

Roche presents new data from its bispecific antibody portfolio across a range of blood cancers

- **Latest data to be presented at ASH 2020 includes results in non-Hodgkin lymphoma and heavily pre-treated multiple myeloma**
- **Portfolio includes two CD20xCD3 bispecifics, mosunetuzumab and glofitamab, and first-of-its-kind FcRH5xCD3 bispecific antibody, cevostamab, building on Roche's legacy of more than 20 years in antibody development**

Basel, 08 December 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that new data on its investigational T-cell engaging bispecific antibodies, mosunetuzumab, glofitamab and cevostamab, were presented at the all-virtual 62nd American Society of Hematology (ASH) Annual Meeting and Exposition, from 5-8 December 2020, showing encouraging activity across multiple types of blood cancer. These antibodies work by binding to two different targets, on two different cells, simultaneously: one on the surface of cancer cells and one on the surface of immune cells called T-cells. This dual targeting approach activates a patient's existing T-cells to engage and eliminate target cancer cells, offering an innovative approach for the treatment of blood cancers including non-Hodgkin lymphoma (NHL) and multiple myeloma (MM); diseases where treatment options are currently limited, and resistance to, or relapse following, treatment is common. These bispecifics are just one of the novel 'off-the-shelf' technologies Roche is exploring, in its quest to improve patient outcomes.

"The data suggest that our novel bispecific antibodies have potential across multiple types of blood cancers, and supports broad exploration of these new immunotherapy approaches across different patient populations and treatment lines," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Lymphoma and multiple myeloma are challenging cancers to treat, especially when patients present with aggressive subtypes or experience multiple relapses, but 'off-the-shelf' therapies like these could provide new options that may potentially enable patients to be treated quickly."

Promising responses with mosunetuzumab and glofitamab in non-Hodgkin lymphoma

To date in clinical trials, Roche's two CD20xCD3 T-cell engaging bispecific antibodies, mosunetuzumab and glofitamab, have shown promising responses across multiple types of NHL, including relapsed or refractory (R/R) follicular lymphoma (FL) and diffuse large B-cell lymphoma (DLBCL). This is reinforced by the latest results from the phase I/Ib GO29781 study in R/R FL, which show that 51.6% of patients (n=32/62) achieved a complete response (CR) when treated with mosunetuzumab.[1] High response rates also continue to be seen with glofitamab. For example, new data from the phase I/Ib NP30179 study in R/R NHL show a CR rate of 53.6% in aggressive NHL (n=15/28).[2] Additionally, both bispecific antibodies have proven to have manageable safety profiles. One of the most common adverse events (AEs) observed with bispecific antibodies is cytokine release syndrome (CRS), which involves the over activation of immune cells, and is a known risk associated with immunotherapies that activate the body's own immune system. [3] Based on

studies so far, CRS events with mosunetuzumab and glofitamab are largely low-grade (mainly Grade 1-2), occur in early treatment cycles, and are mostly reversible.[1,2]

Beyond the R/R setting, mosunetuzumab and glofitamab are also being investigated in earlier treatment lines, including first-line DLBCL. Initial data with single-agent mosunetuzumab in the phase I/II GO40554 study, show a CR rate of 45.5% (n=10/22) in elderly or unfit patients who are unable to tolerate full-dose immunochemotherapy. Additionally, when mosunetuzumab was combined with chemotherapy in the phase Ib/II GO40515 study, the CR rate was 79.4% (n=27/34). These are the first bispecific antibody studies in 1L DLBCL to report data, and while early, these results support the potential for mosunetuzumab to provide a new, much-needed treatment option for these patients.[4,5]

Robust development programmes are ongoing for mosunetuzumab and glofitamab, investigating the treatments as monotherapies and in combination with other molecules, as well as more convenient forms of administration such as subcutaneous administration, with several phase III trials planned in the near future.

Encouraging activity with cevostamab in heavily pre-treated patients with multiple myeloma

The third of Roche's bispecific antibodies in malignant haematology, and latest addition to its pipeline, is cevostamab, a first-of-its kind FcRH5xCD3 bispecific antibody targeting FcRH5 on myeloma cells and CD3 on T-cells. FcRH5 is a unique and differentiated target and is expressed on nearly 100% of myeloma cells. Cevostamab is currently being investigated in the ongoing phase I GO39775 dose-escalation and expansion study in heavily pre-treated patients with MM (with a median of six prior lines of therapy); a population for whom new treatment options are urgently needed.

First clinical safety and efficacy data presented at ASH, showed an encouraging overall response rate of 53% (n=18/34) at active doses. Notably, responses were seen in high-risk patients, including those refractory to five different classes of drug (penta-drug refractory) and those with prior exposure to anti-BCMA therapy. Safety of cevostamab was manageable with the most common treatment-related AE being CRS (76%). The majority of CRS events were Grade 1–2 (Grade 1; 34% and Grade 2; 40%) and occurred in cycle 1. One patient experienced Grade 3 CRS (2%) and no Grade 4 or 5 CRS events were observed.[6] Additional biomarker analyses presented at the congress are also helping to further understand the potential of cevostamab in MM and inform its future development, including strategies to mitigate the risk of CRS.[7]

Roche is excited about the ongoing development of its three bispecific antibodies in malignant haematology and eager to understand their full potential in patients with blood cancers.

