Esperion Announces Publication of Rationale and Design of Landmark CLEAR Cardiovascular Outcomes Trial Evaluating NEXLETOL® (bempedoic acid) Tablet in American Heart Journal

April 27, 2021

– First-of-its-kind outcomes trial designed to assess cardiovascular risk reduction in patients with documented intolerance to statin therapy –

– Nearly half of trial participants are women, a significantly higher proportion than have been included in any other previous cardiovascular outcomes study in history –

– Event driven MACE (major adverse cardiovascular events) trial stopping criteria on track for second half of 2022 –

ANN ARBOR, Mich., April 27, 2021 (GLOBE NEWSWIRE) -- Esperion (NASDAQ: ESPR) today announced the peer reviewed publication of the key design paper outlining the baseline characteristics of the enrolled patient population, rationale and design of the CLEAR Outcomes trial evaluating NEXLETOL® (bempedoic acid) Tablet in patients with documented statin intolerance, the first and only cardiovascular outcomes trial (CVOT) to exclusively study this patient population at high risk of cardiovascular disease (CVD), in the May 2021 issue of the *American Heart Journal*.

"The CLEAR Outcomes CVOT represents a landmark trial, as it is the first LDL-C [low-density lipoprotein cholesterol] lowering CVOT to be conducted in statin intolerant patients, an underserved population with high cardiovascular risk and high baseline LDL-C[1]," said Ashley Hall, Chief Development Officer at Esperion. "Another significant aspect of this trial is that historically women are underrepresented in CVOTs; however, women make up nearly half of the participants enrolled in CLEAR Outcomes compared to one-quarter of participants enrolled in past CVOT studies[2]. We are very excited for the upcoming results from this trial."

"Treatment of statin averse patients, like those enrolled in CLEAR Outcomes, represents a major unmet medical need that affects millions of patients," said Stephen Nicholls, co-principal investigator of CLEAR Outcomes, and Director of MonashHeart and Victorian Heart Institute. "The trial focuses on these patients, and is well represented with women, who are historically understudied in clinical trials, and patients with high baseline LDL-C (on average 139 mg/dL at baseline); this landmark trial could potentially give us more options to lower their risk of cardiovascular disease, as well as data to better understand their needs."

CLEAR Outcomes is a Phase 3, event-driven, randomized, multicenter, double-blind, placebo-controlled trial designed to evaluate whether treatment with NEXLETOL reduces the risk of cardiovascular events in patients with or who are at high risk for CVD with documented statin intolerance and elevated LDL-C levels.

The primary endpoint of the study is the effect of NEXLETOL on four-component major adverse cardiovascular events, or MACE (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization). The study, which was fully enrolled in August 2019, includes over 14,000 patients at over 1,200 sites in 32 countries. Additionally, CLEAR Outcomes has enrolled about 6,000 patients (~42%) with diabetes, with potential to further understand the impact of bempedoic acid on glycemic control[3-4].

CLEAR Outcomes is designed to provide 90 percent power to detect an approximately 15 percent relative risk reduction in the primary endpoint in the bempedoic acid treatment group as compared to the placebo group. The trial is expected to complete with a minimum of 1,620 MACE events with an estimated median treatment duration of 3.5-4 years. This duration is considerably longer (over a year) than other recently completed CVOT's and therefore, this study is anticipated to provide a thorough representation of the benefit-risk profile of bempedoic acid on key cardiovascular endpoints. Based on currently estimated MACE event rates, the CLEAR Outcomes trial is estimated to reach the target number of MACE primary endpoints in the second half of 2022[3-4].

The 2020 approval of NEXLETOL in the U.S. was supported by a global pivotal Phase 3 LDL-C-lowering program conducted in more than 3,000 patients with atherosclerotic cardiovascular disease (ASCVD) and/or heterozygous familial hypercholesterolemia (HeFH). In these studies, NEXLETOL provided an average of 18% placebo-corrected LDL-C lowering at week 12 when used with maximally tolerated statins. The most common (incidence ≥2% and greater than placebo) 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. NEXLETOL is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with HeFH or established ASCVD who require additional lowering of LDL-C. The effect of bempedoic acid on cardiovascular morbidity and mortality has not been determined[1]. Please see important safety information below.

NEXLETOL® (bempedoic acid) Tablet

Indication
NEXLETOL 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 NEXLETOL on cardiovascular morbidity and mortality has not been determined.

Important Safety Information

Warnings and Precautions:

- Hyperuricemia: NEXLETOL 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: NEXLETOL is associated with an increased risk of tendon rupture or injury. In clinical trials, tendon rupture occurred in 0.5% of patients treated with NEXLETOL 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 NEXLETOL. 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 NEXLETOL at the first sign of tendon rupture. Avoid NEXLETOL 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 NEXLETOL be taken during breastfeeding. Discontinue NEXLETOL when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus. Based on the mechanism of action, NEXLETOL may cause fetal harm.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call 1-800-FDA-1088 or report side effects to Esperion at 833-377-7633 (833 ESPRMED).

Please see the full Prescribing Information for NEXLETOL.

Esperion Therapeutics

ESPERION is The Lipid Management Company. Our goal is lipid management for everybody, that's why we work hard to make our medicines easy to get, easy to take and easy to have. We discover, develop and commercialize innovative medicines and combinations to lower cholesterol, especially for patients whose needs aren't being met by the status quo. Our entrepreneurial team of industry leaders is inclusive, passionate and resourceful. We are singularly focused on managing cholesterol so you can improve your health easily. For more information, please visit www.esperion.com and follow us on Twitter at www.twitter.com/EsperionInc.

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 and 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. living 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.[5] In the United States, more than 50 percent of atherosclerotic cardiovascular disease (ASCVD) patients and heterozygous familial hypercholesterolemia (HeFH) patients who are not able to reach their guideline recommended LDL-C levels with statins alone need less than a 40 percent reduction to reach their LDL-C threshold goal[6].

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

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 commercialization plans for bempedoic acid tablet. 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 clinical development and commercialization plans, or approval of expanded indications, that existing cash resources may be used more quickly than anticipated, the impact of COVID-19 on our business, clinical activities and commercial development plans, 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.

References

(1) Nicholls SJ, Lincoff M, Bays HE, et al. Rationale and design of the CLEAR-outcomes trial: Evaluating the effect of bempedoic acid on cardiovascular events in patients with statin intolerance. Am Heart J. 2021; 235:104-112. https://doi.org/10.1016/j.ahj.2020.10.060

(2) Cholesterol Treatment Trialists' (CTT) Collaboration, Baigent C, Blackwell L, Emberson J, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet. 2010 Nov 13;376(9753):1670-81. https://www.thelancet.com/article/S0140-6736(10)61350-5/fulltext. Epub 2010 Nov 8. PMID: 21067804; PMCID: PMC2988224.

(3) Sabatine MS, Giugliano RP, Keech A, et al. Rationale and design of the Further cardiovascular Outcomes Research with PCSK9 Inhibition in subjects with Elevated Risk trial. Am Heart J. 2016; 173:94-101. doi: 10.1016/j.ahj.2015.11.015 (patients 75.4% male).

(4) Schwartz GG, Steg PG, Szarek M, et al. Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. N Engl J Med 2018; 379:2097-2107. DOI: 10.1056/NEJMoa1801174 (patients 74.8% male).

(5) ESPERION market research on file: research project interviewing 350 physicians. ESPERION Therapeutics, Inc. Sept-Oct 2018.

(6) Data on file: analysis of NHANES database. ESPERION Therapeutics, Inc. 2018.

Contact:
Kaitlyn Brosco
Esperion
corporateteam@esperion.com