International Lipid Expert Panel (ILEP) Recommends Use of Bempedoic Acid Ahead of PCSK9 Inhibitors in Managing Lipid Disorders and Cardiovascular Risk

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– International Lipid Expert Group Recommends Earlier Utilization of Bempedoic Acid in Both Secondary Prevention Patients As Well As in Patients with Partial or Complete Statin Intolerance –

– Following the "Lower Is Better For Longer" Approach to Lipid Management, the Recently Published Paper Provides Evidence-Based Guidance on Using Bempedoic Acid in Atherosclerotic Cardiovascular Disease (ASCVD), Heterozygous Familial Hypercholesterolemia (HeFH) and Statin Intolerance –

– Based on This Guidance, Bempedoic Acid, Available as NEXLETOL® or in Combination with Ezetimibe as NEXLIZET® is Cited as a "Rational Choices in Patient-Centered Care of Specific Groups of Primary Prevention Patients" –

ANN ARBOR, Mich., March 08, 2023 (GLOBE NEWSWIRE) -- Esperion (NASDAQ: ESPR) today announced publication of updated recommendations from the ILEP which advance bempedoic acid utilization in front of injectable PCSK9 inhibitors. The article, entitled "Bempedoic acid in the management of lipid disorders and cardiovascular risk. 2023 position paper of the international lipid expert panel (ILEP)," was published in *Progress in Cardiovascular Disease* and can be found here.

"This is only the beginning of the broader acceptance and utilization of NEXLETOL (*bempedoic acid) Tablets* and NEXLIZET *(bempedoic acid and ezetimibe) Tablets* both globally, and in the U.S., and the paradigm shift we were expecting," said Sheldon Koenig, president and chief executive officer of Esperion. "We are encouraged by the positive feedback on our recent late-breaker at the American College of Cardiology's Annual Scientific Session & Expo together with the World Congress of Cardiology (ACC23/WCC) presentation and simultaneous publication in the *New England Journal of Medicine* just four days ago. The significant enthusiasm we have received from the medical, patient and payer communities highlights the relevance of the data from CLEAR Outcomes to real-world clinical practice and signals the potential for rapid adoption. We expect the ILEP recommendation to be a precursor to additional treatment guideline updates both in the U.S. and abroad."

In 2022, the ILEP published recommendations on management of partial or complete statin intolerant patients, utilizing both ezetimibe and PCSK9i therapy ahead of bempedoic acid. Based on the robustness of the CLEAR Outcomes results, the ILEP now recommends bempedoic acid utilization ahead of PSCK9i therapy, either in combination or after ezetimibe treatment. Highlights from the ILEP recommended pathways on the use of bempedoic acid in patients with very high cardiovascular risk are summarized below:

Key ILEP Recommendations in Secondary Prevention Patients

1. In ASCVD/HeFH patients with baseline LDL-C 110-160 mg/dl, utilize an upfront combination of high intensity statin and ezetimibe, and if LDL-C is still > 55 mg/dl, start with bempedoic acid. If patient LDL-C is still > 55 mg/dl start with PCSK9i targeted therapy, if available.
2. In ASCVD/HeFH patients with baseline LDL-C >160 mg/dl, utilize an upfront combination of high intensity statin and fixed dose combination of bempedoic acid and ezetimibe, and if LDL-C is still > 55 mg/dl, start with PCSK9i targeted therapy, if available.

Key ILEP Recommendations in Primary Prevention Patients

1. In very high-risk patients with partial statin intolerance, utilize an upfront combination of high intensity statin and ezetimibe, and if LDL-C is still > 55 mg/dl, start with bempedoic acid. If patient LDL-C is still > 55 mg/dl start with PCSK9i targeted therapy, if available.
2. In very high-risk patients with complete statin intolerance, utilize an upfront combination of bempedoic acid and ezetimibe, and if LDL-C is still > 55 mg/dl, start with PCSK9i targeted therapy, if available.

