Media & Investor Release

Roche announces positive data from global phase III programme for crovalimab in PNH, a rare life-threatening blood condition

- **The COMMODORE 2 study met its co-primary efficacy endpoints, showing crovalimab achieved disease control in people with paroxysmal nocturnal haemoglobinuria (PNH) who have not been previously treated with complement inhibitors**
- **The results of the phase III COMMODORE 1 study in people with PNH switching from currently approved C5 inhibitors, supported the favourable benefit-risk profile of crovalimab, as seen in the pivotal COMMODORE 2 study**
- **Results from both studies will be submitted to regulatory authorities around the world and presented at an upcoming medical meeting**

Basel, 7 February 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the global phase III COMMODORE 2 study, evaluating the efficacy and safety of crovalimab in people with paroxysmal nocturnal haemoglobinuria (PNH) who have not been previously treated with complement inhibitors. The study met its co-primary efficacy endpoints of transfusion avoidance and control of haemolysis (the ongoing destruction of red blood cells measured by lactate dehydrogenase levels). Results showed that crovalimab, a novel, investigational anti-C5 recycling monoclonal antibody, given as a subcutaneous injection every four weeks, achieved disease control and was non-inferior to eculizumab, a current standard of care, which is given intravenously every two weeks.

The efficacy and safety data from the separate phase III COMMODORE 1 study in people with PNH switching from currently approved C5 inhibitors to crovalimab, supported the favourable benefit-risk profile of crovalimab, as seen in the pivotal COMMODORE 2 study.

“People with PNH may benefit from more options to achieve robust disease control with less frequent treatment intervals,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “As the first global phase III data for crovalimab, these results emphasise its potential to address these needs. We look forward to submitting these data to regulatory authorities, bringing us one step closer to making crovalimab available for people with PNH around the world.”

PNH is a rare and life-threatening blood condition in which red blood cells are destroyed by the complement system. This causes symptoms such as anaemia, fatigue, blood clots and kidney disease.[1] C5 inhibitors can be effective in treating the condition.[2] Crovalimab has been engineered to be recycled within the circulation, enabling sustained complement inhibition through low dose, subcutaneous administration every four weeks.[3, 4]

Data from both studies will be submitted to regulatory authorities around the world and presented at an upcoming medical meeting. Positive data from the phase III COMMODORE 3 study in China were presented at the American Society of Hematology (ASH) Annual Meeting and Exposition on 10 December 2022. Data from the COMMODORE 3 study have been submitted via China's Centre for Drug Evaluation Breakthrough Therapy Designation pathway. This submission has been accepted under Priority Review for approval consideration by China's National Medical Products Administration.

About the COMMODORE 1 and 2 studies

The COMMODORE 2 study is a phase III, randomised, open-label study evaluating the efficacy and safety of crovalimab versus eculizumab in people with paroxysmal nocturnal haemoglobinuria (PNH) who have not been previously treated 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) 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-randomised treatment arm and were treated with SC crovalimab every four weeks.[5]

The COMMODORE 1 study is a phase III, randomised, open-label study evaluating the safety of crovalimab in people with PNH switching from currently approved C5 inhibitors. The study's outcome measures evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic properties of crovalimab. The study included people (18 years of age or older) currently treated with eculizumab. In a non-randomised arm, the study also included paediatrics (<18 years of age) currently treated with eculizumab, people currently treated with ravulizumab, people currently treated with off-label doses of eculizumab (higher than the approved dose for PNH: more than 900mg per dose and/or more frequently than every two weeks), or people with known mutations in the C5 gene who do not respond to current therapies.[6]

About Crovalimab

Crovalimab is an investigational, novel anti-C5 recycling monoclonal antibody 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. Crovalimab has been engineered to address the medical needs of people living with complement-mediated diseases, including providing patients with a potential at-home administration option.

Crovalimab works by binding to C5, blocking the last step of the complement cascade and is also recycled into circulation, enabling rapid and sustained complement inhibition.[3, 4] Crovalimab's recycling action also enables low dose SC administration every four weeks. In addition, crovalimab binds to a different C5 binding site from current treatments, which has the potential to provide an effective treatment option for people with specific C5 gene

mutations, who do not respond to current therapies.[3] Crovalimab is being investigated in a clinical development programme, including five ongoing phase III studies.[5, 6, 7, 8, 9] Crovalimab is being evaluated in PNH, atypical haemolytic uraemic syndrome, sickle cell disease, and other complement mediated diseases.

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 endeavor 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 thirteenth 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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