Roche announces full FDA approval for Venclexta combinations for acute myeloid leukaemia

- **Approval supported by data from phase III confirmatory trials, VIALE-A and VIALE-C**
- **VIALE-A study showed Venclexta plus azacitidine significantly improved overall survival in newly diagnosed AML compared to azacitidine alone**
- **Supplemental New Drug Applications approved under the FDA's Real-Time Oncology Review pilot programme and Project Orbis initiative**

Basel, 19 October 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has granted full approval of Venclexta® (venetoclax) in combination with azacitidine, or decitabine, or low-dose cytarabine (LDAC) for the treatment of newly diagnosed acute myeloid leukaemia (AML) in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. Venclexta was previously granted provisional approval in this setting under the FDA's accelerated approval programme in November 2018. Today's FDA approval converts Venclexta's accelerated approval in this setting to a full approval.

"Today's full approval is supported by the significant results that showed that Venclexta in combination with azacitidine extended overall survival for people with newly diagnosed acute myeloid leukaemia who cannot tolerate intensive induction chemotherapy," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are very pleased that this application was reviewed under the FDA's Real-Time Oncology Review pilot and Project Orbis initiative, helping to bring this treatment option more rapidly to patients in the United States and other countries."

The approval is primarily based on the results of two phase III studies, VIALE-A and VIALE-C. Results of the VIALE-A study, which were published in the *New England Journal of Medicine* in August 2020, showed Venclexta plus azacitidine significantly reduced the risk of death by 34% (overall survival; OS) compared to azacitidine alone (median OS=14.7 months vs. 9.6 months; HR=0.66; 95% CI: 0.52-0.85; p<0.001). People treated with Venclexta plus azacitidine had significantly higher rates of complete remission (CR) with 37% (95% CI: 31-43) compared to 18% (95% CI: 12-25) in people treated with azacitidine alone (p<0.001). The Venclexta plus azacitidine combination also led to higher rates of CR and CR with partial haematologic recovery (CR + CRh), with the combination showing a CR + CRh of 65% compared to 23% with azacitidine alone (p<0.001). The most frequent serious adverse reactions (≥5%), reported in 83% of people treated with Venclexta plus azacitidine, were low white blood cell count with fever (30%), pneumonia (22%), blood infection (excluding fungal;19%), and bleeding (6%).

For the VIALE-C study, the approval was based on the rate and duration of CR. Twenty-seven percent (95% CI: 20-35) of people treated with Venclexta plus LDAC achieved a CR (median duration of CR (DOCR)=11.1 months) vs. 7.4% (95% CI: 2.4-16) of people treated with LDAC alone (median DOCR=8.3 months). The median OS for people treated with Venclexta plus LDAC was 7.2 months vs. 4.1 months (HR=0.75; 95% CI:

0.52-1.07; p=0.114) for people treated with LDAC alone. These OS results were not statistically significant. The most frequent serious adverse reactions (≥10%), reported in 65% of people treated with Venclexta plus LDAC, were pneumonia (17%), low white blood cell count with fever (16%), and blood infection (excluding fungal;12%).

Updated results from additional phase I/II studies of Venclexta in people with newly diagnosed AML were included in the FDA submissions as supporting data.

"The results of the VIALE-A study reinforce the clinically meaningful benefit of Venclexta plus azacitidine for people newly diagnosed with AML," said Courtney DiNardo, M.D., Associate Professor of the Department of Leukemia, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center. "Based on the results of this study, this treatment regimen represents a significant advance for older AML patients, including higher response rates, greater transfusion independence, longer durations of remission, and ultimately significantly improved overall survival compared to azacitidine alone."

This is the second time that Venclexta has been reviewed under the FDA's new Real-Time Oncology Review (RTOR) and Assessment Aid pilot programmes. The RTOR pilot programme explores a more efficient review process to ensure safe and effective treatments are available to patients as early as possible. The approval was also granted under the FDA's recently established Project Orbis, which provides a framework for concurrent submission and review of oncology medicines among multiple regulatory agencies worldwide. Simultaneous applications were submitted to regulators in the US, Australia, Canada, Brazil and Switzerland under Project Orbis. Additionally, the FDA has granted five Breakthrough Therapy Designations for Venclexta, two of which are for people with previously untreated AML ineligible for intensive chemotherapy.

Venclexta 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, under the brand name Venclyxto® 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 Venclexta® (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 Venclexta 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 VIALE-C Study
VIALE-C (NCT03069352) is a phase III, randomised, double-blind, placebo-controlled multicentre study evaluating the efficacy and safety of Venclexta (venetoclax) plus LDAC, compared to placebo with LDAC, in

211 people with previously untreated acute myeloid leukaemia who are ineligible for intensive chemotherapy. Two-thirds of patients (n=143) received 600 mg Venclexta daily in combination with LDAC and the remaining patients (n=68) received placebo in combination with LDAC.

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.[1] AML is the most common type of aggressive leukaemia in adults.[2] It has the lowest survival rate of all types of leukaemia.[2] 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%.[3,4] Approximately 20,000 people in the US and 18,000 in Europe are diagnosed with AML each year.[5,6]

About Venclexta (venetoclax)

Venclexta 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 blocks the BCL-2 protein and works to help restore the process of apoptosis.

Venclexta 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, under the brand name Venclyxto 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 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; 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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References

[1] American Cancer Society. What is acute myeloid leukemia? [Internet; cited July 2020]. Available from: http://www.cancer.org/cancer/leukemia-acutemyeloidaml/detailedguide/leukemia-acute-myeloid-myelogenous-what-is-aml.
[2] Leukemia & Lymphoma Society: Facts and statistics overview – Leukemia. [Internet; cited July 2020]. Available from: https://www.lls.org/facts-and-statistics/facts-and-statistics-overview/facts-and-statistics#Leukemia.
[3] Sekeres MA. Treatment Of Older Adults With Acute Myeloid Leukemia: State Of The Art And Current Perspectives. Haematologica 2008;93:1769-1772.
[4] Cancer Research UK: Survival statistics for acute myeloid leukaemia (AML). [Internet; cited July2020]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/leukaemia-aml/survival.
[5] National Cancer Institute. Adult Acute Myeloid Leukemia Treatment (PDQ®)–Health Professional Version. [Internet; cited June 2020]. Available from: https://www.cancer.gov/types/leukemia/hp/adult-aml-treatment-pdq.
[6] Visser, et al. Incidence, survival and prevalence of myeloid malignancies in Europe. Eur J Cancer. 2012; 48(17): 3257-66.

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