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Crovalimab Approved in China as the First Country, for the Treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Crovalimab, the 5th Chugai originated global drug, approved for the first time in the world
- Crovalimab is the second approved drug applying Chugai's proprietary Recycling Antibody® technology, which is expected to improve patient convenience by allowing treatment at home by self-injection through subcutaneous administration every four weeks
- Approval based on several studies including a Chinese phase III clinical trial (COMMODORE 3 study) and a global phase III clinical trial (COMMODORE 2), for PNH without history of complement inhibitor treatment

TOKYO, February 8, 2024 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) today announced that crovalimab (Chinese product name : 派圣凯®), a humanized complement inhibitor C5 monoclonal antibody discovered by Chugai, was approved by the National Medical Products Administration (NMPA) of People's Republic of China for treatment of adults and adolescents (12 years of age and above) with PNH not been previously treated with complement inhibitors. As F. Hoffmann-La Roche Ltd. (hereafter "Roche") [Head Office: Basel, Switzerland. CEO: Thomas Schinecker] is responsible for the development of crovalimab outside Japan and Taiwan, the regulatory application was filed by a China affiliate of Roche. China is the first country in the world to approve crovalimab.

The approval is based on the results of several studies including COMMODORE 3 study, a multicenter, single-arm, phase III clinical trial conducted in China, and COMMODORE 2 study, a randomised, open-label global phase III study, for PNH without history of complement inhibitor treatment.

Crovalimab has been created using Chugai's Recycling Antibody technology. While a typical antibody can bind to an antigen only once, crovalimab is engineered to bind to the antigen repeatedly, enabling sustained complement inhibition at a low dose and achieving subcutaneous administration every four weeks. Crovalimab is the second approved drug applying Chugai's Recycling Antibody technology, following Enspryng® for the treatment of neuromyelitis optica spectrum disorder (NMOSD).

[Reference Information]

Anti-C5 Recycling Antibody Crovalimab Obtains Priority Review in China for the Treatment of Paroxysmal Nocturnal Hemoglobinuria (Press release by Roche issued on August 10, 2022)
https://www.chugai-pharm.co.jp/english/news/detail/20220810160000_942.html

About Crovalimab

Crovalimab (genetical recombination) is an anti-C5 recycling antibody created with Chugai's Recycling Antibody technology. Recycling antibodies are designed to achieve pH-dependent antigen binding so that a

CHUGAI PHARMACEUTICAL CO., LTD. Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku Tokyo, 103-8324 Japan
Media Relations Group TEL:+81-(0)3-3273-0881 E-mail:pr@chugai-pharm.co.jp
Investor Relations Group TEL:+81-(0)3-3273-0554 E-mail:ir@chugai-pharm.co.jp

single antibody molecule can bind with the antigen multiple times, enabling a longer efficacy compared with a conventional antibody. Crovalimab is designed to target C5, a key component of the complement system, and is expected to control complement activity. It is also expected to reduce the treatment burden for patients and their caregivers through subcutaneous administration. Since crovalimab binds to complement C5 at a different site from existing antibody drugs, it can be an effective treatment option for patients with a specific C5 gene mutation reported in Asia (appears in approximately 3.2% of Japanese patients with PNH), which causes existing antibody drugs not to bind to C5.[1,2]
The drug has been filed for approval as a new drug for PNH in Japan, the US, and EU. In addition, clinical trials are ongoing for atypical hemolytic uremic syndrome (aHUS), and Roche is conducting trials for sickle cell disease (SCD) and lupus nephritis overseas.

About paroxysmal nocturnal hemoglobinuria
Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired hematopoietic stem cell disorder characterized by intravascular hemolysis due to complement activation. It is caused by the clonal expansion of hematopoietic stem cells, driven by acquired mutations in the *PIG-A* gene.[3] While symptoms may vary in each individual, there are typically two types. One is symptoms attributed to the characteristic hemolysis in PNH, such as hemoglobinuria and thrombosis. The other is hematopoietic failures similar to those associated with aplastic anemia. PNH may cause complications, including chronic kidney disease and pulmonary hypertension.

Source:
1. Fukuzawa T, et al. Long lasting neutralisation of C5 by SKY59, a novel recycling antibody, is a potential therapy for complement-mediated diseases. 2017; Sci Rep 7, 1080.
2. Nishimura J et al. Genetic variants in C5 and poor response to eculizumab. N Engl J Med. 2014 Feb 13;370(7):632-9.
3. Working group for the development of the reference guide revision of diagnostic criteria and practice for paroxysmal nocturnal hemoglobinuria (PNH). Referenced Guide to Paroxysmal Nocturnal Hemoglobinuria Treatment Revised 2022. (in Japanese only)

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