

## Press Release

### **FDA Grants Breakthrough Therapy Designation for Daiichi Sankyo and Plexxikon's Investigational CSF-1R Inhibitor Pexidartinib (PLX3397) in Tenosynovial Giant Cell Tumor**

- *A rare, potentially destructive tumor of the joint or tendon sheath, tenosynovial giant cell tumor (TGCT) can lead to significant pain, joint destruction, frequent surgery and loss of mobility*
- *No FDA-approved systemic therapy currently exists for the treatment of TGCT*
- *First Breakthrough Therapy Designation for Daiichi Sankyo's innovative portfolio of oncology compounds*

**Parsippany, NJ and Berkeley, CA – (October 30, 2015)** – Daiichi Sankyo, Inc. and Plexxikon Inc., a member of the Daiichi Sankyo Group, today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation to its investigational oral CSF-1R inhibitor pexidartinib (formerly PLX3397) for the treatment of tenosynovial giant cell tumor (TGCT) where surgical removal of the tumor would be associated with potentially worsening functional limitation or severe morbidity.

Breakthrough Therapy Designation is designed to expedite the development and review of medicines that may demonstrate substantial benefit over currently available treatments in order to ensure that patients with serious diseases have access to new treatments as soon as possible. Currently, there is no FDA-approved systemic therapy for the treatment of TGCT.

“Surgery is the primary treatment for TGCT, but for patients with a diffuse form of the condition, the tumor is more difficult to remove and has a high rate of recurrence, resulting in multiple complicated surgeries and even amputation in some patients,” said Mahmoud Ghazzi, MD, PhD, Executive Vice President and Global Head of Development for Daiichi Sankyo. “We are pleased that the FDA recognizes the unmet need for the treatment of TGCT and we look forward to working closely with the Agency on the expedited development of this potential non-surgical treatment for patients with TGCT.”

The Breakthrough Therapy Designation was granted based on results from an extension cohort of a single-arm, multi-center phase 1 study that assessed the safety and efficacy of pexidartinib. Results of this study were published in the July 30, 2015 issue of *The New England Journal of Medicine*.<sup>1</sup>

“The responses seen in our ongoing phase 1 study provided initial proof-of-concept that selective CSF-1R inhibition with pexidartinib may safely and effectively reduce tumor burden in patients with TGCT, providing the rationale to move directly into a phase 3 clinical trial,” said Gideon Bollag, PhD, Chief Executive Officer of Plexxikon. “This Breakthrough Therapy Designation represents another significant milestone in our commitment to develop novel targeted agents that address unmet medical needs in rare conditions such as TGCT.”

A pivotal, phase 3 study of pexidartinib called ENLIVEN is currently enrolling patients with symptomatic TGCT for whom surgical removal of the tumor would be associated with potentially worsening functional limitation or severe morbidity. More information about ENLIVEN is available at <https://www.clinicaltrials.gov/ct2/show/NCT02371369>.

The most common treatment-related adverse events seen in the ongoing Phase 1 study of pexidartinib included fatigue, hair color changes, nausea, dysgeusia (abnormal taste), and periorbital edema (swelling around the eyes), which rarely led to drug discontinuation. Treatment-related severe adverse events included fatigue, diarrhea, anemia, hyponatremia, elevated liver enzymes and neutropenia.

### **About TGCT**

Tenosynovial giant cell tumor (TGCT) – a group of neoplasms including pigmented villonodular synovitis (PVNS) and giant cell tumor of the tendon sheath (GCT-TS) – is a rare, usually non-metastatic tumor that affects the synovium-lined joints, bursae, and tendon sheaths, resulting in swelling, pain, stiffness and reduced mobility in the affected joint or limb.<sup>2</sup> It is estimated that TGCT has an annual incidence of 11 cases per million.<sup>3</sup> Patients are commonly diagnosed in their 20s to 50s,<sup>4</sup> and depending on the type of TGCT, women can be up to twice as likely to develop a tumor as men.<sup>5</sup>

