



Perosphere and Daiichi Sankyo Enter into a Clinical Trial Agreement to Evaluate the Efficacy and Safety of PER977 to Reverse the Anticoagulant Activity of the Investigational, Oral, Once-Daily Factor Xa Inhibitor Edoxaban

Daiichi Sankyo to support and co-sponsor phase 1 Clinical Study

MOUNT KISCO, New York, USA, and Tokyo, Japan (April 25, 2013) -- Perosphere Inc. and Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced today that they have entered into a clinical trial agreement under which Daiichi Sankyo will support and co-sponsor a phase 1 clinical study testing the safety, tolerability and effectiveness of PER977 to reverse the anticoagulant activity of edoxaban, Daiichi Sankyo's investigational oral, once-daily, direct factor Xa-inhibitor.^{1,2,3}

PER977 is a synthetic, small new molecular entity being developed by Perosphere that has been shown in pre-clinical studies to directly bind to heparins as well as circulating direct factor Xa- and IIa-inhibitors and therefore has the potential to reverse their anticoagulant effect.^{4,5,6,7} PER977 does not bind to blood coagulation factors or other blood proteins.⁵ In pre-clinical studies, PER977 has demonstrated the ability to reverse the anticoagulant effects of direct factor Xa- and IIa-inhibitors *in vitro* and *ex vivo* in animal and human models.^{4,6,7} PER977 reverses anticoagulant activity within 30 minutes after intravenous administration and has a clearance half-life of approximately 1.5 hours.⁵

“Novel oral anticoagulants were developed to help address the limitations of older anticoagulant agents, such as the need for frequent dose adjustments and monitoring,” said Jack Ansell, M.D., Professor of Medicine, NYU School of Medicine, and an advisor to Perosphere. “However, during severe bleeding or the need for emergency intervention, there is no established therapy to reverse the anticoagulant activity of these agents.”

Edoxaban is an investigational, oral, once-daily anticoagulant that specifically and reversibly inhibits factor Xa, which is an important factor in the coagulation system that leads to blood clotting.^{1,8} Edoxaban is currently approved only in Japan, since April 2011, for the prevention of venous thromboembolism (VTE) after major orthopaedic surgery, under the brand name Lixiana[®].

Elsewhere, including Europe and the U.S., edoxaban is currently in phase 3 of clinical development and has not been approved. The global edoxaban clinical trial program includes two phase 3 clinical studies, Hokusai-VTE and ENGAGE AF-TIMI 48 (Effective aNticoaGulation with Factor XA Next GEneration in Atrial Fibrillation), which are evaluating edoxaban, administered once-daily, for treatment and prevention of recurrence of VTE in patients with deep vein thrombosis (DVT) and/or pulmonary embolism (PE), and for the prevention of stroke and systemic embolic events (SEE) in patients with non-valvular atrial fibrillation, respectively.^{2,3}



“Some potential reversal agents under evaluation for direct factor Xa- and IIa-inhibitors are recombinant proteins or fully humanized monoclonal antibody fragments,” stated Dr. Solomon S. Steiner, CEO of Perosphere. “PER977 is a synthetic agent that has the potential to be an antidote for both direct factor Xa- and IIa-inhibitors as well as heparins. In pre-clinical studies, PER977 has been shown to remain stable for more than one year.”

“The initiation of this study, in collaboration with Perosphere, is an important next step in the development of edoxaban,” said Mahmoud Ghazzi, M.D., Ph.D., Executive Vice President of Drug Development for the Americas and Chief Medical Advisor for Global Drug Development, Daiichi Sankyo. “Given our focus on optimizing patient care, the development of a reversal agent is a priority for Daiichi Sankyo in the event one may be needed by physicians.”

About Perosphere

Perosphere is a specialty pharmaceutical company with internationally recognized drug delivery expertise. The company identifies market opportunities where application of drug delivery technology to a drug already on the market can create a new medical use for that drug or enhance its safety, efficacy or ease of use. Perosphere also selectively identifies and develops new chemical entities and other therapeutics that can be used as “rescue” drugs. PER977, a clinical-stage anticoagulant reversal agent for direct factor Xa- and IIa-inhibitors, is Perosphere's lead drug candidate. For more information, please visit www.perosphere.com.

