Media & Investor Release

Positive phase III results for Roche's Gazyva/Gazyvaro show superiority to standard therapy alone in people with lupus nephritis

- **The REGENCY study met its primary endpoint, demonstrating statistically significant and clinically meaningful treatment benefits in people with active lupus nephritis**
- **Gazyva/Gazyvaro is designed to target an underlying cause of lupus nephritis, aiming to prevent or delay progression to end-stage kidney disease[1,2]**
- **Lupus nephritis is a potentially life-threatening manifestation of an autoimmune disease affecting 1.7 million people worldwide, primarily women; up to one-third of people on current treatments will progress to end-stage kidney disease within 10 years[3-6]**

Basel, 26 September 2024 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today positive topline results from the phase III REGENCY study of Gazyva®/Gazyvaro® (obinutuzumab) in people with active lupus nephritis. In the study, a higher proportion of people treated with Gazyva/Gazyvaro plus standard therapy (mycophenolate mofetil and glucocorticoids) achieved a complete renal response (CRR) at 76 weeks compared to those treated with standard therapy alone. Safety was in line with the well-characterised profile of Gazyva/Gazyvaro. No new safety signals were identified.

"Gazyva/Gazyvaro achieved a robust complete renal response rate in lupus nephritis, which is associated with long-term preservation of kidney function and delay or prevention of end-stage kidney disease," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Since dialysis or transplants are often required for patients with advanced kidney disease, these findings could represent an important step forward for people living with this devastating disease."

"I am very excited about today's announcement that the phase III REGENCY study has met its primary endpoint," said Dr. Brad H. Rovin, Director of Nephrology and Medical Director of the Center for Clinical Research Management at The Ohio State University Wexner Medical Center, and investigator for the REGENCY study. "The results of REGENCY are compelling. Obinutuzumab could offer the lupus community an effective new treatment option for controlling this difficult disease that can be associated with high morbidity for individuals living with lupus."

Two key secondary endpoints showed statistically significant and clinically meaningful benefits with Gazyva/Gazyvaro - the endpoint proportion of patients achieving CRR with a successful reduction of corticosteroid use, and an improvement in proteinuric response (both at 76 weeks). These endpoints are important indicators for achieving better disease control in lupus nephritis. Other secondary endpoints were not statistically significant, but numerically greater responses were observed for Gazyva/Gazyvaro in several endpoints. *

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Data are being shared with health authorities, including the US Food and Drug Administration (FDA) and the European Medicines Agency, with the goal of making this potential new treatment option for lupus nephritis available as soon as possible. Data are also being submitted for publication in a medical journal and presentation at a future medical congress.

Lupus nephritis is a potentially life-threatening manifestation of an autoimmune disease that affects approximately 1.7 million people worldwide, predominantly women and mostly of colour and childbearing age.[3-5, 7] In lupus nephritis, disease-causing B cells drive persistent inflammation that damages the kidneys.[2] Despite current treatment options, up to a third of people will develop end-stage kidney disease within 10 years, where dialysis or transplant are the only available options and the risk of mortality is high.[6] Data suggest that Gazyva/Gazyvaro depletes disease-causing B cells, helping to limit further damage to the kidneys and potentially preventing or delaying progression to end-stage kidney disease.[8]

Gazyva/Gazyvaro® was granted Breakthrough Therapy Designation by the US FDA in 2019, based on data from the phase II NOBILITY study.[9] Breakthrough Therapy Designation is designed to accelerate the development and regulatory review of medicines intended to treat serious or life-threatening conditions where preliminary clinical evidence has indicated they may demonstrate substantial improvement over existing therapies.

