Media Release

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Roche announces phase III data showing Venclexta/Venclyxto plus MabThera/Rituxan reduced the risk of disease progression or death by 83% compared to a standard of care regimen in previously treated chronic lymphocytic leukaemia

- **This chemotherapy-free combination showed improvements across multiple efficacy measures compared to bendamustine plus MabThera/Rituxan in the pivotal MURANO trial**
- **Results will be presented during the Late-Breaking Abstracts Session at the 59th American Society of Hematology Annual Meeting**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced the first results from the pivotal phase III MURANO study evaluating Venclexta™/Venclyxto™ (venetoclax) plus MabThera®/Rituxan® (rituximab) compared to bendamustine plus MabThera®/Rituxan® (BR) for the treatment of people with relapsed or refractory chronic lymphocytic leukaemia (CLL). The results showed that a fixed duration of treatment with Venclexta/Venclyxto plus MabThera/Rituxan significantly reduced the risk of disease progression or death (progression-free survival; PFS, as assessed by investigator) by 83% compared with BR (HR=0.17; 95% CI 0.11-0.25; p<0.0001). No new safety signals were observed. 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 United States and commercialised by AbbVie outside of the United States.

"The MURANO study results indicate that Venclexta/Venclyxto plus MabThera/Rituxan has the potential to provide an important new chemotherapy-free option for people with previously treated chronic lymphocytic leukaemia," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "We are particularly encouraged by the magnitude of benefit observed across key efficacy measures compared to a current standard of care, and we look forward to discussing these results with health authorities."

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Results from the study were featured in the official press programme of the 59th American Society of Hematology (ASH) Annual Meeting in Atlanta on Monday, 11 December, and will be presented during the Late-Breaking Abstracts Session on Tuesday, 12 December, at 7.45am EST by John F. Seymour, MD, Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Australia (Abstract #LBA-2).

Data from the MURANO study will be submitted to global health authorities, including the US Food and Drug Administration (FDA), which has granted Breakthrough Therapy Designation for Venclexta in combination with Rituxan for the treatment of relapsed or refractory CLL based on promising results from the phase Ib M13-365 study.

Venclexta was granted accelerated approval by the FDA in April 2016 for the treatment of people with CLL with 17p deletion, as detected by an FDA approved test, who have received at least one prior therapy. The MURANO study is part of the company's commitment in the United States to convert the current accelerated approval of Venclexta to a full approval.

A robust clinical development programme for Venclexta/Venclyxto is ongoing, and additional results across multiple blood cancers including acute myeloid leukaemia (AML) and multiple myeloma (MM) were also presented at the ASH Annual Meeting.

About the MURANO Study

MURANO (NCT02005471) is a phase III open-label, international, multicentre, randomised study evaluating the efficacy and safety of Venclexta/Venclyxto in combination with MabThera/Rituxan compared to bendamustine in combination with MabThera/Rituxan (BR). All treatments were of fixed duration. The study included 389 patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) who had been previously treated with at least one, but not more than three, lines of therapy. Patients were randomly assigned in a 1:1 ratio to receive either Venclexta/Venclyxto plus MabThera/Rituxan (Arm A) or BR (Arm B). The primary endpoint of the study is investigator-assessed progression-free survival (PFS). Secondary endpoints include PFS assessed by independent review committee (IRC), overall response rate (ORR), complete response rate (with or without complete blood count recovery, CR/CRi), overall survival (OS), minimal residual disease (MRD) status, duration of response, event-free survival and time to next CLL treatment.

