

New Venclexta/Venclyxto data demonstrate deep responses in two of the most common types of leukaemia

- **New analyses from the phase III MURANO study in previously treated chronic lymphocytic leukaemia show continued benefit from fixed-duration regimen after a median follow-up of three years**
- **Updated results from two studies in newly-diagnosed acute myeloid leukaemia demonstrate Venclexta combinations continued high rates of deep remission**

Basel, 4 December 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new data from the Venclexta®/Venclyxto® (venetoclax) clinical development programme, including longer-term results from the phase III MURANO study in people with previously treated chronic lymphocytic leukaemia (CLL) and updated data from two phase Ib/II studies in people with previously untreated acute myeloid leukaemia (AML) ineligible for intensive chemotherapy due to coexisting medical conditions. Data from the Venclexta/Venclyxto clinical development programme that ranges across multiple blood cancers, including CLL, AML, non-Hodgkin lymphoma and multiple myeloma, will be featured in more than 30 abstracts, including 12 oral presentations, at the 60th American Society of Hematology (ASH) 2018 Annual Meeting.

“We’re excited by the versatility of Venclexta/Venclyxto in treating a range of distinct types of blood cancer, including difficult-to-treat forms with limited options,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “These data support our broad clinical development programme through which we hope to discover more ways Venclexta/Venclyxto can be used alone or in combination with other medicines to treat additional types of cancer.”

Updated data in CLL

Two new analyses of the phase III MURANO study in relapsed or refractory (R/R) CLL demonstrated the continued clinical benefit of Venclexta/Venclyxto plus MabThera®/Rituxan® (rituximab) was sustained after patients completed the chemotherapy-free, two-year fixed-duration course of therapy.

- An analysis showed the combination reduced the risk of disease progression or death (progression-free survival; PFS, as assessed by investigator) by 84% (HR=0.16; 95% CI: 0.12-0.23; p<0.0001) compared to standard of care bendamustine plus MabThera/Rituxan (BR) after a median three-year follow-up. At three years, 71% of patients in the Venclexta/Venclyxto plus MabThera/Rituxan arm had not experienced disease progression, compared to 15% of patients in the BR arm (median PFS: not reached vs. 17.0 months, respectively). A clinically meaningful benefit in overall survival was also observed in the Venclexta/Venclyxto arm compared to the BR arm (88% vs. 80%, HR=0.50; 95 percent CI: 0.30-0.85). Consistent benefit was observed in all patient subgroups for Venclexta/Venclyxto plus MabThera/Rituxan compared to BR, including high-risk and low-risk groups. Data were presented in an oral session on Saturday, 1 December at 14:45 PST (Abstract #184).

- A separate analysis showed higher rates of minimal residual disease (MRD)-negativity observed with Venclexta/Venclyxto plus MabThera/Rituxan compared to BR were sustained after patients completed treatment (62% vs. 13%). MRD-negativity means no cancer can be detected using a specific, highly sensitive test, and was defined as less than 1 CLL cell in 10,000 leukocytes. Importantly, these results were observed in the majority of patients in the Venclexta/Venclyxto arm, including patients in high-risk subgroups and were consistent with the maintained PFS benefit seen with longer follow-up. These data support the utility of MRD in peripheral blood as a predictive marker of clinical outcome. No new safety signals were observed with the treatment combination of Venclexta/Venclyxto plus MabThera/Rituxan. These data will be presented in an oral session on Monday, 3 December at 11:30 PST (Abstract #695).

Updated data in AML

Updated data from the phase Ib M14-358 and phase I/II M14-387 studies evaluating Venclexta/Venclyxto in combination with a hypomethylating agent or low-dose cytarabine (LDAC) in people with previously untreated AML who are ineligible for intensive chemotherapy, will also be presented. These results showed that among patients who were dependent upon blood transfusions at baseline, about half were able to achieve transfusion independence (the absence of transfusions during any consecutive 56 days during the study treatment period). No unexpected safety signals were observed with Venclexta/Venclyxto in combination with hypomethylating agents or LDAC.

- The M14-358 study showed high rates of complete remission (with at least partial blood count recovery, CR+CRh) of 67% for those who received Venclexta/Venclyxto plus azacitidine and 71% for those who received Venclexta/Venclyxto plus decitabine. For people taking Venclexta/Venclyxto and azacitidine or decitabine who were dependent on blood transfusions at baseline, 50% and 52% achieved red blood cell transfusion independence, respectively; and 58% or 60% achieved platelet transfusion independence, respectively.
- The M14-387 study showed rates of complete remission (with or without full recovery of normal blood cell count, CR+CRi) of 54% in people who received Venclexta/Venclyxto in combination with LDAC and a median duration of remission of 8.1 months. For people taking Venclexta/Venclyxto with LDAC, 48% achieved red blood cell transfusion independence and 60% achieved platelet transfusion independence.

Results from the two studies were presented in an oral session on Sunday, December 2 at 7:45 PST and 8:00 PST, respectively (Abstract #284 and #285).

