3, double-blind, randomized placebo-controlled study of bempedoic acid (Study 2, also known as CLEAR Wisdom) were published today in the *Journal of the American Medical Association (JAMA).* Bempedoic acid is being developed as a, convenient, once-daily, oral therapy for the treatment of patients with elevated low-density lipoprotein cholesterol (LDL-C) added onto maximally tolerated statin therapy. Bempedoic acid and the bempedoic acid 180 mg + ezetimibe 10 mg fixed dose combination (FDC) tablets' new drug applications (NDAs) are currently under regulatory review by the U.S. Food and Drug Administration (FDA), and the marketing authorisation applications (MAAs) are currently under centralized review by the European Medicines Agency (EMA).

Study 2 evaluated the long-term safety, tolerability and efficacy, of bempedoic acid 180 mg versus placebo in 779 patients with atherosclerotic cardiovascular disease (ASCVD) and/or heterozygous familial hypercholesterolemia (HeFH) inadequately controlled with current lipid-modifying therapies, added-on to maximally tolerated statin therapy, which may mean no statin at all.

The JAMA publication includes results from the primary efficacy endpoint of LDL-C lowering at 12-weeks and key secondary endpoints of safety and tolerability over 52-weeks, including that bempedoic acid:

- significantly lowered LDL-cholesterol by 17 percent on background maximally tolerated statin therapy at 12 weeks, and the effect was durable through 52-weeks;
- significantly lowered high-sensitivity C-reactive protein (hsCRP), an important marker of the underlying inflammation associated with cardiovascular disease, by 19 percent, and the effect was durable through 52-weeks;
- reduced hemoglobin A1c (HbA1c) by 0.21% vs. placebo in patients with diabetes (n=236) at 12 weeks, favorable glycemic control and less worsening of diabetes persisted over the 52-week treatment period;
- showed overall adverse event rates comparable with placebo (BA 70% vs placebo 71%) at 52 weeks, and the proportion of patients with reported serious adverse events was similar compared with placebo (BA 20% vs placebo 19%) at 52 weeks; and
- showed adjudicated 3-component major adverse cardiac event rates of 2.7% with BA and 4.7% with placebo.

"The CLEAR Wisdom trial demonstrated that bempedoic acid provided additional LDL-cholesterol lowering in patients on background maximally tolerated statin therapy and had an overall adverse event profile that was comparable to placebo," said Anne C. Goldberg MD, FACP, FAHA, FNLA, Professor of Medicine, Division of Endocrinology, Metabolism and Lipid Research at Washington University, St. Louis and lead study author. "These results are consistent with the results reported from the largest long-term Phase 3 study of bempedoic acid, Study 1 or CLEAR Harmony, which were published earlier this year in the New England Journal of Medicine. Results across the Phase 3 development program show that bempedoic acid has the potential to be a treatment option for high-risk patients who require additional LDL-C lowering."

"The results published in JAMA today along with the results from our three other positive Phase 3 studies show that bempedoic acid has the potential to be an important new treatment option for patients with high levels of bad cholesterol despite the use of maximally tolerated statin therapy", said Tim M. Mayleben, president and chief executive officer of Esperion. "While statins clearly benefit many patients, there is a notable segment of patients who need additional LDL-C lowering treatment and that could benefit from a cost-effective and convenient oral, once-daily therapy that can be added to maximally tolerated statin therapy."

Design of Global Pivotal Phase 3 Study 2 (1002-047, also known as CLEAR Wisdom)

The 52-week, global, pivotal Phase 3 randomized, double-blind, placebo-controlled, multicenter study evaluated the efficacy and safety of bempedoic acid 180 mg/day versus placebo. The study was conducted at 86 sites in North America and Europe. A total of 779 patients were randomized 2:1 to receive bempedoic acid or placebo. The primary efficacy objective was to assess the 12-week LDL-C lowering efficacy of bempedoic acid versus placebo. Secondary objectives included evaluating the safety and tolerability of bempedoic acid versus placebo, the 24-week and 52-week LDL-C lowering efficacy of bempedoic acid versus placebo, and bempedoic acid's effects on other markers after 12 weeks of treatment, including HbA1c and hsCRP, versus placebo.

Bempedoic Acid

Bempedoic acid is our lead, non-statin, oral, once-daily, LDL-C lowering therapeutic candidate, currently under regulatory review by the FDA and EMA. With a targeted mechanism of action, bempedoic acid is a first-in-class, ATP Citrate Lyase (ACL) inhibitor that lowers LDL-C by reducing cholesterol biosynthesis and up-regulating the LDL receptor. Bempedoic acid has been observed to reduce hsCRP, a key marker of inflammation associated with cardiovascular disease. Completed Phase 3 studies conducted in more than 4,000 patients, with over 2,600 patients treated with bempedoic acid, demonstrated up to 18 percent placebo corrected LDL-C lowering when used with moderate- and high-intensity statins and 21 to 28 percent placebo corrected LDL-C lowering when used with low dose or no background statin.

