First-In-Class Cholesterol-Lowering Treatment NILEMDO® (NEXLETOL® in the U.S.) and Its Combination with Ezetimibe, NUSTENDI® (NEXLIZET® in the U.S.), Approved In Europe To Treat Hypercholesterolemia and Significantly Reduce Cardiovascular Risk

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– NILEMDO (bempedoic acid), a First-In-Class, Oral Treatment and NUSTENDI (bempedoic Acid / Ezetimibe Fixed-Dose Combination) Receive Label Update Approval from The European Commission as Treatments to Reduce Cardiovascular Risk by Lowering Low-Density Lipoprotein Cholesterol (LDL-C) Levels –

– This Makes Bempedoic Acid the First and Only LDL-C Lowering Treatment Indicated for Primary and Secondary Prevention of Cardiovascular Events –

– Up To 80% Of Patients Do Not Reach Guideline-Recommended LDL-C Goals Despite Receiving Treatments Such as Statins and Remain at an Increased Risk of a Heart Attack or Stroke and In Need of Additional Treatment –

ANN ARBOR, Mich. and MUNICH, Germany, May 22, 2024 (GLOBE NEWSWIRE) -- Daiichi Sankyo Europe GmbH (hereafter, 'Daiichi Sankyo') and Esperion Therapeutics, Inc. jointly announced today that the European Commission (EC) has approved the label update of both NILEMDO® (bempedoic acid) and NUSTENDI® (bempedoic acid / ezetimibe fixed-dose combination (FDC)), as treatments for hypercholesterolemia (high levels of cholesterol) and to reduce the risk of adverse cardiovascular events. The EC's decisions to update the labels of bempedoic acid and bempedoic acid / ezetimibe FDC are based on the positive CLEAR Outcomes trial results and makes them the first and only LDL-C lowering treatments indicated for primary and secondary prevention of cardiovascular events.

The EC decisions follow the previous CHMP opinions received in March this year, and approved bempedoic acid and its fixed-dose combination (bempedoic acid / ezetimibe) for use in adults with established or at high risk for atherosclerotic cardiovascular disease to reduce cardiovascular risk by lowering LDL-C levels, as an adjunct to correction of other risk factors.

In Europe, around one in seven people have high LDL-C levels, and cardiovascular disease is the leading cause of death, responsible for more than 10,000 lives lost every day. However, up to 80% of patients do not reach guideline-recommended LDL-C goals despite receiving treatments such as statins and are at increased risk of a heart attack or stroke.

Bempedoic acid is a first-in-class oral treatment which lowers cholesterol, and which can be combined with other treatments to help lower cholesterol even further. Bempedoic acid provided additional cholesterol lowering of up to 28% on top of statin therapy, compared to placebo. Bempedoic acid / ezetimibe FDC combines two complementary ways of reducing cholesterol in a once-daily tablet, reduced LDL-C by 38% compared to placebo in high-risk patients already taking maximum-tolerated statin therapy.

"Today's announcement marks a pivotal moment in our ongoing efforts to reduce cardiovascular risk. With the new indication, which covers both primary and secondary prevention, we can support healthcare professionals to better meet the treatment needs in their daily practice. At the same time, we're confident it will reassure patients that their medication truly addresses their CV risk. This reaffirms our commitment to be a trusted ally in improving cardiovascular care throughout Europe," said Oliver Appelhans, Head of Europe Specialty Division, Daiichi Sankyo Europe GmbH.

"We are delighted with the European Commission's approval, which reflects the significant cardiovascular risk reduction benefit that the bempedoic acid global franchise brings to patients worldwide," said Sheldon Koenig, President and CEO, Esperion. "This further supports our efforts towards delivering innovative treatment options to manage cardiovascular risk for patients with elevated LDL-C."

"Today's positive label update reaffirms the efficacy of both these treatments for reducing LDL-C levels and ultimately reducing patients' risk of serious cardiovascular events," said Professor Alberico Catapano, University of Milan, Italy. "The announcement will provide doctors across Europe with further confidence in prescribing bempedoic acid, alone or in combination with ezetimibe, for managing the needs of their patients."

