Investor Update

FDA accepts application for Roche's crovalimab for the treatment of PNH, a rare life-threatening blood condition

- **Acceptance based on the phase III COMMODORE 2 study, which demonstrated crovalimab achieved disease control and was well-tolerated in people with paroxysmal nocturnal haemoglobinuria (PNH)[1]**
- **If approved, crovalimab will be the first monthly subcutaneous treatment for PNH, with the option to self-administer outside of a supervised healthcare setting**
- **Filing applications have also been accepted in the EU, China and Japan, and submissions to other regulatory authorities around the world are ongoing**

Basel, 6 September 2023 – Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the US Food and Drug Administration (FDA) has accepted the company's Biologics License Application (BLA) for crovalimab, an investigational, novel anti-C5 recycling monoclonal antibody, for the treatment of paroxysmal nocturnal haemoglobinuria (PNH). The acceptance was based on results from the pivotal phase III COMMODORE 2 study, which demonstrated that in people with PNH, crovalimab achieved disease control and was well-tolerated.[1] Results from the phase III COMMODORE 1 study, demonstrating the consistent benefit-risk profile of crovalimab, also supported the application.[2]

"This filing acceptance reinforces the value of crovalimab, which was engineered to be recycled in the bloodstream with the goal of offering a sustained response while reducing treatment burden," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Crovalimab could provide an option to self-administer as infrequently as every four weeks, thereby reducing clinic visits for people with this lifelong condition."

PNH is a rare and life-threatening blood condition, which affects approximately 20,000 people worldwide.[3] 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.[4] C5 inhibitors – treatments that block part of the complement system cascade – have been shown to be effective in treating PNH.[5] Crovalimab is a novel C5 inhibitor that is recycled within the bloodstream, enabling sustained complement inhibition through low dose, subcutaneous (SC) administration every four weeks.[6,7]

The BLA was based on results from the phase III COMMODORE 2 study in people with PNH who have not been previously treated with complement inhibitors. Results from the study demonstrated that crovalimab, administered as SC injections every four weeks, achieved disease control and was non-

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inferior with comparable safety to eculizumab, a current standard of care, given intravenously every two weeks.[1] Adverse events (AE) in the study occurred in 78% of participants treated with crovalimab and 80% treated with eculizumab, with the most common AE being an infusion-related reaction.[1] The application also included data from the phase III COMMODORE 1 study, which supported the favourable benefit-risk profile of crovalimab in people with PNH switching from currently approved C5 inhibitors.[2] Data from the COMMODORE 1 and 2 studies were recently presented at the European Hematology Association 2023 Hybrid Congress.[1,2]

Global phase III data from the COMMODORE 1 and 2 studies in PNH have been submitted to other regulatory authorities around the world and submissions are ongoing. Positive data from a third phase III single arm study evaluating crovalimab in PNH, the COMMODORE 3 study in China, were presented at the American Society of Hematology 2022 Annual Meeting.[8] Data from the COMMODORE 3 study have been submitted via China's Centre for Drug Evaluation Breakthrough Therapy Designation pathway and crovalimab has been accepted for consideration for approval under Priority Review by China's National Medical Products Administration.

Crovalimab is being investigated in a broad clinical development programme, including five ongoing phase III studies and three earlier phase studies in PNH and other complement mediated diseases.[1,2,8,9,10]

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 certain 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 subcutaneous (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 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 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.[11]

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.[12]

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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References

[1] Roth A, et al. The Phase III, Randomised COMMODORE 2 Trial: Results from a Multicentre Study of Crovalimab vs Eculizumab in Paroxysmal Nocturnal Hemoglobinuria (PNH) Patients Naïve to Complement Inhibitors. Presentation at European Hematology Association (EHA) Annual Congress; 2023 June 08-13. Abstract #S181.
[2] Scheinberg P, et al. Phase III Randomised, Multicentre, Open-Label COMMODORE 1 Trial: Comparison of Crovalimab Vs Eculizumab in Complement Inhibitor-Experienced Patients with Paroxysmal Nocturnal Hemogobinuria (PNH). Presentation

at European Hematology Association (EHA) Annual Congress; 2023 June 08-13. Abstract #S183.
[3] Grand View Research. Paroxysmal nocturnal hemoglobinuria (PNH) treatment market size, share and trends analysis report by treatment and segment forecasts, 2018 – 2025. [Internet; cited August 2023]. Available from: https://www.grandviewresearch.com/industry-analysis/paroxysmal-nocturnal-hemoglobinuria-pnh-market.
[4] National Organization for Rare Diseases. Paroxysmal nocturnal hemoglobinuria. [Internet; cited August 2023]. Available from: https://rarediseases.org/rare-diseases/paroxysmal-nocturnal-hemoglobinuria/.
[5] Bektas M, et al. Paroxysmal nocturnal hemoglobinuria: current treatments and unmet needs. Journal of Managed Care & Specialty Pharmacy 2020; 26:12-b Suppl, S14-S20.
[6] 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.
[7] Nishimura J, et al. An Optimized Crovalimab Dose and Regimen Reduced the Formation of Drug-Target-Drug Complexes in Patients with Paroxysmal Nocturnal Hemoglobinuria From the Phase I/II COMPOSER Trial. Poster presented at: American Society Of Hematology (ASH) Annual Meeting; 2020 December 5-8; Atlanta, GA, USA. Abstract 1550.
[8] Liu H, et al. Results From the First Phase 3 Crovalimab (C5-Inhibitor) Study (COMMODORE 3): Efficacy and Safety in Complement Inhibitor-Naive Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH). Presentation at: ASH Annual Meeting and Exposition; 2022 Dec 10-13 Abstract #293.
[9] COMMUTE-p (NCT04958265). [Internet; cited August 2023] Available at: https://www.clinicaltrials.gov/ct2/show/NCT04958265.
[10] COMMUTE-a (NCT04861259). [Internet; cited August 2023] Available at: https://www.clinicaltrials.gov/ct2/show/NCT04861259.
[11] COMMODORE 2 (NCT04434092). [Internet; cited August 2023] Available at: https://www.clinicaltrials.gov/ct2/show/NCT04434092.
[12] COMMODORE 1 (NCT04432584). [Internet; cited August 2023] Available at: https://www.clinicaltrials.gov/ct2/show/NCT04432584.

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