Media & Investor Release

FDA accepts supplemental Biologics License Application for Roche's Columvi combination for people with relapsed or refractory diffuse large B-cell lymphoma

- **Application is based on data from the phase III STARGLO study where Columvi plus chemotherapy showed a statistically significant and clinically meaningful improvement in overall survival[1,2]**
- **This regimen could provide an off-the-shelf, fixed-duration treatment option for patients to start soon after diagnosis, which is important for those who are at high-risk of disease progression**
- **Improving survival outcomes is needed for people with an aggressive disease like relapsed or refractory DLBCL, especially those who aren't eligible for transplant[3]**

Basel, 5 December 2024 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the U.S. Food and Drug Administration (FDA) has accepted the company's supplemental Biologics License Application (sBLA) for Columvi® (glofitamab) in combination with gemcitabine and oxaliplatin (GemOx) for the treatment of people with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) who have received at least one prior line of therapy and are not candidates for autologous stem cell transplant. The FDA is expected to make a decision on approval by 20 July 2025.

The standard second-line therapy for R/R DLBCL patients has historically been high-dose chemotherapy followed by stem-cell transplant, however, not all patients are a candidate due to age or coexisting medical conditions. While newer therapies are becoming available, barriers remain for many and alternative treatment options are needed for these patients to improve survival outcomes.[3]

"For people with aggressive lymphomas like DLBCL, timely intervention with effective therapies can be crucial to reduce the risk of disease progression and improve long-term outcomes," said Levi Garraway, MD, PhD, Roche's Chief Medical Officer and Head of Global Product Development. "We are encouraged by the overall survival benefit seen with this Columvi combination and hope it can become an important treatment option for those who are in need of alternative therapies."

The sBLA is based on results from the phase III STARGLO study, which were presented at the European Hematology Association Congress earlier this year and recently published in *The Lancet*.[1,2] Data showed Columvi in combination with GemOx demonstrated a statistically significant and clinically meaningful overall survival (OS) improvement versus MabThera®/Rituxan® (rituximab) and GemOx (R-GemOx), making it the first CD20xCD3 bispecific antibody to show a survival benefit in DLBCL in a randomised phase III trial.[1,2] Safety

of the combination appeared consistent with the known safety profiles of the individual medicines.[1,2]

Data from the STARGLO study have been submitted to other health authorities around the world for approval consideration, including the European Medicines Agency.

Columvi is part of Roche's industry-leading CD20xCD3 bispecific antibody programme, which has seen more than 3,000 patients treated in clinical trials and more than 2,600 treated in clinical practice to date.[4] Columvi was the first fixed-duration bispecific antibody to receive accelerated approval by the U.S. FDA and conditional marketing authorisation in the EU as a monotherapy to treat people with R/R DLBCL after two or more lines of systemic therapy and is currently approved in more than 50 countries around the world.

As part of Roche's efforts to elevate treatment standards in the earlier stages of DLBCL, where there is the best opportunity to improve long-term outcomes and prevent relapse, Columvi is also being investigated in combination with Polivy® (polatuzumab vedotin), MabThera/Rituxan, cyclophosphamide, doxorubicin and prednisone (R-CHP) in previously untreated DLBCL in the phase III SKYGLO study.

About the STARGLO study[5]

The STARGLO study [GO41944; NCT04408638] is a phase III, multicentre, open-label, randomised study evaluating the efficacy and safety of Columvi® (glofitamab) in combination with gemcitabine plus oxaliplatin (GemOx) versus MabThera®/Rituxan® (rituximab) in combination with GemOx (R-GemOx) in patients with relapsed or refractory diffuse large B-cell lymphoma who have received at least one prior line of therapy and who are not candidates for autologous stem cell transplant, or who have received two or more prior lines of therapy. Preclinical research indicated an increased antitumour effect when combining Columvi with GemOx over GemOx alone, so the STARGLO study was initiated to further explore the potential complementary effects of the treatment combination. Outcome measures include overall survival (OS; primary endpoint), progression-free survival, complete response rate, objective response rate, duration of objective response (secondary endpoints), and safety and tolerability.

