Roche announces CHMP recommendation for EU approval of Venclyxto plus Gazyvaro for people with untreated chronic lymphocytic leukaemia

- **Positive CHMP recommendation based on pivotal phase III CLL14 study showing that fixed duration of treatment with Venclyxto plus Gazyvaro reduced risk of disease progression or death by 65% compared to current standard-of-care**
- **Venclyxto in combination with Gazyvaro represents a potential new, fixed 12-month, chemotherapy-free option for people with previously untreated chronic lymphocytic leukaemia**

Basel, 31 January 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for Venclyxto® (venetoclax) in combination with Gazyvaro® (obinutuzumab) for the treatment of adults with previously untreated chronic lymphocytic leukaemia (CLL).

"Despite advances in treating chronic lymphocytic leukaemia, many patients cannot tolerate the side effects of chemotherapy-containing regimens," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We're pleased that the CHMP has recognised the potential of Venclyxto plus Gazyvaro as a fixed-duration, chemotherapy-free treatment option for patients with this malignancy, which is the most common type of leukaemia in adults."

The positive CHMP opinion is based on results from the pivotal phase III CLL14 study, which evaluated the combination of 12-month, fixed-duration Venclyxto plus Gazyvaro compared to Gazyvaro plus chlorambucil in adults with previously untreated CLL who had co-existing medical conditions. Results showed that the combination of Venclyxto plus Gazyvaro led to a 65% reduction in the risk of disease worsening or death (progression-free survival [PFS], as assessed by investigators) compared to Gazyvaro plus chlorambucil, a current standard-of-care for CLL (HR=0.35; 95% CI 0.23-0.53; p<0.0001). When PFS was assessed by an independent review committee, this finding was confirmed. Venclyxto plus Gazyvaro showed high response rates compared to Gazyvaro plus chlorambucil, including higher rates of minimal residual disease (MRD)-negativity, meaning that no cancer can be detected using a specific and highly sensitive test. In peripheral blood, MRD-negativity rates were 76% for Venclyxto plus Gazyvaro versus 35% for Gazyvaro plus chlorambucil, and in bone marrow MRD-negativity rates were 57% versus 17%, respectively. The most commonly reported adverse events in people treated with Venclyxto plus Gazyvaro were low white blood cell count (neutropenia), diarrhoea and upper respiratory tract infection.

Previously, the European Commission has approved Venclyxto in combination with MabThera® (rituximab) for the treatment of adults with CLL who have received at least one prior therapy. Based on this positive CHMP recommendation, a final decision regarding the approval of Venclyxto in previously untreated CLL is expected from the European Commission in the near future. The US Food and Drug Administration (FDA) approved Venclexta® in combination with Gazyva® for the treatment of people with previously untreated CLL with co-existing medical conditions in May 2019. This followed rapid review and approval of the

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supplemental New Drug Application under the FDA's Real-Time Oncology Review and Assessment Aid pilot programmes, the former of which explores a more efficient review process to ensure safe and effective treatments are available to patients as early as possible. Additional submissions of the data to health authorities around the world are ongoing.

Venclexta/Venclyxto is being developed by AbbVie and Roche. It is jointly commercialised by AbbVie and Genentech, a member of the Roche Group, in the US, under the brand name Venclexta, and commercialised by AbbVie outside of the US.

About the CLL14 study [1]
CLL14 (NCT02242942) is a randomised phase III study evaluating the combination of fixed-duration Venclyxto plus Gazyvaro compared to Gazyvaro plus chlorambucil in patients with previously untreated chronic lymphocytic leukaemia (CLL) and co-existing medical conditions. 432 patients with previously untreated CLL were randomly assigned to receive either a 12-month duration of Venclyxto alongside six-month duration of Gazyvaro (Arm A) or six-month duration of Gazyvaro alongside 12-month duration of chlorambucil (Arm B). Arm A started with an initial dosing of Gazyvaro followed by a five-week Venclyxto dose ramp-up to help reduce the risk of tumour burden. The primary endpoint of the study is investigator-assessed (INV) progression-free survival (PFS). Secondary endpoints include PFS assessed by independent review committee (IRC), minimal residual disease (MRD) status, overall response rate (ORR), complete response (CR, with or without complete blood count recovery), overall survival, duration of response, event-free survival, time to next CLL treatment, and safety. The CLL14 study is being conducted in cooperation with the German CLL Study Group, headed by Michael Hallek, MD, University of Cologne.

About Venclyxto (venetoclax)
Venclyxto is a first-in-class targeted medicine designed to selectively bind and inhibit the B-cell lymphoma-2 (BCL-2) protein. In some blood cancers and other tumours, BCL-2 builds up and prevents cancer cells from dying or self-destructing, a process called apoptosis. Venclyxto blocks the BCL-2 protein and works to restore the process of apoptosis.

Venclexta/Venclyxto is being developed by AbbVie and Roche. It is jointly commercialised by AbbVie and Genentech, a member of the Roche Group, in the US, under the brand name Venclexta, and commercialised by AbbVie outside of the US. Together, the companies are committed to research with Venclexta/Venclyxto, which is currently being studied in clinical trials across several types of blood and other cancers.

In the US, Venclexta has been granted five Breakthrough Therapy Designations by the US Food and Drug Administration: one for previously untreated chronic lymphocytic leukaemia (CLL), two for relapsed or refractory CLL and two for previously untreated acute myeloid leukaemia.

About Gazyvaro (obinutuzumab)
Gazyvaro is an engineered monoclonal antibody designed to attach to CD20, a protein expressed on certain B-cells, but not on stem cells or plasma cells. Gazyvaro is designed to attack and destroy targeted B-cells both directly and together with the body's immune system. Gazyvaro is marketed as Gazyva in the US.

Gazyva/Gazyvaro is currently approved in more than 90 countries in combination with chlorambucil for people with previously untreated chronic lymphocytic leukaemia, in more than 80 countries in combination with bendamustine for people with certain types of previously treated follicular lymphoma and in more than 70 countries in combination with chemotherapy for previously untreated follicular lymphoma.

Additional combination studies investigating Gazyvaro with other approved or investigational medicines, including cancer immunotherapies and small molecule inhibitors, are underway across a range of blood cancers.

About chronic lymphocytic leukaemia
Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in the Western world.[2] CLL mainly affects men and the median age at diagnosis is about 70 years.[3] Worldwide, the incidence of all leukaemias is estimated to be over 400,000, with an incidence of over 100,000 in Europe.[4] CLL is estimated to affect around one-third of all people newly diagnosed with leukaemia.[2]

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 idasanutlin, a small molecule which inhibits the interaction of MDM2 with p53; T-cell engaging bispecific antibodies targeting both CD20 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 eleventh 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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