Media & Investor Release

FDA accepts supplemental Biologics License Application for Roche's Gazyva/Gazyvaro for the treatment of lupus nephritis

- **Gazyva/Gazyvaro is the only anti-CD20 monoclonal antibody in a randomised phase III study to demonstrate a complete renal response benefit[1]**
- **The filing application is based on data from the phase III REGENCY study, where Gazyva/Gazyvaro showed superiority over standard therapy alone in people with active lupus nephritis[1]**
- **Lupus nephritis affects 1.7 million people worldwide; up to one-third of people on current treatments will progress to end-stage kidney disease within 10 years[2-5]**

Basel, 5 March 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the US Food and Drug Administration (FDA) has accepted the company's supplemental Biologics License Application (sBLA) for Gazyva®/Gazyvaro® (obinutuzumab) for the treatment of lupus nephritis. The filing acceptance is based on positive results from the phase III REGENCY study, which showed improved complete renal response (CRR) with Gazyva/Gazyvaro plus standard therapy compared with standard therapy alone.[1] The FDA is expected to make a decision on approval by October 2025.

"In people with lupus nephritis, Gazyva/Gazyvaro demonstrated a complete renal response benefit, a meaningful clinical outcome linked to preservation of kidney function, and slowing 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. "The FDA's sBLA acceptance for Gazyva/Gazyvaro recognises the need to provide a more effective treatment option for people living with this devastating disease."

"Lupus nephritis is a debilitating and potentially life-threatening condition that can lead to kidney failure and require dialysis or transplantation," said Louise Vetter, President and Chief Executive Officer, Lupus Foundation of America. "Given the relatively young age of onset, people with lupus nephritis experience more years of disease-related complications and decreased quality of life due to the significant burden of this illness. We are hopeful for a new treatment option that can effectively reduce these risks and improve the health of all people affected by this disease."

The phase III REGENCY results, which were simultaneously presented at the World Congress of Nephrology (WCN) and published in the *New England Journal of Medicine* in February 2025, showed that nearly half of patients on Gazyva/Gazyvaro plus standard therapy achieved a CRR, with a statistically significant and clinically meaningful improvement, compared with standard treatment alone. This was accompanied by clinically meaningful improvements in

complement levels and reductions in anti-dsDNA, markers of disease activity and inflammation. A pre-specified subgroup analysis showed consistent CRR benefit across patient subgroups, highlighting treatment potential for a broad patient population with a high unmet need. Gazyva/Gazyvaro's safety profile was consistent with the well-characterised profile observed in its haematology-oncology indications.

Data from the phase III REGENCY study are also being used for a filing submission with the European Medicines Agency.

Gazyva/Gazyvaro is the only anti-CD20 monoclonal antibody in a randomised phase III study to demonstrate a CRR benefit in lupus nephritis.[1] In 2019, Gazyva/Gazyvaro was granted Breakthrough Therapy Designation by the FDA based on data from the phase II NOBILITY study. 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.[6-9]

Our pipeline in immunological kidney and related diseases also includes Sefaxersen (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, RG6382, a CD19xCD3 T-cell engaging bispecific antibody being investigated in SLE, and P-CD19CD20-ALLO1, an allogeneic dual CAR-T.

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.[10] In lupus nephritis, disease-causing B cells drive persistent inflammation that damages the kidneys.[11] We can target disease-causing B cells, an underlying cause of lupus nephritis, with Gazyva/Gazyvaro to help gain better control of the disease, protect the kidneys from further damage and potentially prevent or delay progression to end-stage kidney disease.

Gazyva/Gazyvaro is already approved in 100 countries for various types of lymphoma. In the United States, Gazyva 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 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 REGENCY study met its primary endpoint; nearly half of patients on Gazyva/Gazyvaro plus standard therapy achieved a complete renal response (CRR), with a statistically significant and clinically meaningful improvement, compared to standard treatment alone. In the study, 46.4% of people treated with Gazyva/Gazyvaro plus standard therapy (mycophenolate mofetil and glucocorticoids) achieved CRR at 76 weeks compared with 33.1% of people treated with standard therapy alone (adjusted difference 13.4%, 95% CI, 2.0%-24.8%; P=0.0232). Two key secondary endpoints showed statistically significant and clinically meaningful benefit with Gazyva/Gazyvaro – the endpoint achieving CRR with a successful reduction of corticosteroid use and an improvement in proteinuric response (both at 76 weeks). Other secondary endpoints (mean change in estimated glomerular filtration rate at 76 weeks, overall renal response at 50 weeks) were not statistically significant, however a numerical difference in favour of Gazyva/Gazyvaro was observed. Statistically, significance for death and renal-related events through week 76 cannot be claimed due to the hierarchical design specified in the statistical analysis plan. Gazyva/Gazyvaro's safety profile was consistent with the well-characterised profile observed in its haematology-oncology indications.[1]

About lupus nephritis

Lupus nephritis is a potentially life-threatening manifestation of systemic lupus erythematosus, an autoimmune disease that commonly affects the kidneys.[2] Lupus nephritis affects approximately 1.7 million people worldwide. In lupus nephritis, disease-causing B cells drive persistent inflammation that damages the kidneys.[3,4] Lupus nephritis has a profound impact on the lives and outlook of those affected. 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, and the risk of mortality is high.[5] Lupus nephritis predominantly affects women, mostly women of colour and usually of childbearing age.[12] Currently, there is no cure.[5]

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.

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