

Press Release

Daiichi Sankyo Europe Enters into European Licensing Agreement with Esperion for Bempedoic Acid and the Bempedoic Acid / Ezetimibe Combination Tablet

- *Daiichi Sankyo Europe will market oral bempedoic acid and bempedoic acid / ezetimibe combination tablet in the European Economic Area, the U.K. and Switzerland*
- *Bempedoic acid is a first-in-class, oral, once-daily ATP Citrate Lyase (ACL) inhibitor that reduces cholesterol and fatty acid synthesis in the liver¹*
- *Bempedoic acid and its fixed dose combination tablet with ezetimibe will offer additional treatment options for the large number of patients unable to reach their target LDL-C level*
- *This agreement expands Daiichi Sankyo Europe's commitment to cardiovascular care and the development of innovative, convenient and affordable treatments*
- *The marketing authorization application (MAA) is expected to be submitted to the European Medicines Agency (EMA) in the second quarter of 2019 with an expected approval in 2020*

Munich, Germany (January 7, 2019) – Daiichi Sankyo Europe has entered into an exclusive licensing agreement with Esperion Therapeutics (NASDAQ: ESPR) for Daiichi Sankyo Europe to market bempedoic acid and bempedoic acid / ezetimibe combination tablet in the European Economic Area and Switzerland. Daiichi Sankyo Europe will be responsible for commercialization in these territories while Esperion will be responsible for the development and manufacturing. This agreement will strengthen Daiichi Sankyo's cardiovascular portfolio in Europe and will exploit synergies in the commercialization of the once daily anticoagulant LIXIANA® (edoxaban) and the once daily antiplatelet Efient® (prasugrel).

There is a significant need for additional treatment options for the large number of patients in Europe with hypercholesterolemia who are not at their target LDL-C level. Even in very high risk patients, only 32% are at their target LDL-C level.² This is particularly true for patients who are experiencing adverse drug reactions (ADRs) under statins and are therefore taking statins only at the maximum tolerated dose or no statin at all.³ Bempedoic acid has a liver specific mode of action and therefore has the potential to avoid the muscle related ADRs associated with statin therapy.¹ Bempedoic acid can be used in combination with other lipid lowering drugs and will offer an affordable oral, once daily option for patients not at target.⁴

The robust LDL-C development program that established efficacy and safety of bempedoic acid was completed in October 2018. It included almost 4,800 patients, and approximately 3,100 patients were treated with bempedoic acid with an additional LDL-C lowering of up to 30 percent LDL-C and up to 48 percent LDL-C in combination with ezetimibe. The results demonstrate that bempedoic acid is well tolerated and confirm efficacy over an extended period of time. Rates of treatment-emergent adverse events, muscle-related adverse events and discontinuations were similar in the bempedoic acid and placebo treatment groups.⁵

“We are very pleased to announce this license agreement for bempedoic acid which is a first-in-class treatment that will address a critical unmet need for patients who have limited options and who are not reaching their target LDL-cholesterol level,” said Rodney Smith, MD, Head of Medical Affairs at Daiichi Sankyo Europe. “The Esperion team has conducted a robust, 4,000 patient, high-quality development program to establish bempedoic acid as an efficacious and well tolerated therapeutic option and this supports our great confidence in this product that complements and strengthens our current cardiovascular portfolio, building on the success of LIXIANA[®],” adds Benoit Creveau, Head of Marketing Cardiovascular at Daiichi Sankyo Europe.

Under the terms of the licensing agreement, Daiichi Sankyo Europe will make an upfront payment of \$150 million to Esperion as well as additional milestone payments including \$150 million upon first commercial sales and sales royalties. The potential total milestone payment is up to \$900 million.

“We are very pleased to partner with Daiichi Sankyo Europe to establish bempedoic acid as the most preferred LDL-C lowering treatment option after statins for patients and physicians in Europe. Daiichi Sankyo Europe’s 1,000 person cardiovascular commercial organization has a strong history of successfully commercializing drugs, including their oral anticoagulant, LIXIANA[®], and there is significant overlap among physicians targeted for bempedoic acid.” said Tim Mayleben, president and chief executive officer of Esperion. “This agreement represents the first step in the evolution of Esperion from a pioneering development-stage company to a successful commercial-stage company.”

Esperion completed its Phase 3 LDL-C development program of bempedoic acid and bempedoic acid / ezetimibe combination tablet in October 2018. The company plans to submit New Drug Applications (NDAs) to the Food and Drug Administration (FDA) during the first quarter of 2019 and Marketing Authorization Applications (MAAs) to the European Medicines Agency (EMA) during the second quarter of 2019. FDA and EMA LDL-C approval decisions are expected during the first half of 2020. The global cardiovascular outcomes trial of bempedoic acid, CLEAR Outcomes, is ongoing and cardiovascular risk reduction data are expected during 2022.

