Media & Investor Release

Roche's subcutaneous crovalimab given every four weeks achieves disease control in people with PNH, a life-threatening blood condition

- **The phase III COMMODORE 3 study of crovalimab met primary endpoints of transfusion avoidance and haemolysis control in people with paroxysmal nocturnal hemoglobinuria (PNH) [1]**
- **COMMODORE 3 is the first China-specific study in PNH. Current treatment options are extremely limited in China, resulting in significant levels of disease-related morbidity and mortality for people living with PNH [2]**
- **Based on these data crovalimab has received Breakthrough Therapy Designation and is under Priority Review for approval in China**

Basel, 11 December 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive new data from the phase III COMMODORE 3 study in China, demonstrating that crovalimab, a novel anti-C5 recycling monoclonal antibody, is efficacious and well-tolerated in people with paroxysmal nocturnal haemoglobinuria (PNH). The study met its co-primary efficacy endpoints of transfusion avoidance (TA) and haemolysis control, demonstrating that participants with PNH, who have not been treated previously with complement inhibitors and who received subcutaneous crovalimab injections every four weeks, achieved disease control.[1] The data were presented at the American Society of Hematology (ASH) congress, taking place from 10-13 December 2022.

PNH is an ultra-rare and life-threatening blood condition, where red blood cells are targeted and destroyed by the complement system – part of the innate immune system – causing symptoms such as anaemia, fatigue, blood clots and kidney disease. [3] C5 inhibitors – treatments that block part of the complement system – have been shown to be effective in treating the condition. Crovalimab has been engineered to be recycled into circulation, enabling sustained complement inhibition, and potentially reducing the treatment burden associated with currently available treatments. [4, 5, 6, 7] It is being investigated in a comprehensive clinical development programme, including five ongoing global phase III studies in PNH and other complement mediated diseases. [8, 9, 10, 11, 12]

"We are pleased with the strength of these first phase III data for crovalimab, which we hope will address the urgent need for efficacious and well-tolerated treatment options for this life-threatening condition in China." said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "As crovalimab has been developed to be taken subcutaneously and infrequently, with the option to self-administer, it has the potential to become an important treatment option for people everywhere living with paroxysmal nocturnal haemoglobinuria."

F. Hoffmann-La Roche Ltd
4070 Basel
Switzerland
Group Communications
Roche Group Media Relations
Phone +41 61 688 88 88
www.roche.com

The COMMODORE 3 study included data from 51 participants with PNH, who received crovalimab subcutaneously every four weeks during the primary study period. Results showed that the co-primary efficacy endpoints of haemolysis control and TA, indicators of disease control, were met. The mean proportion of participants with haemolysis control from week five through to week 25 was 78.7% (95% CI: 67.8%, 86.6%).1 The difference between the proportion of participants with TA within 24 weeks prior to screening (0.0%) and the proportion of participants with TA from baseline through to week 25 (51.0%) was statistically significant ($p<0.0001$).[1] 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.[13,14]

In addition, the proportion of participants with breakthrough haemolysis (used to measure a loss of disease control) from baseline through week 25 was 3.9% (95% CI: 0.7%, 14.6%), and the proportion of participants who achieved haemoglobin stabilisation was 51% (95% CI: 36.8%, 65.1%).[1] A rapid and clinically meaningful improvement in fatigue status within two weeks after treatment with crovalimab was also reported and sustained over time, as measured by the FACIT-Fatigue scale.[1] The overall safety data were consistent with the known safety profile of C5 inhibitors and underlying disease, showing that crovalimab was well-tolerated with no new safety signals identified.[1]

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 in PNH by China's National Medical Products Administration. As the availability of C5 inhibitors is extremely limited in China, there remains a high clinical need for people living with PNH there.

Data from the global crovalimab COMMODORE 1 and COMMODORE 2 PNH studies are expected in 2023. Crovalimab is being investigated as a potential treatment option for people living with PNH and other diseases such as atypical haemolytic uraemic syndrome and sickle cell disease.

About COMMODORE 3 (YO42311)

The COMMODORE 3 study is a phase III, single-arm study in China evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of crovalimab in people who have not previously been treated with complement inhibitors.[8] The study included 51 participants with paroxysmal nocturnal hemoglobinuria (PNH), who received crovalimab subcutaneously every four weeks for 24 weeks. Participants enrolled in the study received a loading series of crovalimab including an intravenous dose on day one, followed by weekly crovalimab subcutaneous (SC) doses for four weeks on week one day two, then on weeks two, three, and four. Maintenance SC dosing began at week five and continued every four weeks thereafter for a total of 24 weeks of study treatment. After 24 weeks of crovalimab treatment, participants who derived benefit from the drug can continue to receive crovalimab.

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 infections. Crovalimab has been engineered to address the medical needs of people living with complement-mediated diseases and overcome some of the challenges of currently available treatment options.

Similar to currently approved C5 inhibitors, crovalimab binds to C5, blocking the last step of the complement cascade. [5] However, crovalimab is also recycled into circulation, enabling rapid and sustained complement inhibition, which may potentially overcome the problem of incomplete C5 inhibition with currently available treatments.[4,5,6,7] Crovalimab's recycling action also enables low dose subcutaneous administration every four weeks, potentially removing the need for regular, time-consuming intravenous infusions. 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. [5] Crovalimab is being investigated in a comprehensive clinical development programme, including five ongoing global phase III studies.[8,9,10,11,12] Crovalimab is being evaluated in paroxysmal nocturnal haemoglobinuria, 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.

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F. Hoffmann-La Roche Ltd
4070 Basel
Switzerland
Group Communications
Roche Group Media Relations
Phone +41 61 688 88 88
www.roche.com

Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

Hans Trees, PhD
Phone: +41 79 407 72 58

Nathalie Altermatt
Phone: +41 79 771 05 25

Karsten Kleine
Phone: +41 79 461 86 83

Nina Mählitz
Phone: +41 79 327 54 74

Dr. Barbara von Schnurbein
Phone: +41 79 699 97 44

Sileia Urech
Phone: +41 79 935 81 48

Roche Investor Relations

Dr. Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr. Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr. Gerard Tobin
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com