Primary treatment of TGCT includes surgery to remove the tumor, but in patients with a diffuse form where it can wrap around bone, tendons, ligaments and other parts of the joint, the tumor is more difficult to remove and may require multiple surgeries or joint replacement, eventually advancing to the point where surgery is no longer an option and amputation may be considered. It is estimated that the rate of recurrence in the diffuse form of the disease can be about 45 percent or higher in some case series.<sup>6</sup>

### **About Pexidartinib (PLX3397)**

Pexidartinib is an investigational novel, oral small molecule that potently and selectively inhibits CSF-1R (colony stimulating factor-1 receptor), which is a primary growth driver of abnormal cells in the synovium that causes TGCT. Pexidartinib has not been approved by the U.S. Food and Drug Administration (FDA) or any other regulatory authority for uses under investigation.

In addition to Breakthrough Therapy Designation, pexidartinib has been granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) for the treatment of PVNS and GCT-TS. Pexidartinib also has received Orphan Designation from the European Commission for the treatment of TGCT.

Pexidartinib is being evaluated in several other potential clinical indications including glioblastoma, melanoma, ovarian and breast cancer as well as in combination with anti-PD-1 therapy, pembrolizumab, for advanced melanoma and other multiple solid tumors. Pexidartinib also is being studied in the I-SPY 2 TRIAL, a collaborative research effort studying the effects of adding specific investigational drugs to standard chemotherapy prior to surgery in women with newly diagnosed, locally advanced breast cancer.

### **About Daiichi Sankyo Oncology**

Daiichi Sankyo is focused on the discovery and development of novel oncology agents with the goal of delivering first-in-class and best-in-class treatments that address unmet medical needs. The oncology pipeline of Daiichi Sankyo continues to grow and currently includes both small molecules and monoclonal antibodies with novel targets in both solid and hematological cancers.

Daiichi Sankyo currently has four compounds in phase 3 clinical development in the U.S. each with a unique mechanism of action with three focusing on rare or orphan indications. These investigational compounds include quizartinib, an oral FLT3 inhibitor, for relapsed or refractory FLT3-ITD-positive acute myeloid leukemia (AML); pexidartinib (PLX3397), an oral CSF-1R inhibitor, for tenosynovial giant cell tumor (TGCT) being developed with Plexxikon, a member of the Daiichi Sankyo Group; tivantinib, an oral MET inhibitor, for second-line treatment of hepatocellular carcinoma in partnership with ArQule, Inc.; and patritumab, a HER3 monoclonal antibody, for non-small cell lung cancer.

### **About Plexxikon**

Plexxikon, a member of the Daiichi Sankyo Group since April 2011, is a leader in the structure-guided discovery and development of novel small molecule pharmaceuticals to treat human disease. The company's drug Zelboraf® (vemurafenib/PLX4032) was approved by the FDA in 2011, and is being co-promoted in the U.S. by Daiichi Sankyo Inc. and Genentech. Plexxikon is developing a portfolio of preclinical and clinical stage compounds to address significant unmet medical needs in oncology and other therapeutic areas. Plexxikon's Scaffold-Based Drug Discovery™ platform integrates multiple state-of-the-art technologies, including structural screening as a key component that provides a significant advantage over other drug discovery approaches.

## **About Daiichi Sankyo, Inc.**

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 17,000 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 its strong portfolio of medicines for hypertension, dyslipidemia, bacterial infections, and thrombotic disorders, the Group's research and development is focused on bringing forth novel therapies in cardiovascular-metabolic diseases, pain management, and oncology, including biologics. For more information, please visit:

[www.daiichisankyo.com](http://www.daiichisankyo.com). Daiichi Sankyo, Inc., headquartered in Parsippany, New Jersey, is a member of the Daiichi Sankyo Group. For more information on Daiichi Sankyo, Inc., please visit [www.dsi.com](http://www.dsi.com).

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