In addition to REGENCY, Gazyva/Gazyvaro is being investigated in children and adolescents with lupus nephritis, people with membranous nephropathy, childhood-onset idiopathic nephrotic syndrome and systemic lupus erythematosus (SLE), an autoimmune disease that commonly affects the kidneys and can lead to lupus nephritis.[10-13] Our pipeline also includes RG6299 (ASO factor B), an antisense oligonucleotide therapy being investigated in people with primary immunoglobulin A nephropathy at high risk of progression, Lunsumio® (mosunetuzumab), a first-in-class CD20xCD3 T-cell engaging bispecific antibody being investigated in SLE, PiaSky® (crovalimab), a novel recycling monoclonal antibody being investigated in atypical haemolytic uraemic syndrome and RG6382, a CD19xCD3 T-cell engaging bispecific antibody being investigated in SLE.[14-18]

About Gazyva/Gazyvaro in kidney diseases

Gazyva®/Gazyvaro® (obinutuzumab) is a Type II engineered humanised monoclonal antibody designed to attach to CD20, a protein found on certain types of B cells.[1] In lupus nephritis, disease-causing B cells drive persistent inflammation that damages the kidneys.[2] We can target an underlying cause of lupus nephritis to help gain better control of the disease by depleting disease-causing B cells with Gazyva/Gazyvaro, aiming to protect the kidneys from further damage and potentially prevent or delay progression to end-stage kidney disease.[1,2,8] Gazyva/Gazyvaro is already approved in 100 countries for various types of lymphoma. In the United States, Gazyva/Gazyvaro is part of a collaboration between Genentech and Biogen.

About the REGENCY study

REGENCY [NCT04221477] is a phase III, randomised, double-blind, placebo-controlled, multicentre study investigating the efficacy and safety of Gazyva®/Gazyvaro® (obinutuzumab) plus standard therapy (mycophenolate mofetil and glucocorticoids) in people with active/chronic International Society of Nephrology/Renal Pathology Society 2003 proliferative Class III or IV lupus nephritis, with or without Class V. The study enrolled 271 people, who were randomised 1:1 to receive either biannual intravenous dosing of Gazyva/Gazyvaro plus standard therapy or placebo plus standard therapy. REGENCY was designed based on robust phase II data and conducted during the COVID-19 pandemic. The study population was representative of the real-world population of people with lupus nephritis. The primary endpoint was the proportion of people who achieved complete renal response (CRR) at 76 weeks. Key secondary endpoints included the proportion of people who achieved CRR at week 76 with successful reduction of corticosteroid use (prednisone taper); the proportion who achieved proteinuric response at 76 weeks; mean change in estimated glomerular filtration rate at 76 weeks; death or renal related events through week 76 and overall renal response at 50 weeks. Safety and tolerability were also assessed.

About lupus nephritis

Lupus nephritis is a potentially life-threatening manifestation of systemic lupus erythematosus, an autoimmune disease that commonly affects the kidneys.[3] Lupus nephritis affects approximately 1.7 million people worldwide.[4,5] Lupus nephritis has a profound impact on the lives and outlook of those affected and even with the latest treatments, the damage caused to the kidneys usually gets worse over time, with up to a third of people progressing to end-stage kidney disease within 10 years, where the only options are dialysis or transplant.[6] Lupus nephritis predominantly affects women, mostly women of colour and usually of childbearing age.[7] Currently, there is no cure.[3]

About Roche in kidney diseases

For 20 years, we have combined innovation, scientific expertise and commitment to patients to address unmet needs in kidney diseases. Our industry-leading pipeline includes several ongoing phase I-III clinical studies of immune-mediated investigational therapies with the aim of bringing innovative new treatment options to people living with kidney and kidney-related diseases, including lupus nephritis, membranous nephropathy, immunoglobulin A nephropathy, atypical haemolytic uraemic syndrome, childhood-onset idiopathic nephrotic syndrome and systemic lupus erythematosus, an autoimmune disease that can lead to lupus nephritis.

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.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045. 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.

*Mean change in estimated glomerular filtration rate at 76 weeks, death or renal-related events through week 76, and overall renal response at 50 weeks.

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