Roche presents latest advances with immunotherapies in non-Hodgkin lymphoma

- **Data for investigational CD20xCD3 bispecific antibodies and new combination regimens with Polivy showed enhanced clinical benefits for people with non-Hodgkin lymphoma in early studies**

Basel, 4 June 2021 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that new data on its investigational CD20xCD3 T-cell engaging bispecific antibodies, mosunetuzumab and glofitamab, and its first-in-class anti-CD79b antibody-drug conjugate, Polivy® (polatuzumab vedotin), in non-Hodgkin lymphoma (NHL) will be presented at the 2021 ASCO Annual Meeting from 4-8 June 2021.

"People with difficult-to-treat blood cancers such as non-Hodgkin lymphoma still need more options to help improve outcomes," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are encouraged by promising data from our emerging T-cell engaging bispecific antibodies, mosunetuzumab and glofitamab, and the antibody-drug conjugate, Polivy, that demonstrate the potential of these novel immunotherapeutic approaches for various groups of patients."

While approximately 500,000 people worldwide are diagnosed with NHL each year, treatment options are currently limited and resistance to existing therapies or relapse following treatment is common.[1] The most prevalent form of NHL, accounting for about 40% of newly diagnosed NHL cases, is an aggressive form called diffuse large B-cell lymphoma (DLBCL), that comes with a life expectancy of weeks or months if left untreated.[2,3]

In clinical trials to date, the investigational CD20xCD3 T-cell engaging bispecific antibodies, mosunetuzumab and glofitamab, have shown promising responses across multiple types of NHL, including relapsed or refractory (R/R) DLBCL and follicular lymphoma (FL). Pivotal data for these medicines are expected this year and Roche is targeting a regulatory filing for mosunetuzumab in FL by the end of 2021, following its U.S. Food and Drug Administration Breakthrough Therapy Designation granted in June 2020. Key data on mosunetuzumab and glofitamab to be presented at the meeting include:

- Phase I NP30179 study investigating step-up dosing of glofitamab in heavily pre-treated R/R NHL, showed high, ongoing complete responses (CRs) and an acceptable safety profile. After a median follow-up of 6.3 months, results showed that glofitamab achieved a complete metabolic response rate, defined as the disappearance of metabolic tumour activity, of 71.4% in patients with aggressive (fast-growing) NHL. The most common adverse events (AEs) were cytokine release syndrome (CRS) (63.5%), neutropenia (38.5%), and pyrexia (32.7%); CRS events were mostly low grade and confined to the first cycle of treatment.[4]
- Phase I/II GO40516 study of mosunetuzumab in combination with Polivy in R/R NHL showed promising efficacy and an acceptable safety profile. The regimen achieved a CR of 54.5% in all patients. Eighty six percent of patients evaluated had aggressive NHL, and these patients achieved a

CR rate of 47.4%. The most frequent treatment-related AEs were neutropenia (45.4%), fatigue, nausea, and diarrhoea (all 36.4%) and CRS (9.1%; all Grade 1).[5]

Broad development programmes are ongoing for mosunetuzumab and glofitamab, including the phase III GO42909 trial investigating mosunetuzumab plus lenalidomide versus MabThera®/Rituxan® (rituximab) plus lenalidomide in R/R FL, which will soon be enrolling patients. For glofitamab, the phase III GO41944 open-label, randomised trial designed to evaluate the safety and efficacy of glofitamab plus gemcitabine and oxaliplatin (glofit-GemOx) versus MabThera/Rituxan plus GemOx in patients with R/R DLBCL, is also ongoing.

Roche is committed to pursuing treatment solutions that can be tailored to meet the various needs of both people living with NHL and healthcare professionals. Polivy is already a treatment option for people with R/R DLBCL and continues to show potential in multiple combinations. Key data at the meeting include:

- New triplet combination of Polivy with MabThera/Rituxan and lenalidomide, which demonstrated promising activity in difficult-to-treat R/R DLBCL, based on results from the phase Ib/II GO29834 study. With a median follow-up of 9.7 months, median overall survival was 10.9 months (95% CI: 7.4–NE) and median progression-free survival was 6.3 months (95% CI: 4.5–9.7) in patients treated with the triplet. The most commonly reported Grade 3-4 AEs were neutropenia (58.0%), thrombocytopenia (14.0%), infections (14.0%) and anaemia (11.0%).[6]

As a leader in haematology development, Roche will continue to follow the science to expand and improve upon treatment options for healthcare providers and people with difficult-to-treat blood cancers.

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About Roche's investigational bispecifics in haematology
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 redirects 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 strategy to explore multiple bispecific formats, to identify those that maximise potential 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 called '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 (NHL), including diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL).

About Polivy® (polatuzumab vedotin)
Polivy is a first-in-class anti-CD79b antibody-drug conjugate (ADC). The CD79b protein is expressed specifically in the majority of B-cells, an immune cell impacted in some types of NHL, making it a promising target for the development of new therapies.[7,8] Polivy binds to CD79b and destroys these B-cells through the delivery of an anti-cancer agent, which is thought to minimise the effects on normal cells.[9,10] Polivy is being developed by Roche using Seagen ADC technology and is currently being investigated for the treatment of several types of NHL. Polivy is marketed in the US by Genentech as Polivy (polatuzumab vedotin-piiq), with piiq as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the U.S. Food and Drug Administration.

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 (R/R) B-cell NHL. Outcome measures include overall response rate, complete response rate per Lugano 2014 criteria, maximum tolerated dose and tolerability.

About the GO40516 study
The GO40516 study [NCT03671018] is a phase I/II, multicentre, open-label study, evaluating the efficacy, safety, tolerability and pharmacokinetics of mosunetuzumab in combination with Polivy in people with B-cell NHL. It consists of a dose finding portion followed by an expansion phase for second line or later (2L+) participants with R/R DLBCL and 2L+ R/R FL. Outcome measures include best overall response rate, maximum tolerated dose and tolerability.

About the GO29834 study
The GO29834 study [NCT02600897] is a phase Ib/II, multicentre, open-label study, evaluating the efficacy and safety of Polivy with MabThera® /Rituxan® (rituximab) and lenalidomide in R/R DLBCL. Outcome measures include complete response and tolerability.

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, Gazyva/Gazyvaro, Polivy, 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 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, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

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. In recent years, Roche has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

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 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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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