About Roche's CD20xCD3 bispecific antibodies

Roche is currently developing two T-cell engaging bispecific antibodies, mosunetuzumab and glofitamab, designed to target CD20 on the surface of B-cells and CD3 on the surface of T-cells. This dual targeting activates and re-directs a patient's existing T-cells to engage and eliminate target B-cells by releasing cytotoxic proteins into the B-cells. Mosunetuzumab and glofitamab differ in their structures, and both are

being developed by Roche as part of our ongoing haematology research and development strategy to explore multiple bispecific formats, to identify those that may maximise clinical benefits for patients. Mosunetuzumab has a structure similar to that of a natural human antibody in that it has two 'Fab' regions, but is different from naturally-occurring antibodies in that one 'Fab' region targets CD20 and the other 'Fab' region targets CD3. Glofitamab is based on a novel structural format which we call '2:1', which refers to the structure of the antibody. It is engineered to have two 'Fab' regions which bind to CD20, and one 'Fab' region which binds to CD3. The clinical development programmes for mosunetuzumab and glofitamab include ongoing investigations of these molecules as monotherapies and in combination with other medicines, for the treatment of people with CD20-positive B-cell non-Hodgkin lymphomas, including diffuse large B-cell lymphoma and follicular lymphoma, and other blood cancers.

About cevostamab (FcRH5xCD3 bispecific antibody)

Cevostamab (BFCR4350A) is an FcRH5xCD3 T-cell engaging bispecific antibody designed to target FcRH5 on myeloma cells and CD3 on T-cells. FcRH5 is a unique and differentiated target, expressed on nearly 100% of myeloma cells.[8] Cevostamab has a structure similar to that of a natural human antibody in that it has two 'Fab' regions, but is different from naturally-occurring antibodies in that one 'Fab' region targets FcRH5 and the other 'Fab' region targets CD3. This dual targeting activates and re-directs a patient's existing T-cells to engage and eliminate target FcRH5-expressing myeloma cells by releasing cytotoxic proteins into the myeloma cells.

About the GO29781 study

The GO29781 study [[NCT02500407](#)] is a phase I/Ib, multicentre, open-label, dose-escalation study evaluating the safety and pharmacokinetics of mosunetuzumab in people with relapsed or refractory B-cell non-Hodgkin lymphoma. Outcome measures include best objective response rate by revised International Working Group criteria, maximum tolerated dose and tolerability.

About the GO40554 study

The GO40554 study [[NCT03677154](#)] is a phase I/II, multicentre, open-label, randomised study evaluating the safety, pharmacokinetics, and preliminary efficacy of mosunetuzumab following first-line diffuse large B-cell lymphoma (DLBCL) immunochemotherapy, or in participants with previously untreated DLBCL who are unable to tolerate full-dose, first-line immunochemotherapy. Primary objectives include complete response rate at time of primary response assessment, as measured by PET-CT, according to Lugano 2014 Response Criteria, and safety. Secondary objectives include assessment of pharmacokinetics, objective response rate, duration of response and progression-free survival.

About the NP30179 study

The NP30179 study [[NCT03075696](#)] is a phase I/Ib, multicentre, open-label, dose-escalation study, evaluating the efficacy, safety, tolerability and pharmacokinetics of glofitamab. In this study, glofitamab is assessed as a single-agent and in combination with Gazyva®/Gazyvaro® (obinutuzumab), following pre-treatment with a one-time, fixed-dose of Gazyva/Gazyvaro, in people with relapsed or refractory B-cell non-

Hodgkin lymphoma. Outcome measures include overall response rate, complete response rate per Lugano 2014 criteria, maximum tolerated dose and tolerability.

About the GO39775 study

The GO39775 study [[NCT03275103](#)] is a phase I, multicentre trial evaluating the safety and activity of cevostamab (BFCR4350A) monotherapy in adult patients with relapsed or refractory multiple myeloma for which no established therapies are available, appropriate or tolerable. Prior exposure to CAR T-cells, T-cell engaging bispecific antibodies, bispecific T-cell engagers (BiTEs) and antibody-drug conjugates, including those targeting BCMA, is allowed. Primary objectives are to evaluate safety (including the maximum tolerated dose and dose-limiting toxicities) and to identify a recommended phase II dose. Secondary objectives include assessment of pharmacokinetics, activity, immunogenicity and pharmacodynamic biomarkers.

About Roche in haematology

Roche has been developing medicines for people with malignant and non-malignant blood diseases for over 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, and Hemlibra® (emicizumab). Our pipeline of investigational haematology medicines includes T-cell engaging bispecific antibodies, glofitamab and mosunetuzumab, targeting both CD20 and CD3, and 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

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving

antibiotics, antimalarials and cancer medicines. Moreover, for the twelfth consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 billion. 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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