Bempedoic Acid / Ezetimibe Fixed Dose Combination Tablet

Through the complementary mechanisms of action of inhibition of cholesterol synthesis (bempedoic acid) and inhibition of cholesterol absorption (ezetimibe), the bempedoic acid / ezetimibe fixed dose combination tablet is a non-statin, orally available, once-daily, LDL-C lowering therapeutic candidate, currently under review by the FDA and EMA. Inhibition of ATP Citrate Lyase (ACL) by bempedoic acid lowers LDL-C by reducing cholesterol biosynthesis and up-regulating the LDL receptor. Inhibition of Niemann-Pick C1-Like 1 (NPC1L1) by ezetimibe results in reduced absorption of cholesterol from the gastrointestinal tract, thereby reducing delivery of cholesterol to the liver. Phase 3 data demonstrated that this combination resulted in a 29 percent placebo corrected LDL-C lowering when used with maximally tolerated statins, a 44 percent LDL-C lowering when used with no background statin (post-hoc analysis), and a 34 percent reduction in high sensitivity C-reactive protein (hsCRP).

CLEAR Cardiovascular Outcomes Trial

The effect of bempedoic acid on cardiovascular morbidity and mortality has not yet been determined. Esperion initiated a global cardiovascular outcomes trial (CVOT) to assess the effects of bempedoic acid on the occurrence of major cardiovascular events in patients with, or at high risk for, cardiovascular disease (CVD) who are only able to tolerate less than the lowest approved daily starting dose of a statin and considered "statin averse." The CVOT — known as CLEAR Cardiovascular Outcomes Trial — is an event-driven, global, randomized, double-blind, placebo-controlled study that completed enrollment in August 2019 of 14,032 patients with hypercholesterolemia and high CVD risk at over 1,400 sites in 32 countries.

Esperion Therapeutics' Commitment to Patients with Hyperlipidemia

High levels of LDL-C can lead to a build-up of fat and cholesterol in and on artery walls (known as atherosclerosis), potentially leading to cardiovascular events, including heart attack or stroke. In the U.S., 96 million people, or more than 37 percent of the adult population, have elevated LDL-C. There are approximately 18 million people in the U.S. with atherosclerotic cardiovascular disease (ASCVD) who live with elevated levels of LDL-C despite taking maximally tolerated lipid-modifying therapy — including individuals considered statin averse — leaving them at high risk for cardiovascular events[1]. In the United States, more than 50 percent of ASCVD patients who are not able to reach their LDL-C goals with statins alone need less than a 40 percent reduction to reach their LDL-C threshold[2].

Esperion's mission as the Lipid Management Company is to deliver once-daily, oral therapies that complement existing oral drugs to provide the additional LDL-C lowering that these patients need.

Esperion Therapeutics

Through scientific and clinical excellence, and a deep understanding of cholesterol biology, the experienced Lipid Management Team at Esperion is committed to developing new LDL-C lowering therapies that will make a substantial impact on reducing global cardiovascular disease, the leading cause of death around the world. For more information, please visit www.esperion.com and follow us on Twitter at https://twitter.com/EsperionInc.

Forward-Looking Statements

This press release contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding the regulatory approval pathway for bempedoic acid tablet and the bempedoic acid / ezetimibe fixed dose combination tablet, the therapeutic potential of, and the clinical development plan for bempedoic acid tablet and the bempedoic acid / ezetimibe fixed dose combination tablet, including Esperion's timing, designs, plans for announcement of results regarding its CLEAR Outcomes study and other ongoing clinical studies for bempedoic acid tablet and the bempedoic acid / ezetimibe combination fixed dose tablet, timing for the review and approval of the NDAs and the MAAs, and Esperion's expectations for the market for therapies to lower LDL-C, including the market adoption of bempedoic acid tablet and the bempedoic acid / ezetimibe fixed dose combination tablet, if approved. Any express or implied statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Forward-looking statements involve risks and uncertainties that could cause Esperion's actual results to differ significantly from those projected, including, without limitation, delays or failures in Esperion's studies, that positive results from a clinical study of bempedoic acid may not be sufficient for FDA or EMA approval or necessarily be predictive of the results of future or ongoing clinical studies, that notwithstanding the completion of Esperion's Phase 3 clinical development program for LDL-C lowering, the FDA or EMA may require additional development in connection with seeking regulatory approval, that existing cash resources may be used more quickly than anticipated, and the risks detailed in Esperion's filings with the Securities and Exchange Commission. Esperion disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this press release, other than to the extent required by law.

References

[1] Esperion market research on file: research project interviewing 350 physicians. Esperion Therapeutics, Inc. Sept-Oct 2018.

[2] Data on file: analysis of NHANES database. Esperion Therapeutics, Inc. 2018.

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