



Press Release

Company name: DAIICHI SANKYO COMPANY, LIMITED

Representative: Sunao Manabe, Representative Director, President and CEO

(Code no.: 4568, First Section, Tokyo Stock Exchange)

Please address inquiries to Junichi Onuma

Vice President, Corporate Communications Department

Telephone: +81-3-6225-1126

<https://www.daiichisankyo.com>

Daiichi Sankyo Announces Positive Results from ESAX-DN Phase 3 Study in Japan of Esaxerenone in Patients with Diabetic Nephropathy

Tokyo, Japan (November 8th, 2019)– Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that the primary objective has been achieved from ESAX-DN, a Phase 3 pivotal study of esaxerenone, a non-steroidal, selective novel mineralocorticoid receptor (MR) blocker, for patients in Japan with diabetic nephropathy.

The ESAX-DN results were presented in a late-breaking presentation during Kidney Week 2019, the annual meeting of the American Society of Nephrology, in Washington, USA.

ESAX-DN is a phase 3 randomized, double-blind, 2-arm, parallel group comparison study with placebo in incipient diabetic nephropathy patients*¹ who are taking an angiotensin II receptor blocker (ARB) or an angiotensin converting enzyme (ACE) inhibitor in Japan.

The study showed the esaxerenone-based regimen had a significantly higher Urine Albumin-to-Creatinine Ratio (UACR) remission*² rate (esaxerenone: 22.1% vs. placebo: 4.0%) and significantly reduced UACR (esaxerenone:-58.3% vs. placebo: 8.3) compared with the placebo group. As the secondary endpoint, significant reduction of progression from incipient to overt diabetic nephropathy*³ (esaxerenone: 1.4% vs. placebo: 7.5%) was confirmed in the esaxerenone group compared to the placebo group.

Additionally, no new safety concerns were identified in this study. 8.8% of confirmed hyperkalemia was observed in the esaxerenone group compared with 2.2% in the placebo group, and elevated serum potassium was recovered after discontinuation of administration.

Daiichi Sankyo will further contribute to medical care by using the scientific knowledge around esaxerenone, which has been expanded through the ESAX-DN study results.

*1 Incipient diabetic nephropathy means type 2 diabetes with microalbuminuria, which is defined $45 \leq \text{UACR} < 300 \text{ mg/g} \cdot \text{Cr}$ in this study.

*2 Satisfying both reversal to normal range of UACR, which is an index of kidney function, and sustainment; defined as achieving two consecutive $\text{UACR} < 30 \text{ mg/g} \cdot \text{Cr}$ (normoalbuminuria) values at the end of treatment, and 30% reduction of UACR from baseline.

*3 Overt diabetic nephropathy is defined as type 2 diabetes with UACR which is increased to equal or more than $300 \text{ mg/g} \cdot \text{Cr}$

About the ESAX-DN Phase 3 Pivotal Trial

ESAX-DN is a phase 3 randomized, double-blind, 2-arm, parallel group comparison study with placebo in patients with type 2 diabetes with microalbuminuria who are taking an angiotensin II receptor blocker (ARB) or an angiotensin converting enzyme (ACE) inhibitor in Japan. The primary endpoint is rate of remission to normoalbuminuria after 52-week treatment, and the secondary endpoints are change rate in urinary albumin to creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR). Four hundred and fifty-five (455) patients were enrolled at 135 clinical sites in Japan. Additional information on the study is available at <http://www.clinicaltrials.jp/user/showCteDetailE.jsp?japicId=JapicCTI-173695>.

About Diabetic Nephropathy

Diabetic nephropathy is one of the most significant long-term complications in terms of morbidity and mortality for individual patients with diabetes. In Japan, approximately 10 million people, or 12.1 % of the population, are estimated to have diabetes, with a growing incidence. Approximately 50% of all type 2 diabetics will develop evidence of diabetic nephropathy *1. It is the leading cause of dialysis (42.5%, 2017) in Japan *2.