Bempedoic Acid / Ezetimibe Combination Tablet

Through the complementary mechanisms of action of inhibition of cholesterol synthesis (bempedoic acid) and inhibition of cholesterol absorption (ezetimibe), the bempedoic acid / ezetimibe combination tablet is a non-statin, orally available, once-daily, LDL-C lowering therapy. Inhibition of ATP Citrate Lyase (ACL) by bempedoic acid reduces cholesterol biosynthesis and lowers LDL-C by up-regulating the LDL receptor. Inhibition of Niemann-Pick C1-Like 1 (NPC1L1) by ezetimibe results in reduced absorption of cholesterol from the gastrointestinal tract, thereby reducing delivery of cholesterol to the liver, which in turn upregulates the LDL receptors. Phase 3 data demonstrated that this well tolerated combination results in a 35 percent lowering of LDL-C when used with maximally tolerated statins, a 43 percent lowering of LDL-C when used as a monotherapy, and a 34 percent reduction in high sensitivity C-reactive protein (hsCRP). Rates of treatment-emergent adverse events, muscle-related adverse events and discontinuations were similar in the bempedoic acid and placebo treatment groups.⁶

Bempedoic Acid

With a targeted mechanism of action, bempedoic acid is a first-in-class, complementary, oral, once-daily ATP Citrate Lyase (ACL) inhibitor that, reduces cholesterol and fatty acid biosynthesis, and lowers LDL-C by up-regulating the LDL receptor. Similar to statins, bempedoic acid also reduces high sensitivity C-reactive protein (hs-CRP), a key marker of inflammation associated with cardiovascular disease.⁵ Bempedoic acid is a prodrug that requires activation by the very long-chain acyl-Co synthetase-1 (ACSVL1). Furthermore, it was demonstrated that the absence of ACSVL1 in skeletal muscle provides a mechanistic basis for bempedoic acid to potentially avoid the myotoxicity associated with statin therapy.¹ Completed Phase 2 and Phase 3 studies conducted in almost 4,800 patients, and approximately 3,100 patients treated with bempedoic acid, have produced an additional 20 percent LDL-C lowering when used with maximally tolerated statins, up to 30 percent LDL-C lowering as monotherapy, 35 percent LDL-C lowering in combination with ezetimibe when used with maximally tolerated statins and up to 48 percent LDL-C lowering in combination with ezetimibe as monotherapy.⁵

The effect of bempedoic acid on cardiovascular morbidity and mortality has not yet been determined. The company initiated a global cardiovascular outcomes trial (CVOT) to assess the effects of bempedoic acid on the occurrence of major cardiovascular events in patients with, or at high risk for, cardiovascular disease (CVD) who are only able to tolerate less than the lowest approved daily starting dose of a statin and considered "statin intolerant." The CVOT — known as CLEAR Outcomes — is an event-driven, randomized, double-blind, placebo-controlled study expected to enroll approximately 12,600 patients with hypercholesterolemia and high CVD risk at over 1,000 sites in approximately 30 countries.⁷

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for hypertension and thrombotic disorders, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology", Daiichi Sankyo research and development is primarily focused on bringing forth novel therapies in oncology, including immuno-oncology, with additional focus on new horizon areas, such as pain management, neurodegenerative diseases, heart and kidney diseases, and other rare diseases. For more information, please visit:

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¹ Pinkosky L. *et al.* Liver-specific ATP-citrate lyase inhibition by bempedoic acid decreases LDL-C and attenuates atherosclerosis. *Nature*. 2016; 10.1038.

² De Backer G. *et al.* Lipid Management of Patients with Coronary Heart Disease in 27 Countries in Europe: Results of EUROASPIRE V Survey of the European Society of Cardiology. Presented at EAS 2018. Available at <https://www.eas-society.org/news/399857/EAS2018-Late-Breaking-Clinical-Trial-EUROASPIRE-V.htm>. Last accessed 20 December 2018.

³ Rosei EA *et al.* Management of Hypercholesterolemia, Appropriateness of Therapeutic Approaches and New Drugs in Patients with High Cardiovascular Risk. *High Blood Press Cardiovasc Prev*. 2016; 23(3): 217–230.

⁴ Thompson PD *et al.* Treatment with ETC-1002 alone and in combination with ezetimibe lowers LDL cholesterol in hypercholesterolemic patients with or without statin intolerance. *Journal of Clinical Lipidology*. 2016; 10:5560567.

⁵ Phase 3 Top-Line Results from Study 2 & Cumulative Phase 3 Program Results. Esperion Investor Presentation. Oct 29, 2018. Available at <https://investor.esperion.com/static-files/32936da0-96f9-40e5-a12b-bd00ece6698d>. Last accessed December 12, 2018.

⁶ Top-Line Results from the Bempedoic Acid / Ezetimibe Combination Pill Phase 3 Study. Esperion Investor Presentation. Aug 27, 2018. Available at <https://investor.esperion.com/static-files/1639de53-9494-4299-98a5-0b6f1317678a>. Last accessed December 12, 2018.

⁷ Evaluation of Major Cardiovascular Events in Patients With, or at High Risk for, Cardiovascular Disease Who Are Statin Intolerant Treated with Bempedoic Acid (ETC-1002) or Placebo (CLEAR Outcomes). Available at <https://clinicaltrials.gov/ct2/show/NCT02993406?term=bempedoic+acid&rank=4>. Last accessed December 12, 2018.