EC approval is based on results of the Phase 3 CLEAR (Cholesterol Lowering via Bempedoic Acid, an ATP citrate lyase (ACL)-Inhibiting Regimen) Outcomes trial. The trial randomized a total of 13,970 patients aged 18–85 years old and was conducted at 1,250 sites in 32 countries, including 485 sites across Europe. Results from the Phase 3 CLEAR Outcomes trial demonstrated:

- a 13% reduction in the relative risk of major adverse cardiovascular events defined as a four-component composite of death from cardiovascular (CV) causes, non-fatal myocardial infarction, non-fatal stroke or coronary revascularization (MACE-4).
- Results of the key secondary endpoints and subgroup analyses have also been published.

INDICATION
NEXLIZET and NEXLETOL are indicated:

- The bempedoic acid component of NEXLIZET and NEXLETOL is indicated to reduce the risk of myocardial infarction and coronary revascularization in adults who are unable to take recommended statin therapy (including those not taking a statin) with:
    - established cardiovascular disease (CVD), or

- at high risk for a CVD event but without established CVD.

- As an adjunct to diet:
  - NEXLIZET, alone or in combination with other LDL-C lowering therapies, to reduce LDL-C in adults with primary hyperlipidemia, including HeFH.
  - NEXLETOL, in combination with other LDL-C lowering therapies, or alone when concomitant LDL-C lowering therapy is not possible, to reduce LDL-C in adults with primary hyperlipidemia, including HeFH.

IMPORTANT SAFETY INFORMATION
NEXLIZET and NEXLETOL are contraindicated in patients with a prior hypersensitivity to bempedoic acid or ezetimibe or any of the excipients. Serious hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria have been reported.

Hyperuricemia: Bempedoic acid, a component of NEXLIZET and NEXLETOL, may increase blood uric acid levels, which may lead to gout. Hyperuricemia may occur early in treatment and persist throughout treatment, returning to baseline following discontinuation of treatment. 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, a component of NEXLIZET and NEXLETOL, is associated with an increased risk of tendon rupture or injury. Tendon rupture may occur more frequently in patients over 60 years of age, in those taking corticosteroid or fluoroquinolone drugs, in patients with renal failure, and in patients with previous tendon disorders. Discontinue NEXLIZET or NEXLETOL at the first sign of tendon rupture. Consider alternative therapy in patients who have a history of tendon disorders or tendon rupture.

The most common adverse reactions in the primary hyperlipidemia trials of bempedoic acid, a component of NEXLIZET and NEXLETOL, in ≥2% of patients and greater than placebo were upper respiratory tract infection, muscle spasms, hyperuricemia, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anemia, and elevated liver enzymes.

Adverse reactions reported in ≥2% of patients treated with ezetimibe (a component of NEXLIZET) and at an incidence greater than placebo in clinical trials were upper respiratory tract infection, diarrhea, arthralgia, sinusitis, pain in extremity, fatigue, and influenza.

In the primary hyperlipidemia trials of NEXLIZET, the most commonly reported adverse reactions (incidence ≥3% and greater than placebo) observed with NEXLIZET, but not observed in clinical trials of bempedoic acid or ezetimibe, were urinary tract infection, nasopharyngitis, and constipation.

The most common adverse reactions in the cardiovascular outcomes trial for bempedoic acid, a component of NEXLIZET and NEXLETOL, at an incidence of ≥2% and 0.5% greater than placebo were hyperuricemia, renal impairment, anemia, elevated liver enzymes, muscle spasms, gout, and cholelithiasis.

Discontinue NEXLIZET or NEXLETOL when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus. Because of the potential for serious adverse reactions in a breast-fed infant, breastfeeding is not recommended during treatment with NEXLIZET or NEXLETOL.

Report pregnancies to Esperion Therapeutics, Inc. Adverse Event reporting line at 1-833-377-7633.

Please see full Prescribing Information for NEXLIZET and NEXLETOL.

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 X at twitter.com/EsperionInc.

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.

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 net sales, profitability, and growth of Esperion's commercial products, clinical activities and results, supply chain, commercial development and launch plans, the outcomes and anticipated benefits of legal proceedings and settlements, 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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