European Commission approves Venclyxto-based combinations for adults with newly diagnosed acute myeloid leukaemia who are ineligible for intensive chemotherapy

- **With hypomethylating agents significantly improved complete response rates in certain adults with newly diagnosed acute myeloid leukaemia**
- **In the VIALE-A study, Venclyxto plus azacitidine significantly improved overall survival in patients ineligible for intensive chemotherapy, a patient population who typically have a five-year overall survival rate of less than 10%[1]**
- **Study data reinforces the potential of Venclyxto-based combinations to provide clinically meaningful benefits in difficult to treat blood cancers**

Basel, 25 May 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission has approved Venclyxto® (venetoclax) in combination with hypomethylating agents, azacitidine and decitabine, for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for intensive chemotherapy.

"This Venclyxto approval is a critical step in providing new therapeutic options for patients in the EU newly diagnosed with AML who cannot tolerate the side effects of, or are ineligible for, intensive chemotherapy," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Venclyxto-based combinations continue to show meaningful clinical benefits in AML patients, who would otherwise have a poor prognosis."

The approval is based on the results of two key studies, phase III VIALE-A and phase I/II M14-358, of Venclyxto in combination with hypomethylating agents in adults with newly diagnosed AML, who are ineligible for intensive chemotherapy. Results from the VIALE-A study showed Venclyxto plus azacitidine significantly reduced the risk of death by 34%, compared to azacitidine alone (HR=0.66; 95% CI: 0.52, 0.85; $p<0.001$). The median overall survival was 14.7 months (95% CI: 11.9, 18.7) in the Venclyxto group and 9.6 months (95% CI: 7.4, 12.7) in the control group. The Venclyxto combination more than doubled the complete responses (CRs), with a CR rate of 37% (95% CI: 31, 43) compared to 18% (95% CI: 12, 25) in the comparator arm ($p<0.001$). The Venclyxto plus azacitidine combination also led to higher rates of composite complete remission (CR + CR with incomplete blood count recovery [CR + CRi]) at 66% (95% CI: 61, 72) compared to 28% (95% CI: 21, 36) with azacitidine alone ($p<0.001$). The most frequently reported serious adverse reactions (≥5%) in patients receiving Venclyxto in combination with azacitidine were febrile neutropenia, pneumonia, sepsis and haemorrhage.

Results from the M14-358 study demonstrated that patients receiving Venclyxto in combination with decitabine achieved a CR + CRi rate of 74% (95% CI: 55, 88). The most frequently reported serious adverse reactions (≥5%) were febrile neutropenia, pneumonia, bacteraemia and sepsis.

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Today's approval reinforces the potential of Venclyxto-based combinations to provide clinically meaningful benefits across several disease areas, including AML. Venclexta® (venetoclax) is already approved in the US in combination with azacitidine, decitabine, or low dose cytarabine for the treatment of newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. Venclexta/Venclyxto is also approved in the US and EU in combination with MabThera®/Rituxan® (rituximab) for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy; in combination with Gazyva®/Gazyvaro® (obinutuzumab) for the treatment of adult patients with previously untreated CLL; and as a monotherapy for the treatment of CLL in the presence of 17p deletion or TP53 mutation in people who are unsuitable for or have failed a B-cell receptor pathway inhibitor.

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 VIALE-A study
VIALE-A [NCT02993523] is a phase III, randomised, double-blind, placebo-controlled multicentre study evaluating the efficacy and safety of Venclyxto® (venetoclax) plus azacitidine, a hypomethylating agent, compared to placebo with azacitidine, in 431 people with previously untreated acute myeloid leukaemia who are ineligible for intensive chemotherapy. Two-thirds of patients (n=286) received 400 mg Venclyxto daily, in combination with azacitidine, and the remaining patients (n=145) received placebo tablets in combination with azacitidine. Patients enrolled in the study had a range of mutational subtypes, including IDH1/2 and FLT3. VIALE-A met its primary and key secondary endpoints.

About the M14-358 study
M14-358 [NCT02203773] is a phase I/II, open-label, non-randomised, multicentre study evaluating the efficacy and safety of Venclyxto® (venetoclax) plus azacitidine or decitabine, in patients with previously untreated acute myeloid leukaemia who are ineligible for intensive chemotherapy. Oral Venclyxto was given in combination with azacitidine in 84 patients and in combination with decitabine in 31 patients.

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.[2] AML is the most common type of aggressive leukaemia in adults, approximately 42,000 people in Europe are currently diagnosed with AML.[3,4,5] Even with the best available therapies, it has the lowest survival rate of all types of leukaemia.[6]

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 help 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, 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 U.S. 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 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 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 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 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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