Media & Investor Release

New England Journal of Medicine publishes new data for Roche's Gazyva/Gazyvaro which shows superiority over standard therapy in people with active lupus nephritis

- **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[1]**
- **Analysis showed consistent CRR benefit across patient subgroups, highlighting potential to treat a broad patient population with high unmet need[1]**
- **Gazyva/Gazyvaro is the only anti-CD20 monoclonal antibody in a phase III study to demonstrate CRR benefit,[1] which is associated with preservation of kidney function and delay or prevention of end-stage kidney disease**

Basel, 7 February 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that a detailed analysis of its phase III REGENCY trial of Gazyva®/Gazyvaro® (obinutuzumab) in people with active lupus nephritis (LN) was published in the *New England Journal of Medicine*.[1] The study demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of complete renal response (CRR), showing that 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). This was accompanied by clinically meaningful improvements in complement levels and reductions in anti-dsDNA, markers of disease activity and inflammation.[1]

Data were presented at the World Congress of Nephrology (WCN) 2025 and are being shared with health authorities, including the US Food and Drug Administration (FDA) and the European Medicines Agency.

"The fact that nearly half of lupus nephritis patients achieved a complete renal response, together with clinically meaningful benefits observed consistently across subgroups, indicates superior disease control with Gazyva/Gazyvaro compared to standard treatment alone," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Lupus nephritis disproportionately affects younger women, mostly women of colour, often leading to end-stage kidney disease. Our goal is to address this urgent need by providing a more effective treatment option."

"The positive REGENCY study results confirmed the findings of an earlier trial that administration of obinutuzumab, a therapy which targets B cells, benefitted patients with lupus nephritis more than standard treatment alone," said Dr. Richard Furie, the Marilyn and Barry Rubenstein Chair in Rheumatology and Chief of the Division of Rheumatology at Northwell Health, US. "It is also gratifying to see that patients who received obinutuzumab

were not only more likely to achieve the desired outcome but were able to taper corticosteroids at the same time."

Gazyva/Gazyvaro's safety profile was consistent with the well-characterised profile observed in its haematology-oncology indications. Key secondary endpoints showed that at week 76, patients who received Gazyva/Gazyvaro plus standard therapy were more likely to achieve CRR, with a successful reduction of corticosteroid use than standard therapy alone.[1] In addition, a higher proportion of patients showed improvement in proteinuric response when treated with Gazyva/Gazyvaro plus standard therapy versus standard therapy alone.[1] These endpoints are important indicators for achieving better disease control in lupus nephritis. As seen in pre-specified subgroup analyses, a benefit in CRR with Gazyva/Gazyvaro over standard therapy alone was consistent across all subgroups of patients, including indicators of more active lupus nephritis, Class IV lupus nephritis, concomitant Class V disease, higher baseline proteinuria levels, and/or greater serologic activity.[1]

Further results for key secondary endpoints can be found in the table below and additional post hoc analysis is ongoing.

Key secondary endpoints	Obinutuzumab (n=135) Response % (95% CI)	Placebo (n=136) Response % (95% CI)	Treatment Difference (95% CI)	*P* value
CRR with prednisone taper (prednisone ≤7.5 mg/day Week 64 through Week 76)	42.7 (34.3, 51.1)	30.9 (23.1, 38.7)	11.9 (0.6, 23.2)	0.0421
Proteinuric response at Week 76 (UPCR <0.8 g/g)	55.5 (47.1, 64.0)	41.9 (33.6, 50.2)	13.7 (2.0, 25.4)	0.0227
Change in eGFR from baseline to Week 76, adjusted mean	2.31 (2.71)	-1.54 (2.71)	3.84 (-1.83, 9.51)	0.1842
Death or renal-related events through Week 76	18.9 (12.1, 25.6)	35.6 (27.5, 43.8)	-16.83 (-27.4, -6.2)	0.0026*
ORR at Week 50	59.1 (50.8, 67.4)	50.7 (42.2, 59.2)	8.4 (-3.4, 20.1)	0.1670
Change in FACIT-F from baseline to Week 76, adjusted mean	1.8 (1.2)	3.1 (1.2)	-1.4 (-3.9, 1.2)	0.2991

*** Statistical significance cannot be claimed as endpoints earlier in the hierarchy were not met**

Lupus nephritis is a potentially life-threatening manifestation of an autoimmune disease that affects approximately 1.7 million people worldwide, predominantly women, mostly of colour and childbearing age.[2-5] 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]

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

2019.[7] 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, an autoimmune disease that commonly affects the kidneys and can lead to lupus nephritis.[8-11]

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 a 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; mean change in FACIT-F at week 76; death or renal-related events through week 76 and overall renal response at 50 weeks. Safety and tolerability were also assessed.

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.[12] In lupus nephritis, disease-causing B cells drive persistent inflammation that damages the kidneys.[13] We can target an underlying cause of lupus nephritis to help gain better control of the disease by depleting disease-causing B cells. 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.[12-14]

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 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 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.[6] Lupus nephritis predominantly affects women, mostly women of colour and usually of childbearing age.[5] Currently, there is no cure.[6]

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, childhood-onset idiopathic nephrotic syndrome and systemic lupus erythematosus (SLE), an autoimmune disease that can lead to lupus nephritis.

Our pipeline 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, RG6382, a CD19xCD3 T-cell engaging bispecific antibody being investigated in SLE, and P-CD19CD20-ALLO1, an allogeneic dual CAR-T therapy being investigated in SLE.

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.

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