

Esperion Announces Publication of Bempedoic Acid Study 1 Results in The New England Journal of Medicine

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- Study 1 Demonstrated Bempedoic Acid Significantly Lowered LDL-Cholesterol and Reduced hsCRP –
- Over 52-Weeks, Bempedoic Acid was Observed to be Safe, Well-Tolerated, and Did Not Lead to Higher Overall Adverse Events Compared With Placebo –
- Bempedoic Acid is an Oral, Once-daily ATP Citrate Lyase (ACL) Inhibitor that Reduces Cholesterol and Fatty Acid Synthesis in the Liver –
- Research by Professor Kausik Ray, published in the March 14th, 2019 New England Journal of Medicine –

ANN ARBOR, Mich., March 13, 2019 (GLOBE NEWSWIRE) -- Esperion (NASDAQ:ESPR) announced that results from the 2,230 patient, 52-week, Phase 3 long-term safety study of bempedoic acid (CLEAR Harmony, also known as Study 1 or 1002-040) were published today in *The New England Journal of Medicine (NEJM)*. Bempedoic acid is being developed as a complementary, cost-effective, convenient, once-daily, oral therapy for the treatment of patients with elevated low-density lipoprotein cholesterol (LDL-C). Bempedoic acid and the bempedoic acid / ezetimibe combination tablet new drug applications have been submitted to the United States Food and Drug Administration, as well as are under regulatory review for marketing authorization by the European Medicines Agency.

Study 1 evaluated the long-term safety, tolerability and efficacy of bempedoic acid 180 mg versus placebo in 2,230 high-risk patients with atherosclerotic cardiovascular disease (ASCVD) that are inadequately controlled with current lipid-modifying therapies, including maximally tolerated statins.

The NEJM publication highlights results from the primary endpoint of adverse event rates over 52-weeks along with key efficacy endpoints at 12-weeks, including that bempedoic acid:

- significantly lowered LDL-cholesterol by 18 percent on background maximally tolerated statin therapy;
- significantly reduced high-sensitivity C-reactive protein (hsCRP), an important marker of the underlying inflammation associated with cardiovascular disease, by 22 percent;
- did not lead to higher overall adverse events compared with placebo (BA 78.5% vs placebo 78.7%), and the proportion of patients with reported serious adverse events was small and similar compared with placebo (BA 14.5% vs placebo 14.0%);
- showed fewer adjudicated major adverse cardiac events compared with placebo (BA 4.6% vs placebo 5.7%);
- showed lower rates of new-onset or worsening of diabetes compared with placebo (BA 3.3% vs 5.4% placebo);
- was observed to be safe and well-tolerated.

“The publication of the largest bempedoic acid study to date further confirms what leading experts have said, that bempedoic acid is a safe, well-tolerated and efficacious potential treatment option that can significantly lower LDL-cholesterol as well as reduce hsCRP,” said Bill Sasiela, Senior Vice President, Clinical Development at Esperion.

“This latest study shows that bempedoic acid could be another addition to the arsenal of once-daily, oral cholesterol-lowering treatments available to patients. Overall, these recent studies show that not only is the treatment generally well-tolerated, being comparable with placebo, and potentially safe over longer periods, but that when added to high intensity statin treatment it can help to further reduce LDL-cholesterol levels,” said Professor Kausik Ray, from the Imperial Centre for Cardiovascular Disease Prevention at Imperial College London’s School of Public Health, who led the study. “Whilst this was not an outcomes study, our parallel paper in the same issue of the Journal suggests comparing the mechanism of cholesterol lowering with bempedoic acid with statins using genetics suggests that we can hope to expect similar benefit to statins per mmol/L lowering of LDL-cholesterol. The ongoing trial, ‘CLEAR OUTCOMES’, is specially testing even longer-term safety and whether this approach reduces cardiovascular disease risk in addition to lowering cholesterol.”

