Esperion Presents Results from CLEAR Outcomes Primary Prevention Analysis at 83rd American Diabetes Association Scientific Sessions

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– 30% risk reduction of MACE-4 composite of death from cardiovascular causes, and >25% risk reduction across four key secondary endpoints in primary prevention population, including 27% reduction in all-cause mortality –

– Bempedoic acid is the first LDL-lowering therapy since statins to demonstrate cardiovascular risk reduction in a primary prevention population –

– Of the patients included in the primary prevention population, nearly two-thirds were diabetic –

– Results simultaneously published in the Journal of the American Medical Association (JAMA) –

ANN ARBOR, Mich., June 24, 2023 (GLOBE NEWSWIRE) -- Esperion (NASDAQ: ESPR) announced the results from the pre-specified, primary prevention CLEAR Outcomes subgroup analysis at the 83rd American Diabetes Association (ADA) Scientific Sessions.

Results from this primary prevention analysis show a significant reduction in cardiovascular risk, including a 36% risk reduction of MACE-3 (composite of major adverse cardiovascular events including non-fatal myocardial infarction, non-fatal stroke and cardiovascular death), and a 30% risk reduction of MACE-4 (composite of major adverse cardiovascular events including non-fatal myocardial infarction, non-fatal stroke, coronary revascularization and cardiovascular death) in the primary prevention population. The data were simultaneously published in the renowned peer-reviewed *Journal of the American Medical Association (JAMA).* The article, entitled "Bempedoic Acid for Primary Prevention of Cardiovascular Events in Statin-Intolerant Patients," can be found here.

"We are thrilled with the results from the primary prevention analysis of the CLEAR Outcomes study presented at the ADA Scientific Sessions and simultaneously published in the *Journal of the American Medical Association,*" said Sheldon Koenig, President and CEO of Esperion. "This analysis represents a significant opportunity to expand how many people can benefit from bempedoic acid, to the tune of 70 million patients. This large subgroup analysis supports the use of bempedoic acid, available as NEXLETOL® or in combination with ezetimibe as NEXLIZET®, in the primary prevention population, for those patients at high risk for atherosclerotic cardiovascular disease (ASCVD) or a cardiovascular event. Now, more than ever, we believe that bempedoic acid offers an evidence-based option for patients who are not on statins and those not able to tolerate statins, as well as those who would benefit from primary or secondary cardiovascular event prevention strategies."

"These findings demonstrate the importance of lowering LDL cholesterol in people who are at high risk of having a heart attack, but who have not had one to date," noted Stephen Nicholls, MD, Director of the Victorian Heart Hospital and Institute and Monash University, Melbourne, Australia. "Many of these patients could not tolerate statins and needed a new option, and CLEAR Outcomes demonstrated that bempedoic acid proved to be effective not only in lowering LDL cholesterol, but also in lowering the rate of cardiovascular risk in primary prevention patients."

JoAnne Foody, MD, FACC, FAHA, Chief Medical Officer of Esperion commented, "Patients at high risk of cardiovascular disease without a history of ASCVD, including those with diabetes, have few proven lipid lowering therapies that reduce cardiovascular risk. Bempedoic acid's novel ATP citrate lyase inhibition is the first LDL-C lowering mechanism since statins to demonstrate cardiovascular risk reduction in primary prevention patients in a cardiovascular outcomes trial. Other non-statin LDL-C lowering therapies, such as ezetimibe and PCSK9s, have only been studied in secondary prevention (ASCVD) populations. We believe this analysis from CLEAR Outcomes supports the use of bempedoic acid earlier in the treatment paradigm to achieve LDL-C goals and reduce cardiovascular risk in a broad range of primary and secondary prevention patients."

Key Highlights from the Primary Prevention Analysis:

The primary prevention patient population included 4,206 statin-intolerant patients from the CLEAR Outcomes trial (30% of the total 13,970 patients) who had no prior cardiovascular events, LDL-C level greater than or equal to 100 mg/dL at the start of the study, and who were at high risk for cardiovascular events ("primary prevention group"). Patients were randomized to receive oral bempedoic acid 180 mg daily (n=2,100) or placebo (n=2,106). Notable groups represented in this analysis included 59% (n=2,481) female, 18.5% (n=777) Hispanic/Latino ethnicity, and 66.1% (n=2,781) patients with diabetes.

