CHMP Issues Positive Opinions For Both Bempedoic Acid And The Bempedoic Acid / Ezetimibe Fixed-Dose Combination Tablet As Treatments For Hypercholesterolemia And Significantly Reducing Cardiovascular Events

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– Positive CHMP Opinions Are Based On The Analyses Of The Phase 3 Of The CLEAR (Cholesterol Lowering via Bempedoic Acid, an ATP Citrate Lyase (ACL)-Inhibiting Regimen) Outcomes Trial[1] –

– European Commission Decision On Label Update Authorization Applications Are Expected To Be Made In 1H 2024 –

ANN ARBOR, Mich. and MUNICH, Germany, March 22, 2024 (GLOBE NEWSWIRE) -- Daiichi Sankyo Europe GmbH (hereafter, 'Daiichi Sankyo') and Esperion Therapeutics, Inc. jointly announced today, that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted positive opinions for the label update of both bempedoic acid (*marketed as NILEMDO®▼)* and the bempedoic acid / ezetimibe fixed dose combination (FDC) (*marketed as NUSTENDI®▼)*, recommending their approval as treatments to reduce low-density lipoprotein cholesterol (LDL-C) and cardiovascular risk.[2] The existing label of bempedoic acid (*NILEMDO®▼)* provides authorisation for adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:[2]

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin, or[2]
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.[2]

The CHMP recommended adopting an update to this label, with which bempedoic acid is also indicated 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:[2]

- in patients on a maximum tolerated dose of a statin with or without ezetimibe, or[2]
- alone or in combination with ezetimibe in patients who are statin-intolerant, or for whom a statin is contraindicated.[2]

The existing label of bempedoic acid / ezetimibe FDC tablet (*NUSTENDI®▼)* provides authorisation of its use in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:[2]

- in combination with a statin in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin in addition to ezetimibe[2], or
- alone in patients who are either statin-intolerant or for whom a statin is contraindicated, and are unable to reach LDL-C goals with ezetimibe alone[2],
- in patients already being treated with the combination of bempedoic acid and ezetimibe as separate tablets with or without statin[2].

Additionally, the CHMP recommends an update of the bempedoic acid / ezetimibe label to amend its indication 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[2]:

- in patients on a maximum tolerated dose of a statin and not adequately controlled with additional ezetimibe treatment[2] or,
- in patients who are either statin-intolerant, or for whom a statin is contraindicated, and not adequately controlled with ezetimibe treatment[2] or ,
- in patients already being treated with the combination of bempedoic acid and ezetimibe as separate tablets[2].

"*The positive CHMP opinion is a crucial milestone towards improved treatment outcomes, as we are now able to address even better the unmet needs of cardiovascular care and prevention among patients in Europe. This first-in-class medicine with proven efficacy in reducing hypercholesterolaemia and preventing cardiovascular risks, is a testament to our tireless efforts to help improve the cardiovascular treatment landscape. The opinion further reinforces our confidence towards continued commitment of supporting clinical communities and healthcare ecosystems across Europe*," said **Oliver Appelhans, Head of Europe Specialty Division, Daiichi Sankyo Europe GmbH.**

"We are thrilled with the positive CHMP opinion, 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 latest regulatory milestone further bolsters our efforts to work towards delivering innovative treatment options to manage cardiovascular risk for patients with elevated LDL-C."*

The CHMP positive opinions are based on analysis from the Phase 3 CLEAR (Cholesterol Lowering via Bempedoic Acid, an ATP citrate lyase (ACL)-Inhibiting Regimen) Outcomes trial[1]. The study enrolled a total of 13,970 patients aged 18-85 years old, and took place at 1,250 sites in 32 countries, including 485 sites across Europe[1]. 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 revascularisation (MACE-4)[1].
- Results of the key secondary endpoints and subgroup analyses have been published[1].

The CHMP is a scientific committee of the EMA that reviews medical product applications on their scientific and clinical merit. The European Commission will review the CHMP opinions and is expected to deliver its final decision in the mid of the year 2024.

INDICATION

NEXLETOL® (bempedoic acid) Tablet/NEXLIZET® (bempedoic acid and ezetimibe) Tablet is indicated as an adjunct to diet and statin therapy for the treatment of primary hyperlipidemia in adults with heterozygous familial hypercholesterolemia (HeFH) or atherosclerotic cardiovascular disease, who require additional lowering of LDL-C.

IMPORTANT SAFETY INFORMATION

NEXLIZET is contraindicated in patients with a known hypersensitivity to ezetimibe tablets. Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria have been reported with ezetimibe, a component of NEXLIZET.

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, 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, a component of NEXLIZET and NEXLETOL, is associated with an increased risk of tendon rupture or injury. Tendon rupture occurred within weeks to months of starting NEXLIZET or 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 NEXLIZET or NEXLETOL at the first sign of tendon rupture. Avoid NEXLIZET or NEXLETOL in patients who have a history of tendon disorders or tendon rupture.

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

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 the Esperion Therapeutics, Inc. Adverse Event reporting line at 1-833-377-7633.

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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References

[1] Nissen SE, et al. Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients. N Engl J Med. 2023. 13;388(15):1353-1364.

[2] European Medicines Agency (EMA) March 2024. Available at: Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 18-21 March 2024 | European Medicines Agency (europa.eu)