News Release

September 9, 2019
Maruho Co., Ltd.

Maruho Preparing to Resume US Development For Anti-Herpes Virus Agent “Amenalief® Tab. 200mg”

Osaka (Japan), September 9, 2019 – Maruho Co., Ltd (“Maruho”, Head Office: Osaka, Japan, President and CEO: Koichi Takagi) announces it is preparing to resume US development for anti-herpes virus agent “Amenalief® Tab. 200mg” (INN: amenamevir; hereinafter referred to as “the product”).

In 2011, development of the product was temporarily suspended in the US. In July 2019, at a Pre-Investigational New Drug (IND) meeting with the US Food and Drug Administration (FDA), the development plan for phase 3 clinical studies (2 studies) and a phase 2 exploratory study was accepted by the FDA. Maruho will now proceed with preparations for development of the product in the United States including out-licensing.

The product has been observed to show high antiviral activity against the proliferation of the varicella-zoster virus (hereinafter “VZV”) and herpes simplex virus (hereinafter “HSV”) by inhibiting the activity of the helicase-primase complex, which is essential for viral DNA replication. Results of clinical studies for herpes zoster (shingles) [*1] conducted with patients in Japan, showed that 400mg of the product administered once a day after meals was effective. In addition, safety was also determined to be acceptable in considerations of the recognized benefits, and in July 2017 Maruho obtained manufacturing and marketing approval for the treatment of herpes zoster (shingles) in Japan, and launched the product in Japan on September 7, 2017.

Aiming for manufacturing and marketing approval of the product in the US, Maruho hopes to further contribute to the treatment and improvement of quality of life for patients suffering from infectious diseases as a result of VZV and HSV infections.

<Reference>
Background information
The product is an anti-herpes virus agent with a novel mechanism of action created by Astellas Pharma Inc. ("Astellas", Head Office: Tokyo, Japan, President and CEO: Kenji Yasukawa, Ph.D.). In 2009, Astellas completed a phase 2 clinical study for patients with herpes simplex*2 (recurrent genital herpes) in the US. Then, during a long term administered phase 1 clinical study (28 day safety study) on healthy adults for an additional indication (relapse suppression treatment), a case of thrombocytopenia was reported as a serious adverse event. Based on this result, Astellas discontinued the development of the product in 2011.
In August 2012, Maruho entered into a license agreement with Astellas for development and commercialization of the product in Japan. The product was launched in Japan in 2017 and administered to approximately 400,000* patients. Maruho accumulated safety information and included this in reports to the FDA. In 2019, the FDA accepted a development plan to conduct phase 3 clinical studies (2 studies) and phase 2 exploration studies with the product. Currently, Maruho has determined that there is no clear causal relationship with the product and thrombocytopenia.
*Note: As of January 2019

***1 About herpes zoster (shingles)**
Herpes zoster (shingles) is an infection caused by the reactivation of the chickenpox varicella-zoster virus (hereinafter "VZV"). Possible causes of VZV reactivation include aging, underlying diseases that tend to suppress the immune system, stress, or overwork, etc. It is characterized by neuralgia-like pain and sensory abnormalities, followed by a rash outbreak in striped bands at the site of the pain.
(Reference: Clinical strategy in the prevention era. Herpes zoster (Medical Tribune) Supervision: Prof. Niimura, General Editor: Prof. Honda)

***2 About herpes simplex**
Herpes simplex is a disease caused by the herpes simplex virus (HSV) initially infecting the skin and mucosa, or reactivation of the virus in latently-infected nerve ganglia. Once infection occurs, symptomatic recurrences may occur. Classifications of the disease include herpes labialis, herpes facialis, herpes genitalis, and Kaposi varicelliform eruption, depending on the affected area and clinical condition. Initial symptoms include itching and discomfort, followed by the outbreak of cutaneous lesions. Lesions begin with erythema and papules. These are followed by vesicles, pustules, erosion, and ulcers, which lead to the development of crusts. The skin eventually heals as the crusts fall off. Although initial infection is often asymptomatic, the disease may cause severe systemic symptoms such as pyrexia, lymphadenopathy, and pain.
(Reference: Institute of Medical Information Science, Diseases Vol.6 Immune / Collagen Disease / Infectious Diseases, 1st Edition, Medic Media, 2009)

About Maruho
Maruho Co., Ltd. has its headquarters in Osaka and leads Japan in research and development, manufacturing and commercialization of dermatological products. Founded in 1915, Maruho has 1,512 employees (as of the end of September 2018), and net sales were approximately 78.57 billion yen in its fiscal year ending September 30, 2018. Pursuing its long-term corporate vision of "Excellence in Dermatology," Maruho is striving to improve the health and quality of life of people all over the world.
For more information, please visit www.maruho.co.jp/english/

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