For the primary endpoint, bempedoic acid demonstrated the following versus placebo:

- 30% reduced risk [hazard ratio (HR) 0.70 (95% CI 0.55-0.89)] of the primary efficacy endpoint of MACE-4
  - This equates to 43 patients being treated with bempedoic acid to prevent one primary cardiovascular event

For key secondary endpoints, bempedoic acid demonstrated the following versus placebo:

- 39% reduced risk for cardiovascular mortality; HR 0.61 (95% CI 0.41-0.92)
- 39% reduced risk of myocardial infarction; HR 0.61 (95% CI 0.39-0.98)
- 36% reduced risk of MACE-3; HR 0.64 (95% CI 0.48-0.84)
- 27% reduced risk for all-cause mortality; HR 0.73 (95% CI 0.54-0.98)

Bempedoic Acid Effects on LDL Cholesterol and High-Sensitivity C-Reactive Protein:

- 21.5% reduction in high sensitivity C-reactive protein (hsCRP) after 12 months of treatment vs. placebo

- 21.3% reduction in LDL-C after 6 months of treatment vs. placebo

Adverse events in this primary prevention subpopulation were consistent with those seen in the overall study population and included higher incidences of hyperuricemia (12.1% vs. 6.3%), gout (2.6% vs. 2.0%), and cholelithiasis (2.5% vs. 1.1%) for those receiving bempedoic acid versus placebo.

INDICATION
Bempedoic acid is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C. *Limitations of Use:* The effect of bempedoic acid on cardiovascular morbidity and mortality has not been determined.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions: *Hyperuricemia:* Bempedoic acid may increase blood uric acid levels. Hyperuricemia may occur early in treatment and persist throughout treatment, and may lead to the development of gout, especially in patients with a history of gout. Assess uric acid levels periodically as clinically indicated. Monitor for signs and symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate.
Tendon Rupture: Bempedoic acid is associated with an increased risk of tendon rupture or injury. In clinical trials, tendon rupture occurred in 0.5% of patients treated with bempedoic acid versus 0% of patients treated with placebo, and involved the rotator cuff (the shoulder), biceps tendon, or Achilles tendon. Tendon rupture occurred within weeks to months of starting bempedoic acid. Tendon rupture may occur more frequently in patients over 60 years of age, patients taking corticosteroid or fluoroquinolone drugs, patients with renal failure, and patients with previous tendon disorders. Discontinue bempedoic acid at the first sign of tendon rupture. Avoid bempedoic acid in patients who have a history of tendon disorders or tendon rupture.

Adverse Reactions: In clinical trials, the most commonly reported adverse reactions were upper respiratory tract infection, muscle spasms, hyperuricemia, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anemia, and elevated liver enzymes. Reactions reported less frequently, but still more often than with placebo, included benign prostatic hyperplasia and atrial fibrillation.

Drug Interactions: *Simvastatin and Pravastatin:* Concomitant use results in increased concentrations and increased risk of simvastatin or pravastatin-related myopathy. Use with greater than 20 mg of simvastatin or 40 mg of pravastatin should be avoided.

Lactation and Pregnancy: It is not recommended that bempedoic acid be taken during breastfeeding. Discontinue bempedoic acid when pregnancy is recognized, unless the benefits of therapy outweigh the potential risks to the fetus. Based on the mechanism of action, bempedoic acid may cause fetal harm.

Please see full Prescribing Information here.

CLEAR Cardiovascular Outcomes Trial
CLEAR Outcomes is part of the CLEAR clinical research program for NEXLETOL® (bempedoic acid) Tablet and NEXLIZET® (bempedoic acid and ezetimibe) Tablet. The CLEAR Program seeks to generate important clinical evidence on the safety and efficacy of bempedoic acid, a first in a class ATP citrate lyase inhibitor contained in NEXLETOL and NEXLIZET and its potential role in addressing additional critical unmet medical needs. More than 60,000 people will have participated in the program by the time of its completion. The CLEAR Program includes 5 label-enabling Phase III studies as well as other key Phase IV studies with the potential to reach more than 70 million people with or at risk for CVD based on elevated LDL-C.

Esperion Therapeutics
At Esperion, we discover, develop, and commercialize innovative medicines to help improve outcomes for patients with or at risk for cardiovascular and cardiometabolic diseases. The status quo is not meeting the health needs of millions of people with high cholesterol – that is why our team of passionate industry leaders is breaking through the barriers that prevent patients from reaching their goals. Providers are moving toward reducing LDL-cholesterol levels as low as possible, as soon as possible; we provide the next steps to help get patients there. Because when it comes to high cholesterol, getting to goal is not optional. It is our life's work. For more information, visit esperion.com and esperionscience.com and follow us on Twitter at 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 marketing strategy and commercialization plans, current and planned operational expenses, future operations, commercial products, clinical development, including the timing, designs and plans for the CLEAR Outcomes study and its results, plans for potential future product candidates, financial condition and outlook, including expected cash runway, and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "suggest," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions. 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, the impact of the ongoing COVID-19 pandemic on our business, revenues, results of operations and financial condition, the net sales, profitability, and growth of Esperion's commercial products, clinical activities and results, supply chain, commercial development and launch plans, the outcomes of legal proceedings, and the risks detailed in Esperion's filings with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and 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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