Media & Investor Release

European Commission approves Roche's fixed-duration Columvi (glofitamab) for people with relapsed or refractory diffuse large B-cell lymphoma

- **Columvi is the first CD20xCD3 T-cell-engaging bispecific antibody available in Europe to treat the most common and aggressive form of lymphoma**
- **Approval is based on results from the phase I/II NP30179 study, where Columvi given as a fixed course induced early and long-lasting complete responses in people with heavily pre-treated or refractory diffuse large B-cell lymphoma[1]**
- **Columvi is given for a fixed period of time and made to be readily available, providing patients with a treatment end date and treatment-free period**

Basel, 11 July 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the European Commission (EC) has granted conditional marketing authorisation for Columvi® (glofitamab) for the treatment of adult patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. With this approval, Columvi is the first CD20xCD3 T-cell-engaging bispecific antibody available to treat people in Europe with the most common and aggressive form of lymphoma following multiple lines of therapy. Columvi has the potential to change the current standard of care in DLBCL. As well as inducing early and long-lasting responses in people with heavily pre-treated or refractory DLBCL, Columvi is designed to be given for a fixed period of time meaning that people have a target end date for their course of treatment and the possibility of a treatment-free period. It is also a chemotherapy-free treatment option that is off-the-shelf, meaning that people do not have to wait for cell collection and genetic engineering - a multistep process that can take several weeks - before starting treatment. This could be particularly important for patients who are at a high-risk of their disease progressing.

DLBCL is an aggressive (fast-growing) type of lymphoma and is one of the most prevalent types of blood cancer among adults.[2] Each year in Europe, an estimated 36,000 people are diagnosed with DLBCL.[3] While many patients with DLBCL are responsive to initial treatment, four out of ten are not cured with the current standard of care, frontline treatment, and the majority of patients who require subsequent lines of therapy have poor outcomes.[4,5]

"As pioneers in the development of innovative T-cell-engaging bispecific antibodies, we are delighted that we can now offer Columvi as the first approved treatment of its kind to people in Europe," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are confident that thanks to its off-the-shelf availability, fixed-duration regimen and durability, Columvi will positively transform the treatment experience for relapsed or refractory diffuse large B-cell lymphoma."

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"As the lead investigator for the NP30179 study, I have seen first-hand the early and long-lasting responses that Columvi can induce, when given to patients for a fixed period of time," said Michael Dickinson, M.D., Ph.D., principal study investigator and Associate Professor, Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Australia. "It is exciting that with this approval, patients in Europe with heavily pre-treated or refractory diffuse large B-cell lymphoma will now have a new, potentially practice-changing treatment option that will allow them time off of therapy to resume their routine activities, helping to alleviate some of the physical and emotional burdens caused by cancer treatment."

The approval is based on positive results from a pivotal cohort in the phase I/II NP30179 study, where Columvi given as a fixed course induced early and long-lasting responses in people with R/R DLBCL. Overall, 83.3% of patients were refractory to their most recent therapy, 90% were refractory to any previous line of therapy, and about one-third (35.2%) had received prior CAR T-cell therapy. Results showed that Columvi given as a fixed course, induced a complete response (CR; a disappearance of all signs of cancer) in 35.2% (n =38/108) of people, and 50% (n=54/108) achieved an overall response (OR; the combination of CR and partial response, a decrease in the amount of cancer in their body). Among those who achieved a CR, 74.6% (95% CI: 59.19-89.93) continued to experience a response at 12 months, while the median duration of CR was not reached. The median follow-up for duration of response (DOR) was 12.8 months. Median time to first CR was 42 days (95% CI: 41-47). The most common adverse events (AEs) were cytokine release syndrome (CRS; 64.3%), neutropenia (a reduction in white blood cells [37.7%]), anaemia (30.5%) and thrombocytopenia (low blood platelet count [24.7%]). CRS was generally low grade (Grade 1: 48.1%; Grade 2: 12.3%). One patient discontinued treatment due to CRS.[1]