In the primary analysis (conducted after a median follow-up of 11.3 months) patients treated with Columvi plus GemOx lived significantly longer, with a 41% reduction in the risk of death (hazard ratio [HR]=0.59, 95% CI: 0.40-0.89, p=0.011) versus R-GemOx.[1,2] Median OS was not reached with the Columvi regimen versus nine months for R-GemOx.[1,2] Safety of the combination appeared consistent with the known safety profiles of the individual medicines.[1,2] Adverse event (AE) rates were higher with the Columvi combination versus R-GemOx, noting higher median number of cycles received with the Columvi combination (11 versus 4).[1,2] One of the most common AEs was cytokine release syndrome, which was generally low grade (Any

Grade: 44.2%, Grade 1: 31.4%, Grade 2: 10.5%, Grade 3: 2.3%) and occurred primarily in Cycle 1.[1,2]

STARGLO is intended as a confirmatory study to convert the accelerated approval of Columvi in the US and conditional marketing authorisation in the EU to full approvals for people with R/R DLBCL after two or more lines of systemic therapy based on the pivotal phase I/II NP30179 study [NCT03075696].

About Columvi® (glofitamab)

Columvi is a CD20xCD3 T-cell engaging bispecific antibody designed to target CD3 on the surface of T-cells and CD20 on the surface of B-cells. Columvi was designed with a novel 2:1 structural format. This T-cell engaging bispecific antibody is engineered to have one region that binds to CD3, a protein on T-cells, a type of immune cell, and two regions that bind to CD20, a protein on B-cells, which can be healthy or malignant. This dual-targeting brings the T-cell in close proximity to the B-cell, activating the release of cancer cell-killing proteins from the T-cell. Columvi is part of Roche's broad and industry-leading CD20xCD3 T-cell-engaging bispecific antibody clinical development programme that also includes Lunsumio® (mosunetuzumab), which aims to provide tailored treatment options that suit the diverse needs, preferences, and experiences of people with blood cancers and healthcare systems. Roche is investigating Columvi as a monotherapy and in combination with other medicines for the treatment of diffuse large B-cell lymphoma and mantle cell lymphoma.

About diffuse large B-cell lymphoma (DLBCL)

DLBCL is the most common form of non-Hodgkin lymphoma (NHL), accounting for about one in three cases of NHL.[6] DLBCL is an aggressive (fast-growing) type of NHL.[6] While it is generally responsive to treatment in the frontline, as many as 40% of people will relapse or have refractory disease, at which time salvage therapy options are limited and survival is short.[7] Improving treatments earlier in the course of the disease and providing much needed alternative options could help to improve long-term outcomes. Approximately 160,000 people worldwide are diagnosed with DLBCL each year.[6,8]

About Roche in haematology

Roche has been developing medicines for people with malignant and non-malignant blood diseases for more than 25 years; our experience and knowledge in this therapeutic area runs deep. Today, we are investing more than ever in our effort to bring innovative treatment options to patients across a wide range of haematologic diseases. Our approved medicines include MabThera®/Rituxan® (rituximab), Gazyva®/Gazyvaro® (obinutuzumab), Polivy® (polatuzumab vedotin), Venclexta®/Venclyxto® (venetoclax) in collaboration with AbbVie, Hemlibra® (emicizumab), PiaSky® (crovalimab), Lunsumio® (mosunetuzumab) and Columvi® (glofitamab). Our pipeline of investigational haematology medicines includes T-cell engaging bispecific antibody cevostamab, targeting both FcRH5 and CD3 and Tecentriq®

(atezolizumab). Our scientific expertise, combined with the breadth of our portfolio and pipeline, also provides a unique opportunity to develop combination regimens that aim to improve the lives of patients even further.

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.

References

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