The results showed:

- Patients in the study who received Venclexta/Venclyxto plus MabThera/Rituxan lived significantly longer without their disease worsening (PFS, as assessed by investigator) compared to those who received BR (HR=0.17; 95% CI, 0.11-0.25; p<0.0001; median PFS: not reached vs. 17.0 months, respectively).
    - At two years, 84.9% of patients in the Venclexta/Venclyxto plus MabThera/Rituxan arm had not experienced disease progression, compared to 36.3% of patients in the BR arm.
    - Consistent benefit was observed in all patient subgroups for Venclexta/Venclyxto plus MabThera/Rituxan compared to BR, including high-risk and low-risk groups.
    - IRC assessment was consistent; as assessed by IRC, Venclexta/Venclyxto plus MabThera/Rituxan reduced the risk of disease progression or death by 81% compared to BR (HR=0.19; 95% CI 0.13, 0.28; p<0.0001).
- Clinical benefit observed for Venclexta/Venclyxto plus MabThera/Rituxan compared to BR was consistent across key secondary endpoints, including OS (HR=0.48, 95% CI 0.25-0.90; medians not yet reached), ORR as assessed by investigator (93.3% vs. 67.7%), CR/CRi as assessed by investigator (26.8% vs. 8.2%). These results were not statistically significant. In addition, higher rates of MRD-negativity at any time were observed with Venclexta/Venclyxto plus MabThera/Rituxan compared to BR (83.5% vs. 23.1%). MRD negativity was defined as less than one CLL cell in 10,000 leukocytes.
- No new safety signals were observed with the treatment combination of Venclexta/Venclyxto plus MabThera/Rituxan. The most common Grade 3-4 adverse events with Venclexta/Venclyxto plus MabThera/Rituxan compared to BR, respectively, were low white blood cell count (57.7% vs. 38.8%), low red blood cell count (10.8% vs. 13.8%), low platelet count (5.7% vs. 10.1%), low white blood cell count with fever (3.6% vs. 9.6%), pneumonia (5.2% vs. 8.0%) and infusion reactions (1.5% vs. 5.3%).

About Venclexta/Venclyxto

Venclexta/Venclyxto is a small molecule designed to selectively bind and inhibit the BCL-2 protein, which plays an important role in a process called apoptosis (programmed cell death). Overexpression of the BCL-2 protein in CLL has been associated with resistance to certain therapies. It is believed that blocking BCL-2 may restore the signalling system that tells cells, including cancer cells, to self-destruct. Venclexta/Venclyxto is being developed by Roche and AbbVie. It is jointly commercialised by AbbVie and Genentech, a member of the Roche Group, in the United States and commercialised by AbbVie outside of the United States.

Together, the companies are committed to further research with Venclexta/Venclyxto, which is currently being evaluated in phase III clinical trials for the treatment of CLL, along with studies in several other types of cancers. In the United States, Venclexta has been granted four breakthrough therapy designations by the FDA: in combination with Rituxan for people with relapsed or refractory CLL, as a monotherapy for people with relapsed or refractory CLL with 17p deletion; in combination with hypomethylating agents (azacitidine or decitabine) for people with untreated acute myeloid leukaemia (AML) ineligible for intensive chemotherapy, and in combination with low-dose cytarabine (LDAC) for people with untreated AML ineligible for intensive chemotherapy.

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 350,000[1] and CLL is estimated to affect around one-third of all people newly diagnosed with leukaemia.[3]

About Roche in haematology

For more than 20 years, Roche has been developing medicines that redefine treatment in haematology. Today, we are investing more than ever in our effort to bring innovative treatment options to people with diseases of the blood. In addition to approved medicines MabThera /Rituxan (rituximab), Gazyva®/Gazyvaro® (obinutuzumab), and Venclexta / Venclyxto (venetoclax) in collaboration with AbbVie, Roche's pipeline of investigational haematology medicines includes Tecentriq® (atezolizumab), an anti-CD79b antibody drug conjugate (polatuzumab vedotin/RG7596) and a small molecule antagonist of MDM2 (idasanutlin/RG7388). Roche's dedication to developing novel molecules in haematology expands beyond malignancy, with the development of Hemlibra® (emicizumab), a bispecific monoclonal antibody for the treatment of haemophilia A.

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. 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 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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