Innovation all for the patients

CHUGAI

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PiaSky Approved in the EU as the First Monthly Subcutaneous Treatment for People with PNH

- With the option to self-administer*, PiaSky has the potential to reduce treatment burden for people with paroxysmal nocturnal hemoglobinuria (PNH) and their caregivers in Europe
- Approval based on COMMODORE 2 study, which demonstrated efficacy of monthly (every four weeks) subcutaneous (SC) PiaSky was non-inferior to intravenous eculizumab every two weeks in the maintenance dosing period
- Chugai's proprietary Recycling Antibody Technology applied, which enables its monthly SC administration

TOKYO, September 2, 2024 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that Roche has received approval from the European Commission for PiaSky® (generic name: crovalimab (genetical recombination)), a Chugai originated pH-dependent binding humanized anti-complement (C5) monoclonal antibody, for adults and adolescents (12 years of age or older with a weight of 40 kg and above) with paroxysmal nocturnal hemoglobinuria (PNH) who are either new to, or have been previously treated with C5 inhibitors. PNH is a rare and life-threatening blood condition where red blood cells are destroyed by the complement system - part of the innate immune system - causing symptoms such as anemia, fatigue and blood clots, and potentially leading to kidney disease.[1]

"We are very pleased that the Chugai originated PiaSky has been approved in Europe. C5 inhibitors, a standard treatment for PNH, require long-term treatments. Therefore, reducing the burden on people with PNH and caregivers is an important issue. PiaSky is designed to exert its effect with a small volume of medicine and with low frequency of treatment, by applying our proprietary Recycling Antibody® technology. This allows monthly subcutaneous administration during the maintenance period. We expect that PiaSky, which allows self-administration*, will greatly contribute to reducing the treatment burden for people with PNH," said Chugai's President and CEO, Dr. Osamu Okuda.

PiaSky is the first monthly (every four weeks) subcutaneous (SC) treatment for PNH in the European Union, with the option to self-administer following adequate training. This could help to reduce treatment burden and disruption to the lives of people with PNH and their caregivers.[2]

C5 inhibitors, treatments that block the terminal phase of the complement system cascade, have been shown to be effective in treating PNH.[3] PiaSky has been developed to address the patients' needs and issues in PNH treatment. It advances complement inhibition through Chugai's proprietary Recycling Antibody technology, which enables monthly SC administration by allowing the medicine to bind and inhibit the C5 protein multiple times and to act longer in the body with a small volume of medicine.[2,4]

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This approval is based on the results from the Phase III COMMODORE 2 study in people with PNH who have not been previously treated with C5 inhibitors. The study demonstrated that PiaSky, administered as SC injections every four weeks, achieved disease control and was well-tolerated. PiaSky was non-inferior in efficacy to eculizumab, an existing standard of care C5 inhibitor, given intravenously every two weeks. The rate of adverse events in people treated with PiaSky and eculizumab was 78% and 80%, respectively.[4,5] The application included supportive data from two additional Phase III studies, the COMMODORE 1 study in people with PNH switching from currently approved C5 inhibitors, and the COMMODORE 3 study in people new to C5 inhibitor treatment in China.[4-8]

PiaSky is the first monthly SC treatment for PNH, approved in multiple territories around the world, including the US and Japan. It is being investigated in a broad clinical development program, including five Phase III studies and three earlier phase studies in complement-mediated diseases, including atypical hemolytic uremic syndrome and sickle cell disease, in addition to PNH.[5,6,8-13]

*Self-administration is currently not included in the Japanese electronic package insert

About the COMMODORE 2 Study

The COMMODORE 2 study is a phase III, randomized, open-label global study evaluating the efficacy and safety of crovalimab versus eculizumab in people with paroxysmal nocturnal hemoglobinuria (PNH) who have not been treated previously with C5 inhibitors. The study's co-primary efficacy endpoints measure transfusion avoidance and control of hemolysis (the ongoing destruction of red blood cells measured by lactate dehydrogenase levels). The adults** enrolled in the study were randomized in a 2:1 ratio to be treated with either subcutaneous (SC) crovalimab every four weeks or intravenous (IV) eculizumab every two weeks. The participants who were less than 18 years old were included in a non-randomized treatment arm and were treated with SC crovalimab every four weeks.[4,5]

**Including two patients aged less than 18 years old enrolled before the revision of the protocol

About PiaSky

PiaSky is a Chugai originated anti-C5 recycling antibody created with our proprietary Recycling Antibody technology. Recycling antibodies are designed to achieve pH-dependent antigen binding so that a single antibody molecule can bind with the antigen multiple times, enabling a longer efficacy compared with a conventional antibody. Additionally, by introducing surface charge modification technology, it increases the clearance rate of the antigen from the blood, enabling more efficient neutralization of the antigen compared to conventional recycling antibodies, thereby reducing the required dosage. PiaSky 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 people with PNH and their caregivers through subcutaneous administration every 4 weeks with a small volume of medicine. Since PiaSky binds to complement C5 at a different site from existing antibody drugs, it can be an effective treatment option for people with PNH with a specific C5 gene mutation reported in Asia (appears in approximately 3.2% of Japanese people with PNH), which causes existing antibody drugs not to bind to C5.[2,14]

PiaSky has been approved in China for the first time in February 2024, for the treatment of adults and adolescents (12 years of age and above) with PNH who have not been previously treated with complement inhibitors. In Japan, it was approved in March 2024 for the treatment of PNH and launched in May of the

same year. It also obtained approval in the US in June 2024. Currently, it is under review by regulatory authorities in various countries, including Taiwan, as a new drug for PNH. In addition, clinical trials are ongoing for atypical hemolytic uremic syndrome (aHUS), and Roche is conducting trials for sickle cell disease (SCD) 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.[15] 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. In Japan, PNH is a rare disease that is listed as one of the designated intractable diseases (designated intractable disease 62). 1,035 individuals have been granted the medical care recipient certificate for PNH as of the end of FY2022.[16]

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Source:

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