Additional data from a larger cohort in the NP30179 study, published in the *New England Journal of Medicine* reinforce the durability of Columvi. Fixed-duration Columvi resulted in early and long-lasting responses in people with heavily pre-treated or refractory DLBCL, with 39.4% of patients (n=61/155) achieving a CR and a median DOR of 18.4 months. Median time to CR was 42 days (95% CI: 42-44), with the majority of responses reported at the first scheduled response assessment (approximately 1.4 months after the start of treatment). Half of patients (51.6%; n=80/155) achieved an OR. The most common AE was CRS, which was generally low grade (Grade 1: 47.4%; Grade 2: 11.7%) and occurred at initial doses. Columvi-related AEs leading to treatment discontinuation occurred in 3.2% of patients.[6]

The U.S. Food and Drug Administration (FDA) recently approved Columvi for the treatment of adult patients with R/R DLBCL not otherwise specified or large B-cell lymphoma (LBCL) arising from FL, after two or more lines of systemic therapy for the treatment of people with R/R large B cell lymphoma. Columvi is also approved in Canada for the treatment of adult patients with R/R DLBCL not otherwise specified, DLBCL arising from follicular lymphoma (FL), or primary mediastinal B-cell lymphoma, who have received two or more lines of systemic therapy and are

ineligible to receive or cannot receive CAR T-cell therapy or have previously received CAR T-cell therapy. Submissions to additional health authorities worldwide are ongoing.

Roche is continually building on its long-standing expertise in haematology by investigating innovative solutions that redefine treatment standards for patients and improve on existing standards of care. In a broad and industry-leading CD20xCD3 T-cell-engaging bispecific antibody clinical development programme, Roche is exploring the potential of both Columvi and Lunsumio® (mosunetuzumab) in earlier lines of treatment and in combination with other novel and chemotherapy-free agents, such as Polivy® (polatuzumab vedotin), with the goal of providing patients with long-lasting outcomes.

Roche continues to expand Columvi's clinical development programme, which includes the phase III STARGLO trial, evaluating Columvi in combination with gemcitabine and oxaliplatin (GemOx) versus rituximab in combination with GemOx in patients with second-line plus DLBCL who are ineligible for autologous stem cell transplant. Additional phase III studies are also planned, including in first-line DLBCL.

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. A clinical development programme for Columvi is ongoing, investigating the molecule as a monotherapy and in combination with other medicines for the treatment of people with B-cell non-Hodgkin lymphomas, including diffuse large B-cell lymphoma and other blood cancers.

About the NP30179 study

The NP30179 study [NCT03075696] is a phase I/II, multicentre, open-label, dose-escalation and expansion study evaluating the safety, efficacy and pharmacokinetics of Columvi® (glofitamab) in people with relapsed or refractory diffuse large B-cell lymphoma. Outcome measures include complete response rate by an independent review committee (primary endpoint), overall response rate, duration of response, progression-free survival, safety, and tolerability (secondary endpoints).

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.[2] DLBCL is an aggressive (fast-growing) type of NHL.[2] 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.[4,5] Improving treatments earlier in the course of the disease and providing needed alternative options could help to improve long-term outcomes. Each year in Europe, it is estimated that 36,000 people are diagnosed with DLBCL.[3]

About Roche in haematology

Roche has been developing medicines for people with malignant and non-malignant blood diseases for more than 20 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), Lunsumio® (mosunetuzumab) and Columvi® (glofitamab). Our pipeline of investigational haematology medicines includes a T-cell-engaging bispecific antibody cevostamab, targeting both FcRH5 and CD3; Tecentriq® (atezolizumab), a monoclonal antibody designed to bind with PD-L1 and crovalimab, an anti-C5 antibody engineered to optimise complement inhibition. 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.

In recognising our endeavour 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.

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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