Media & Investor Release

CHMP recommends EU approval of Roche's PiaSky for people with PNH, a rare, life-threatening blood condition

- **If approved, PiaSky will be the first monthly subcutaneous (SC) treatment for paroxysmal nocturnal haemoglobinuria (PNH) in the EU**
- **Additionally, with the option to self-administer, PiaSky may provide an alternative to existing intravenous (IV) C5 inhibitors, potentially helping to reduce treatment burden[1]**
- **The recommendation is based on the COMMODORE 2 study results, where SC PiaSky given every month demonstrated equivalent disease control and comparable safety to IV eculizumab given every two weeks[2,3]**

Basel, 28 June 2024 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for PiaSky® (crovalimab) for the treatment of paroxysmal nocturnal haemoglobinuria (PNH). The CHMP has recommended PiaSky, a novel recycling monoclonal antibody that inhibits the complement protein C5, for use in adults and adolescents (12 years of age or older with a weight of 40 kg) who are either new to, or have been previously treated with C5 inhibitors. If approved, PiaSky will be the first monthly subcutaneous (SC) treatment for PNH in the European Union, with the option to self-administer following adequate training. This may provide an alternative option to current C5 inhibitors that require regular intravenous (IV) infusions, potentially helping to reduce treatment burden and disruption to the lives of people with PNH and their caregivers.[1] A final decision regarding the approval of PiaSky is expected from the European Commission in the near future.

"People living with PNH face lifelong treatment, often requiring frequent intravenous infusions and time-consuming clinic visits," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "With the option to self-administer once a month, today's recommendation may therefore offer patients and caregivers in Europe more freedom in their day-to-day lives."

PNH is a rare and life-threatening blood condition, which affects approximately 20,000 people worldwide. In PNH, red blood cells are destroyed by the complement system – part of the innate immune system. This causes symptoms such as anaemia, fatigue and blood clots, and can lead to kidney disease. C5 inhibitors – treatments that block part of the complement system cascade – have been shown to be effective in treating PNH. PiaSky is a novel C5 inhibitor that is recycled within the bloodstream, 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. This

enables SC administration every four weeks, following an initial IV infusion and weekly SC loading doses in the first month of treatment.[1,2,4-6]

The CHMP recommendation 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. Results from the study demonstrated that PiaSky, administered as SC injections every four weeks, achieved disease control and was well-tolerated. PiaSky was non-inferior with comparable safety to eculizumab, an existing standard of care C5 inhibitor, given intravenously every two weeks. The rate of adverse events in people treated with PiaSky was similar to treatment with eculizumab (78% versus 80%, respectively). 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.[2,7,8,9]

PiaSky is the first monthly SC treatment approved in the US, Japan and China for people with PNH based on results of the COMMODORE studies.[2,7,9]

PiaSky is being investigated in a broad clinical development programme, including five ongoing Phase III studies and three earlier phase studies in complement-mediated diseases, including PNH, atypical haemolytic uremic syndrome and sickle cell disease.[2,7,9-14]

About PiaSky® (crovalimab)

PiaSky® (crovalimab) is a novel recycling monoclonal antibody that inhibits the complement protein C5 and is designed to block the complement system – a vital part of the innate immune system that acts as the body's first line of defence against infection. PiaSky has been engineered by Chugai Pharmaceutical Co. Ltd to address certain needs of people living with complement-mediated diseases, including providing patients with a potential for self-administration following adequate training.

PiaSky works by binding to C5, blocking the last step of the complement cascade and delivering rapid and sustained complement inhibition. It is also recycled within the bloodstream, enabling small volume subcutaneous administration every four weeks. In addition, PiaSky binds to a different C5 binding site from current treatments, which has the potential to provide a treatment option for people with specific C5 gene mutations who do not respond to current therapies.

PiaSky is a monthly subcutaneous treatment approved in the US, Japan and China for people with paroxysmal nocturnal haemoglobinuria, based on the Phase III COMMODORE studies. It is also being evaluated in atypical haemolytic uremic syndrome and sickle cell disease.[1,2,7,9-14]

About the COMMODORE 2 study

The COMMODORE 2 study is a Phase III, randomised, open-label study evaluating the efficacy and safety of PiaSky® (crovalimab) versus eculizumab in people with paroxysmal nocturnal haemoglobinuria (PNH) who have not been treated previously with C5 inhibitors. The study's co-primary efficacy endpoints measure transfusion avoidance and control of haemolysis (the ongoing destruction of red blood cells measured by lactate dehydrogenase levels). The adults enrolled in the study were randomised in a 2:1 ratio to be treated with either subcutaneous (SC) PiaSky every four weeks or intravenous eculizumab every two weeks. The participants who were less than 18 years old were included in a non-randomised treatment arm and were treated with SC PiaSky every four weeks.[3]

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognising our endeavour to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the fifteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

For more information, please visit www.roche.com.

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