

New data show Roche’s subcutaneously administered crovalimab achieved disease control and was well-tolerated in people with paroxysmal nocturnal haemoglobinuria (PNH)

- **The COMMODORE 2 study demonstrated that subcutaneous crovalimab every four weeks was non-inferior to intravenous eculizumab every two weeks, with comparable safety, in people new to C5 inhibitors¹**
- **Monthly self-administration of subcutaneous crovalimab has the potential to address the high burden of a disease that requires lifelong treatment including in settings where access to current C5 inhibitors is limited^{1,2}**
- **The COMMODORE 1 study in people switching from currently approved C5 inhibitors supported the consistent benefit-risk profile of crovalimab as seen in the COMMODORE 2 study³**

Basel, 09 June 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that positive results from the global phase III COMMODORE 1 and 2 studies, evaluating the efficacy and safety of crovalimab, an investigational, novel anti-C5 recycling monoclonal antibody, compared to eculizumab, a current standard of care in paroxysmal nocturnal haemoglobinuria (PNH) were presented at the European Hematology Association (EHA) Hybrid Congress, taking place in Frankfurt, Germany on 8-11 June 2023.

“With the option for subcutaneous self-administration, crovalimab could help meet the lifelong needs of people living with PNH and their caregivers,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “Data from the COMMODORE studies will be submitted to regulatory authorities around the world.”

PNH is a rare and life-threatening blood condition, in which red blood cells are destroyed by the complement system – part of the innate immune system – causing symptoms such as anaemia, fatigue, blood clots and kidney disease.⁴ C5 inhibitors have been shown to be effective in treating the condition.⁵ Crovalimab has been engineered to be recycled within the bloodstream, enabling sustained complement inhibition through low dose, subcutaneous (SC) administration every four weeks.^{6,7}

In the COMMODORE 2 study, 79.3% (95% CI: 72.9, 84.5) of participants randomised to be treated with crovalimab achieved haemolysis control from week five to week 25 compared with 79.0% (95% CI: 69.7, 86.0) with eculizumab. Additionally, 65.7% (95% CI: 56.9, 73.5) achieved transfusion avoidance (TA) from baseline to week 25 with crovalimab and 68.1% (95% CI: 55.7, 78.5) with eculizumab. TA is defined as people who become transfusion-free and do not require transfusion per protocol-specified guidelines. Blood transfusion requirements are important clinical measures of haemolysis caused by complement dysregulation in PNH. A

clinically meaningful improvement in FACIT-Fatigue score from baseline to week 25 occurred in both arms, with a numerically greater improvement with crovalimab (adjusted mean change 7.8 (95% CI: 6.5, 9.1)), versus eculizumab (adjusted mean change 5.2 (95% CI: 3.4, 6.9)).¹

Adverse events (AEs) occurred in 78% of participants treated with crovalimab and 80% treated with eculizumab in the COMMODORE 2 study. Serious infections occurred in 3% of participants treated with crovalimab and 7% of participants treated with eculizumab, with no meningococcal infections. The most common AE, occurring in 16% of people treated with crovalimab and 13% of people treated with eculizumab was an infusion-related reaction. One participant in each arm experienced an AE that led to treatment discontinuation.¹

The results from the COMMODORE 1 study indicate that crovalimab maintained disease control in people switching from currently approved complement inhibitors.³ The data support the consistent benefit-risk profile of crovalimab, as well as SC administration with the option to self-administer, as seen in the COMMODORE 2 study.

Roche also presented preliminary data from the COMMODORE Burden of Illness study, which suggest that despite currently available C5 inhibitor treatments, people with PNH continue to experience substantial burden of disease, which can translate into diminished quality of life and considerable costs. These data suggest that people with PNH may benefit from alternative treatment options.⁸

Global phase III data from the COMMODORE 1 and 2 studies in PNH will be submitted to regulatory authorities around the world. Positive data from a third phase III study evaluating crovalimab in PNH, the 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 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, which was created by Chugai Pharmaceutical Co., Ltd, has been engineered to address the medical needs of people living with complement-mediated diseases, including providing patients with a potential self-administration option.

Crovalimab works by binding to C5, blocking the last step of the complement cascade and is also recycled within the bloodstream, enabling rapid and sustained complement inhibition.^{6,7} Crovalimab's recycling properties 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 a treatment option for people with specific C5 gene mutations, who do not respond to current therapies.⁶ It is also being evaluated in atypical haemolytic uraemic syndrome, sickle cell disease, and other complement mediated diseases.

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 treated previously with C5 inhibitors. The 204 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 six participants who were less than 18 years old were included in a non-randomised arm, to be treated with SC crovalimab every four weeks.⁹

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 included 89 people (18 years of age or older) currently treated with eculizumab, randomised in a 1:1 ratio to be treated with either SC crovalimab every four weeks or IV eculizumab every two weeks. 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.¹⁰

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 thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

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