

March 5, 2009

## **Nissan Chemical Industries and Teijin Pharma License Ex-Japan Rights for Atrial Fibrillation/Flutter Drug to Bristol-Myers Squibb**

Nissan Chemical Industries, Ltd.  
Teijin Pharma Limited

Nissan Chemical Industries, Ltd. (Headquarters: Chiyoda-ku, Tokyo; President: Kojiro Kinoshita) (“Nissan Chemical”) and Teijin Pharma Limited (Headquarters: Chiyoda-ku, Tokyo; President: Osamu Nishikawa) (“Teijin Pharma”) have concluded a licensing agreement with Bristol-Myers Squibb Company (NYSE:BMJ) (Headquarters: New York City, New York, US; Chairman and CEO: James M. Cornelius) (“BMS”) for the novel atrial fibrillation and flutter treatment and preventive drug NTC-801, which was discovered by Nissan Chemical and is being jointly developed in Japan by Nissan Chemical and Teijin Pharma.

Nissan Chemical has focused on the discovery of potential pharmaceutical compounds, leveraging its unique precision organic synthesis technology. Though it has launched a calcium antagonist and a cholesterol reduction agent positioned as a “super-statin,” it aims to accelerate the development of NTC-801 even further and on a global scale with this licensing agreement.

Teijin Pharma is striving to enhance its pipeline with its core areas being respiratory, bone and joint, and cardiovascular and metabolic diseases and is proactively pushing forward with product launches, joint development, and proprietary research to expand its presence. The Phase I clinical trials for NTC-801 in Japan are underway, and with this overseas licensing agreement with BMS, it will strive to advance domestic development in coordination with overseas development.

The details are as follows:

### **1. Outline of the license agreement**

Nissan Chemical and Teijin Pharma grant exclusive development and distribution rights to BMS for NTC-801 and backup compounds in all areas of the world except Japan. As payment for the grant, an upfront cash payment of \$40 million, potential development based milestone payments of up to \$170 million, sales based milestones of up to \$175 million and royalties on net sales for licensed products will be received. The active pharmaceutical ingredient will be produced and supplied by Nissan Chemical. Note that in Japan, Nissan Chemical has granted exclusive development and distribution rights to Teijin Pharma.

## **2. NTC-801**

NTC-801, which will be licensed to BMS at this time, is a substance that suppresses atrial fibrillation due to a novel mechanism (inhibition of the acetylcholine-activated potassium channel (IKACH)) that differs from anti-arrhythmic drugs that are currently clinically used. Since the active points are only in the atrium, NTC-801 selectively acts on the atrium. Therefore, it has the potential to be used safely without triggering dangerous side effects that are observed with some anti-arrhythmic drugs and hoped that it will be an innovative new drug that may change the existing atrial fibrillation treatment regime.

## **3. Market needs**

(1) Incidences of atrial fibrillation have been reported to increase with older age, and the number of patients is predicted to grow with the probable increase in the elderly population. The number of atrial fibrillation patients is predicted to reach 1 million in Japan and 8.4 million in the US and Europe by around 2015.

(2) Currently, a pharmaceutical agent (anti-arrhythmic drug) that acts to normalize (bring to sinus rate) irregular atrial rhythms is used for rhythm control treatment of atrial fibrillation. However, because it generally acts on both the atrium and ventricle, there are concerns about adverse effects on the ventricle such as triggering dangerous ventricular arrhythmia based on long QT in electrocardiograms (one type of abnormality in electrocardiograms) or reducing heart function. A pharmaceutical agent that can effectively and safely overcome these issues is necessary.

## **4. Atrial fibrillation**

(1) The atrium functions as a pump to send blood that has returned to the heart from the body or from the lungs into the ventricle. Normally, it contracts regularly in time with the heartbeat (50 to 100 times per minute). Atrial fibrillation is the symptom where the atrium contracts irregularly at about 400 to 600 times per minute, and as a result, the atrium cannot function properly to send blood to the ventricle.

(2) When atrial fibrillation occurs, small clusters of blood (blood clots) are formed in the atrium and flow throughout the body through the bloodstream. This disease is the most significant risk factor for infarctions and especially cerebral infarctions. In addition, its relation to increased risk rate of cardiovascular mortality and as a precipitating factor for cardiac failure has been suggested. Controlling the rhythm of the atrium through anti-arrhythmic drugs is an extremely important treatment strategy to suppress conditions from moving onto such dangerous states that may be fatal.

## **5. Outline of Nissan Chemical Industries**

Since Nissan Chemical Industries was founded in 1887, the company has grown to be a leading manufacturer of a wide range of basic and specialty chemicals, electronic materials, agrochemicals, and pharmaceuticals. More background information on Nissan Chemical is available at the company web site:

<http://www.nissanchem.co.jp/english/index.html>

## **6. Outline of Teijin Pharma Limited**

Teijin Pharma Limited, the core company of Teijin Group's medical and pharmaceuticals business, focuses on three key therapeutic areas: respiratory, bone/joint, and cardiovascular/metabolic diseases, with about 1,700 employees. Teijin Pharma has strong marketing positions particularly in the respiratory and bone/joint areas with pharmaceutical products and home healthcare business, including home oxygen therapy (HOT), which has the top market share in Japan. In the cardiovascular/metabolic diseases area, as well as in the other focused areas, Teijin Pharma is trying to enhance its presence through in-licensing and out-licensing products, effective co-developments, and in-house R&D activities. For more information, visit [www.teijin-pharma.co.jp/english/](http://www.teijin-pharma.co.jp/english/)

## **7. Outline of BMS**

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to extend and enhance human life. For more information visit [www.bms.com](http://www.bms.com)

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