Design of Global Pivotal Phase 3 Study 1 (1002-040, also known CLEAR Harmony)

The 52-week, global, pivotal Phase 3 randomized, double-blind, placebo-controlled, multicenter study evaluated the long-term safety and tolerability of bempedoic acid 180 mg/day versus placebo in high-risk patients with ASCVD and/or heterozygous familial hypercholesterolemia (HeFH) with LDL-C levels of at least 70 mg/dL (1.8 mmol/L) who are inadequately controlled with current lipid-modifying therapies, including maximally tolerated statin therapy. The study was conducted at 117 sites in the U.S., Canada and Europe. A total of 2,230 patients were randomized 2:1 to receive bempedoic acid or placebo. The secondary objective was to assess the 12-week LDL-C lowering efficacy of bempedoic acid versus placebo. Tertiary objectives were to assess the effect of bempedoic acid on other lipid parameters and risk markers, including hsCRP.

An open-label extension study (1002-050) was initiated in early 2017 and is fully enrolled with 1,462 patients.

Bempedoic Acid / Ezetimibe 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 combination tablet is our lead, non-statin, orally available, once-daily, LDL-C lowering therapy. Inhibition of ATP Citrate Lyase (ACL) by bempedoic acid reduces cholesterol biosynthesis and lowers LDL-C by 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, which in turn upregulates the LDL receptors. Phase 3 data demonstrated that this safe and well-tolerated combination results in a 35 percent lowering of LDL-C when used with maximally tolerated statins, a 43 percent lowering of LDL-C when used as a monotherapy,

and a 34 percent reduction in high sensitivity C-reactive protein (hsCRP).

Bempedoic Acid

With a targeted mechanism of action, bempedoic acid is a first-in-class, complementary, orally available, once-daily ATP Citrate Lyase inhibitor that, reduces cholesterol biosynthesis and lowers LDL-C by up-regulating the LDL receptor. Similar to statins, bempedoic acid also reduces hsCRP, a key marker of inflammation associated with cardiovascular disease. Completed Phase 2 and Phase 3 studies conducted in almost 4,800 patients, and approximately 3,100 patients treated with bempedoic acid, have demonstrated an additional 20 percent LDL-C lowering when used with maximally tolerated statins, up to 30 percent LDL-C lowering as monotherapy, 35 percent LDL-C lowering in combination with ezetimibe when used with maximally tolerated statins and up to 48 percent LDL-C lowering in combination with ezetimibe as monotherapy.

The effect of bempedoic acid on cardiovascular morbidity and mortality has not yet been determined. The company 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 intolerant." The CVOT — known as CLEAR Outcomes — is an event-driven, global, randomized, double-blind, placebo-controlled study expected to enroll approximately 12,600 patients with hypercholesterolemia and high CVD risk at over 1,000 sites in approximately 30 countries.

Esperion's Commitment to Patients with Hypercholesterolemia

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 intolerant — leaving them at high risk for cardiovascular events. 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.

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.

The Lipid Management Company

Esperion is the Lipid Management Company passionately committed to developing and commercializing complementary, cost-effective, convenient, once-daily, oral therapies for the treatment of patients with elevated LDL-C. 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. Bempedoic acid and the company's lead product candidate, the bempedoic acid / ezetimibe combination tablet, are targeted therapies that have been shown to significantly lower elevated LDL-C levels in patients with hypercholesterolemia, including patients inadequately treated with current lipid-modifying therapies. For more information, please visit www.esperion.com and follow us on Twitter at <https://twitter.com/EsperionInc>.

Forward Looking Statement: Esperion

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 the bempedoic acid / ezetimibe combination tablet and bempedoic acid and the therapeutic potential of, clinical development plan for, the bempedoic acid / ezetimibe combination tablet and bempedoic acid, including Esperion's timing, designs, plans and announcement of results regarding its CLEAR Outcomes study and other ongoing clinical studies for bempedoic acid and the bempedoic acid / ezetimibe combination tablet, Esperion's expectations for the market for therapies to lower LDL-C, including the market adoption of bempedoic acid and the bempedoic acid / ezetimibe combination tablet, if approved, the expected upcoming milestones described in this press release, and Esperion's cash position and financial outlook. 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 Esperion or its strategic collaborators are able to successfully commercialize the bempedoic acid / ezetimibe combination tablet and bempedoic acid, if approved, 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.

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