Multifactorial intensive therapy, including control of blood glucose, lipid, and blood pressure and using ARB or ACE inhibitor are recommended in the several treatment guidelines for suppressing the onset and progression of early diabetic nephropathy *3·4·5. However, these traditional therapies are suboptimal and there is a clear, unmet need for additional treatments.*6

The progression to advanced stages of diabetic nephropathy is associated with increased risk of dialysis and cardiovascular events. The effect of medication on the suppression of diabetic nephropathy at the advanced stage is not clear. In order to diminish the deterioration of kidney function, it would be desirable to promote remission to normoalbuminuria in diabetic nephropathy in early stages of the disease. *7·8

About Esaxerenone for diabetic nephropathy (CS-3150)

Esaxerenone is an orally administered, non-steroidal, selective blocker of MR. As recently reported, aldosterone is regarded as a potent mediator of organ damage. Esaxerenone may have a role in preventing these organ damaging effects.

Collaboration with Exelixis

In March 2006, Daiichi Sankyo and Exelixis entered into a research collaboration agreement to discover, develop and commercialize novel therapies targeted for MR. Under the terms of the agreement, Daiichi Sankyo has exclusive development, manufacturing and commercialization rights for the compounds worldwide. Esaxerenone is one of the in-licensed compounds identified during the research collaboration with Exelixis, and has subsequently been developed by Daiichi Sankyo.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical therapies to improve standards of care and address diversified, unmet medical needs of people globally by leveraging our world-class science and technology. With more than 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 cardiovascular diseases, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo is primarily focused on providing novel therapies in oncology, as well as other research areas centered around rare diseases and immune disorders. For more information, please visit: www.daiichisankyo.com

About Exelixis

Founded in 1994, Exelixis, Inc. (Nasdaq: EXEL) is a commercially successful, oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Following early work in model system genetics, we established a broad drug discovery and development platform that has served as the foundation for our continued efforts to bring new cancer therapies to patients in need. Our discovery efforts have resulted in four commercially available products, CABOMETYX® (cabozantinib), COMETRIQ® (cabozantinib), COTELLIC® (cobimetinib) and MINNEBRO® (esaxerenone), and we have entered into partnerships with leading pharmaceutical companies to bring these important medicines to patients worldwide. Supported by revenues from our marketed products and collaborations, we are committed to prudently reinvesting in our business to maximize the potential of our pipeline. We are supplementing our existing therapeutic assets with targeted business development activities and internal drug discovery – all to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Exelixis is a member of Standard & Poor's (S&P) MidCap 400 index, which measures the performance of profitable mid-sized companies. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

References

- *1 Parving HH, et al., Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients:a global perspective. *Kidney Int* 69:2057-2063, 2006.
- *2 Nitta K, *et al.*, An overview of regular dialysis treatment in Japan as of Dec. 31, 2017. *J Jpn Soc Dial Ther* 2018;51(12): 699-766

- *3 Japanese Society of Nephrology. Evidence-based Clinical Practice Guideline for CKD (2013). Clinical and Experimental Nephrology June 2014, Volume 18, Issue 3, pp 346–423
- *4 The Japan Diabetes Society. Evidence-based Practice Guideline for the Treatment for Diabetes in Japan 2016
- *5 The Japanese Society of Hypertension. Guidelines for the Management of Hypertension (JSH 2014). Hypertens Research 2014; 37: 253-392.
- *6 Shirakami S. Drug development for unmet medical needs. OPIR Views and Actions 2015;45:30-3
- *7 Gaede P, Tarnow L, Vedel P, et al., Remission to normoalbuminuria during multifactorial treatment preserves kidney function in patients with type 2 diabetes and microalbuminuria. Nephrol Dial Transplant. 2004 Nov; 19 (11):2784-8.
- *8 Ruggenenti P, Fassi A, Ilieva AP, et al., Effects of verapamil added-on trandolapril therapy in hypertensive type 2 diabetes patients with microalbuminuria: the BENEDICT-B randomized trial. J Hypertens. 2011 Feb;29 (2):207–16.