Based on earlier results from the M14-358 and M14-387 studies, Venclexta was granted accelerated approval by the US Food and Drug Administration (FDA) for the treatment of people with newly-diagnosed AML who are age 75 years or older, or for those ineligible for intensive induction chemotherapy due to coexisting medical conditions. A robust clinical development programme for Venclexta/Venclyxto in AML is ongoing, including two ongoing phase III studies evaluating Venclexta/Venclyxto in combination with azacitidine or with LDAC for people with previously untreated AML who are ineligible for intensive chemotherapy based on results from the M14-358 and M14-387 studies.

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.

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) in patients with relapsed or refractory chronic lymphocytic leukaemia (CLL). 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 CLL 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 (PFS). Secondary endpoints included overall survival, overall response rate and complete response rate (with or without complete blood count recovery).

About the M14-358 study

The M14-358 study (NCT02203773) is an open-label, non-randomised, phase Ib dose escalation and expansion study evaluating the safety and efficacy of Venclexta/Venclyxto in combination with hypomethylating agents, azacitidine or decitabine, in 115 newly-diagnosed people with acute myeloid leukaemia who were 60 years or older, or ineligible to receive intensive induction chemotherapy due to coexisting medical conditions. Study endpoints included complete remission rates, transfusion independence, overall survival and safety.

About the M14-387 study

The M14-387 study (NCT02287233) is an open-label, single-arm, phase I/II dose escalation and expansion study evaluating the safety and efficacy of Venclexta/Venclyxto in combination with low-dose cytarabine (LDAC) in 82 newly-diagnosed people with acute myeloid leukaemia who were 60 years or older, or ineligible to receive intensive induction chemotherapy due to coexisting medical conditions. Study endpoints included complete remission rates, transfusion independence, overall survival and safety.

About Venclexta/Venclyxto

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 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. 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 four Breakthrough Therapy Designations by the FDA: in combination with Rituxan for people with relapsed or refractory chronic lymphocytic leukaemia (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 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 more than 400,000^[3] and CLL is estimated to affect around one-third of all people newly diagnosed with leukaemia.^[1]

About Acute Myeloid Leukaemia

Acute myeloid leukaemia (AML) is an aggressive form of leukaemia that starts in immature forms of blood-forming cells, known as myeloid cells, found in the bone marrow.^[4] AML is the most common type of aggressive leukaemia in adults. It has the lowest survival rates of all types of leukaemia.^[5] Even with the best available therapies, older patients aged 65 and over have survival rates comparable to patients with advanced lung cancer, with a five year overall survival rate of <5%.^[6;7] Approximately 20,000 people in the US and 18,000 in Europe are diagnosed with AML each year.^[8;9]

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®/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 which inhibits the interaction of MDM2 with p53 (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. Moreover, for the tenth consecutive year, Roche has been recognised as the most sustainable company 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 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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.

All trademarks used or mentioned in this release are protected by law.

References

- [1] Wendtner CM, et al. Chronic lymphocytic leukemia. Onkopedia guidelines 2012 [Internet; cited 2018]. Available from: <https://www.onkopedia-guidelines.info/en/onkopedia/guidelines/chronic-lymphocytic-leukemia-cll/@@view/html/index.html>
- [2] SEER Stat Fact Sheets: Chronic Lymphocytic Leukemia (CLL) [Internet; cited 2018]. Available from: <http://seer.cancer.gov/statfacts/html/clyl.html>.
- [3] GLOBOCAN 2018. World Fact Sheet. [Internet; accessed 2018]. Available from: <http://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf>
- [4] American Cancer Society: What is acute myeloid leukemia? [Internet; cited 2018]. Available from: <https://www.cancer.org/cancer/acute-myeloid-leukemia/about/what-is-aml.html>
- [5] Leukemia & Lymphoma Society: Facts and statistics overview – Leukemia. [Internet; cited 2018]. Available from: <http://www.lls.org/http%3A//llsorg.prod.acquia-sites.com/facts-and-statistics/facts-and-statistics-overview/facts-and-statistics#Leukemia>.
- [6] Sekeres MA. Treatment Of Older Adults With Acute Myeloid Leukemia: State Of The Art And Current Perspectives. *Haematologica* 2008;93:1769-1772
- [7] Cancer Research UK: Survival statistics for acute myeloid leukaemia (AML). [Internet; cited 2018]. Available from: http://www.cancerresearchuk.org/about-cancer/acute-myeloid-leukaemia-aml/survival?_ga=2.239561667.1384102361.1500450925-993068745.1500450925
- [8] National Cancer Institute. Adult Acute Myeloid Leukemia Treatment (PDQ®)–Health Professional Version [Internet; cited 2018 May]. Available from: <https://www.cancer.gov/types/leukemia/hp/adult-aml-treatment-pdq>.
- [9] Visser O, et al. (RARECARE Working Group). Incidence, survival and prevalence of myeloid malignancies in Europe. *Eur J Cancer*. 2012;48:3257-3266.

Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Simone Oeschger
- Anja von Treskow