"Achieving cholesterol goals for those at highest risk continues to be a vexing problem," noted Kausik Ray, BSc (hons), MBChB, FRCP (Lon), FRCP (Ed), MD, MPhil (Cantab), FACC, FESC, FAHA, Professor of Public Health and Honorary Cardiologist at Imperial College London, and President of the European Atherosclerosis Society. "With an increasing awareness that achieving LDL cholesterol goals for those at highest risk is not feasible through statin monotherapy, increasingly pragmatic guidance is being sought. Cost limits uptake of injectable therapies. Whilst statins and ezetimibe are a good start many will remain above 55 mg/dl. This updated ILEP now firmly places the evidence-based treatment bempedoic acid before injectables where cost in particular is an issue."

CLEAR Cardiovascular Outcomes Trial
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 cardiovascular disease with documented statin intolerance (inability to tolerate 2 or more statins, one at a low dose) and elevated LDL-C levels (fasting blood LDL-C ≥ 100 (2.6 mmol/L). The study, which includes nearly 14,000 patients at over 1,200 sites in 32 countries, accumulated the targeted 1,620 primary major adverse cardiovascular events (MACE-4) in August 2022.

INDICATION

NEXLETOL and NEXLIZET are indicated as adjuncts 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 and NEXLIZET on cardiovascular morbidity and mortality has not been determined.

IMPORTANT SAFETY INFORMATION
Contraindications: NEXLETOL has no contraindications. 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.

Warnings and Precautions: Hyperuricemia: Bempedoic acid, a component of NEXLETOL and NEXLIZET, 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 NEXLETOL or NEXLIZET at the first sign of tendon rupture. Avoid NEXLETOL and NEXLIZET in patients who have a history of tendon disorders or tendon rupture**.**

***Adverse Reactions*:** In NEXLETOL 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.
In the NEXLIZET clinical trial, the most commonly reported adverse reactions observed with NEXLIZET, but not observed in clinical trials of bempedoic acid or ezetimibe, a component of NEXLIZET, and occurring more frequently than with placebo, were urinary tract infection, nasopharyngitis, and constipation.
Adverse reactions reported in clinical trials of ezetimibe, and occurring at an incidence greater than with placebo, included upper respiratory tract infection, diarrhea, arthralgia, sinusitis, pain in extremity, fatigue, and influenza. Other adverse reactions reported in postmarketing use of ezetimibe included hypersensitivity reactions, including anaphylaxis, angioedema, rash, and urticaria; erythema multiforme; myalgia; elevated creatine phosphokinase; myopathy/rhabdomyolysis; elevations in liver transaminases; hepatitis; abdominal pain; thrombocytopenia; pancreatitis; nausea; dizziness; paresthesia; depression; headache; cholelithiasis; cholecystitis.

Drug Interactions: *Simvastatin and Pravastatin*: Concomitant use with bempedoic acid results in increased concentrations and increased risk of simvastatin or pravastatin-related myopathy. Use of either NEXLETOL or NEXLIZET with greater than 20 mg of simvastatin or 40 mg of pravastatin should be avoided.
Cyclosporine: Caution should be exercised when using NEXLIZET and cyclosporine concomitantly due to increased exposure to both ezetimibe and cyclosporine. Monitor cyclosporine concentrations in patients receiving NEXLIZET and cyclosporine. In patients treated with cyclosporine, the potential effects of the increased exposure to ezetimibe from concomitant use should be carefully weighed against the benefits of alterations in lipid levels provided by NEXLIZET.

***Fibrates*:** Coadministration of NEXLIZET with fibrates other than fenofibrate is not recommended. Fenofibrate and ezetimibe may increase cholesterol excretion into the bile, leading to cholelithiasis. If cholelithiasis is suspected in a patient receiving NEXLIZET and fenofibrate, gallbladder studies are indicated and alternative lipid-lowering therapy should be considered.
Cholestyramine: Concomitant use of NEXLIZET and cholestyramine decreases ezetimibe concentration. This may result in a reduction of efficacy. Administer NEXLIZET either at least 2 hours before, or at least 4 hours after, bile acid sequestrants.

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

Please see full Prescribing Information here.

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 expected operational expenses, expected revenue of our commercial products, future operations, expected milestone payments from partners, commercial products and expected growth, clinical development and regulatory submissions, 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, 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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