About Daiichi Sankyo

The Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address the diversified, unmet medical needs of patients in both mature and emerging markets. While maintaining its portfolio of marketed pharmaceuticals for hypertension, hyperlipidemia, and bacterial infections, the Group is engaged in the development of treatments for thrombotic disorders and focused on the discovery of novel oncology and cardiovascular-metabolic therapies. Furthermore, the Daiichi Sankyo Group has created a "Hybrid Business Model," which will respond to market and customer diversity and optimize growth opportunities across the value chain. For more information, please visit www.daiichisankyo.com.



Contact

Solomon S. Steiner, Ph.D.
CEO
Perosphere Inc.
914-241-0191
s.steiner@perosphere.com

Philip N. Sussman
CFO
Perosphere Inc.
212-769-0916
p.sussman@perosphere.com

Michaela Paudler-Debus, Ph.D.
Director Corporate Communications
Daiichi Sankyo Europe
+49 89 7808 685
michaela.paudler-debus@dainichi-sankyo.eu

Forward-looking statements

This press release contains forward-looking statements and information about future developments in the sector, and the legal and business conditions of DAIICHI SANKYO, Co. Ltd and DAIICHI SANKYO, Inc. Such forward-looking statements are uncertain and are subject at all times to the risks of change, particularly to the usual risks faced by a global pharmaceutical company, including the impact of the prices for products and raw materials, medication safety, changes in exchange rates, government regulations, employee relations, taxes, political instability and terrorism as well as the results of independent demands and governmental inquiries that affect the affairs of the company. All forward-looking statements contained in this release hold true as of the date of publication. They do not represent any guarantee of future performance. Actual events and developments could differ materially from the forward-looking statements that are explicitly expressed or implied in these statements. DAIICHI SANKYO, Co. Ltd and DAIICHI SANKYO, Inc. assume no responsibility for the updating of such forward-looking statements about future developments of the sector, legal and business conditions and the company.

References

1. Ogata, K et al. Clinical Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of the Novel Factor Xa Inhibitor Edoxaban in Healthy Volunteers. *J Clin Pharmacol.* 2010;50:743-753.
2. Clinicaltrials.gov: NCT00986154. Comparative Investigation of Low Molecular Weight (LMW) Heparin/Edoxaban Tosylate (DU176b) Versus (LMW) Heparin/Warfarin in the Treatment of Symptomatic Deep-Vein Blood Clots and/or Lung Blood Clots (The Edoxaban Hokusai-VTE Study). Available at: <http://clinicaltrials.gov/show/NCT00986154>. [Last accessed: April 2013].
3. Clinicaltrials.gov: NCT00781391. Global Study to Assess the Safety and Effectiveness of Edoxaban (DU-176b) vs Standard Practice of Dosing With Warfarin in Patients With Atrial Fibrillation (ENGAGEAFTIMI48). Available at: <http://clinicaltrials.gov/show/NCT00781391>. [Last accessed: April 2013].
4. Laulicht, B et al. Small Molecule Antidote for Anticoagulants. *Circulation.* 2012;126:A11395.
5. Perosphere Inc. Data on File.
6. Bakhr, S et al. Small Molecule Antidote for Anticoagulants. Presentation at the Thrombosis and Hemostasis Summit of North America, Chicago, Illinois, May 4, 2012. Available at http://www.perosphere.com/pdf/PER977-THSNA-Presentation_Slides.pdf. [Last accessed: April 2013].
7. Laulicht, B et al. Small Molecule Antidote for Anticoagulants. Presentation at the American Heart Association Meeting, Los Angeles, California, November 5, 2012. Available at: http://www.perosphere.com/pdf/PER977_AHA-presentation.pdf. [Last accessed: April 2013].
8. Comp, P. Selective Factor Xa Inhibition Improves Efficacy of Venous Thromboembolism Prophylaxis in Orthopedic Surgery. *Pharmacotherapy.* 2003;23(6):772-787.