Media Release

New data demonstrate the continued clinical benefit of fixed-duration, chemotherapy-free Venclexta/Venclyxto-based treatments in chronic lymphocytic leukaemia

- **In an updated analysis of the CLL14 study, Venclexta/Venclyxto plus Gazyva/Gazyvaro achieved remissions that were sustained over time in people with previously untreated chronic lymphocytic leukaemia**
- **At four-year follow-up of the MURANO study, Venclexta/Venclyxto plus MabThera/Rituxan continued to reduce disease progression compared to a standard-of-care therapy in previously treated chronic lymphocytic leukaemia**
- **Data presented on both studies include results on minimal residual disease, which is currently emerging as a potential surrogate endpoint**

Basel, 8 December 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced updated data from two pivotal phase III Venclexta®/Venclyxto® (venetoclax) studies (MURANO and CLL14) that highlight Venclexta/Venclyxto combination treatments as chemotherapy-free, fixed-duration options that achieve minimal residual disease (MRD)-negativity, in people with chronic lymphocytic leukaemia (CLL). These data and others from the Venclexta/Venclyxto clinical development programme will be featured in more than 50 abstracts at the 61st American Society of Hematology (ASH) Annual Meeting.

"Venclexta/Venclyxto plus anti-CD20 monoclonal antibody-based regimens continue to demonstrate improved long-term outcomes for people with chronic lymphocytic leukaemia," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "These results reinforce the sustained clinical benefits observed in patients with this common type of blood cancer, after completing this fixed-duration, chemotherapy-free treatment."

The pivotal phase III CLL14 study evaluated the combination of Venclexta/Venclyxto plus Gazyva®/Gazyvaro® (obinutuzumab) in people with previously untreated CLL, who had co-existing medical conditions. At a median follow-up of more than three years (39.57 months), when all patients had been off therapy for a minimum of two years, Venclexta/Venclyxto plus Gazyva/Gazyvaro showed high response rates, including MRD-negativity. Specifically:

- Higher rates of MRD-negativity in peripheral blood (76% vs. 35%; p<0.001) and bone marrow (57% vs. 17; p<0.001%) were observed at the end of treatment in people treated with Venclexta/Venclyxto plus Gazyva/Gazyvaro versus Gazyva/Gazyvaro plus chlorambucil, respectively. MRD-negativity indicates that no cancer can be detected using a specific, highly sensitive test, and was defined as less than one CLL cell in 10,000 white blood cells.
- MRD-negativity was observed in 42 % of people treated with Venclexta/Venclyxto plus Gazyva/Gazyvaro who achieved a complete response (CR) in the peripheral blood, and 14% of people treated with Gazyva/Gazyvaro plus chlorambucil (p<0.001). In bone marrow, MRD-negativity was observed in 34% of people who achieved a complete response with

Venclexta/Venclyxto plus Gazyva/Gazyvaro and 11% of people treated with Gazyva/Gazyvaro plus chlorambucil ($p<0.001$).

- At this updated analysis, the fixed-duration, chemotherapy-free combination of Venclexta/Venclyxto plus Gazyva/Gazyvaro reduced the risk of disease worsening or death by 69% compared to Gazyva/Gazyvaro plus chlorambucil (PFS, as assessed by investigator; HR=0.31; 95% CI 0.22-0.44; $p<0.0001$).
- The most common Grade 3-4 adverse events (AEs) in people treated with Venclexta/Venclyxto plus Gazyva/Gazyvaro were blood and lymphatic system disorders, and infections.
- These data were presented on Saturday, December 7, 2019 at 08:45 ET in an oral session (Abstract #36).

The pivotal phase III MURANO study evaluated the combination of Venclexta/Venclyxto plus MabThera®/Rituxan® (rituximab) in relapsed or refractory (R/R) CLL. Four-year, follow-up data from the study showed sustained OS and PFS benefits with Venclexta/Venclyxto plus MabThera/Rituxan compared to bendamustine plus MabThera/Rituxan (BR). No new safety events were reported in the study. Specifically:

- Results showed that Venclexta/Venclyxto plus MabThera/Rituxan significantly reduced the risk of disease progression or death by 81% (HR=0.19; 95% CI: 0.14, 0.25; $p<0.0001$) compared to BR, with four-year PFS estimates of 57.3% (95 % CI: 49.4, 65.3) vs. 4.6% (95% CI: 0.1, 9.2), respectively.
- Venclexta/Venclyxto plus MabThera/Rituxan also reduced the risk of death by 59% (HR=0.41; 95% CI: 0.26, 0.65; $p<0.0001$), compared to BR, with the Venclexta/Venclyxto plus MabThera/Rituxan treatment arm demonstrating greater sustained OS compared to the BR arm, with four-year OS rates of 85.3% vs. 66.8%, respectively.
- Venclexta/Venclyxto plus MabThera/Rituxan showed that people who achieved MRD-negativity showed an improvement in PFS at the end of treatment.
- No new safety signals were identified with the combination in this extended follow-up. Common grade 3-4 adverse events with Venclexta/Venclyxto plus MabThera/Rituxan compared to BR, respectively, were low white blood cell count (58.8% vs. 39.9%), anaemia (11.3% vs 13.8%) and low platelet count (5.7% vs 10.1%).
- Results from the MURANO study were the basis of regulatory approvals for Venclexta/Venclyxto plus MabThera/Rituxan as a treatment option for people with R/R CLL around the world.
- These data will be presented in an oral session on Sunday, December 8, 2019 at 07:30 ET (Abstract #355).

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 and commercialised by AbbVie outside of the US.

About the CLL14 study

CLL14 (NCT02242942) is a randomised phase III study evaluating the combination of fixed-duration Venclexta/Venclyxto (venetoclax) plus Gazyva/Gazyvaro (obinutuzumab) compared to Gazyva/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 Venclexta/Venclyxto alongside six-month duration of Gazyva/Gazyvaro (Arm A) or six-month duration of Gazyva/Gazyvaro alongside 12-month duration of chlorambucil (Arm B). Arm

A started with an initial dosing of Gazyva/Gazyvaro followed by a five-week Venclexta/Venclyxto dose ramp-up to help reduce the risk of tumour burden. The primary endpoint of the study is investigator-assessed progression-free survival (PFS). Secondary endpoints include PFS assessed by independent review committee, minimal residual disease status, overall response rate, complete response (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 the MURANO study
MURANO (NCT02005471) is a phase III open-label, international, multicentre, randomised study evaluating the efficacy and safety of fixed duration Venclexta/Venclyxto (venetoclax) in combination with MabThera/Rituxan (rituximab) compared to bendamustine in combination with MabThera/Rituxan (BR). All treatments were of fixed duration. Following a five-week dose ramp-up schedule for Venclexta/Venclyxto, patients on the Venclexta/Venclyxto plus MabThera/Rituxan arm received six cycles of Venclexta/Venclyxto plus MabThera/Rituxan followed by Venclexta/Venclyxto monotherapy for up to two years total. Patients on the BR arm received six cycles of BR. The study included 389 patients with chronic lymphocytic leukaemia, with or without 17p deletion, who had been previously treated with at least one line of therapy. Patients were randomly assigned in a 1:1 ratio to receive either Venclexta/Venclyxto plus MabThera/Rituxan or BR. The primary endpoint of the study was progression-free survival. Secondary endpoints included overall survival, overall response rate and complete response rate (with or without complete blood count recovery).

About chronic lymphocytic leukaemia
Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in the Western world.[1] CLL mainly affects men and the median age at diagnosis is about 70 years.[2] Worldwide, the incidence of all leukaemias is estimated to be over 400,000 [3] and CLL is estimated to affect around one-third of all people newly diagnosed with leukaemia.[1]

About Venclexta/Venclyxto (venetoclax)
Venclexta/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. Venclexta/Venclyxto blocks the BCL-2 protein and works to restore the process of apoptosis.

Venclexta/Venclyxto is being developed by AbbVie and Genentech, a member of the Roche Group. It is jointly commercialised by the companies in the United States and commercialised by AbbVie outside of the United States. 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 United States, Venclexta has been granted five Breakthrough Therapy Designations by the US Food and Drug Administration: one for previously untreated CLL, two for relapsed or refractory CLL and two for previously untreated acute myeloid leukaemia.

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 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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.

References

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