Media Release

Positive phase III results for Venclexta/Venclyxto combination in acute myeloid leukaemia presented at EHA 2020

- **Phase III VIALE-A study showed Venclexta/Venclyxto plus azacitidine helped people with the most common type of aggressive adult leukaemia live longer compared to azacitidine alone**
- **Data will be presented as a late-breaking abstract at the 25th European Hematology Association Virtual Congress**

Basel, 13 June 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the phase III VIALE-A study, evaluating Venclexta®/Venclyxto® (venetoclax) in combination with azacitidine in people with previously untreated acute myeloid leukaemia (AML) who were ineligible for intensive induction chemotherapy. VIALE-A results were featured in the 25th European Hematology Association Virtual Congress Press Briefing on Saturday 13 June 2020 at 08:30 CEST and will be presented at the congress during the Late-breaking Oral Session (abstract #LB2601) on Sunday 14 June 2020.

"We are very pleased to present these important results from people with acute myeloid leukaemia, especially those who are unable to tolerate intensive chemotherapy and therefore have limited treatment options," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "The significant survival benefits observed in the VIALE-A study reinforce the potential utility of this Venclexta/Venclyxto-based combination for people with this aggressive disease."

Results from the VIALE-A study showed that the Venclexta/Venclyxto combination reduced the risk of death (overall survival [OS]) by 34% 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) in people with previously untreated AML. The Venclexta/Venclyxto plus azacitidine combination also led to higher rates of composite complete remission (CR + CR with incomplete blood count recovery [CR + CRi]) at 66.4% compared to 28.3% with azacitidine alone (p<0.001).

Safety for Venclexta/Venclyxto plus azacitidine appeared consistent with the known safety profile of these medicines and no unexpected safety signals were identified with the combination. Notable grade 3 or higher adverse events in the Venclexta/Venclyxto plus azacitidine and azacitidine alone arms included low platelet count (thrombocytopenia; 45% vs. 38%), low white blood cell count (neutropenia; 42% vs. 29%; leukopenia; 21% vs. 12%), low white blood cell count with fever (febrile neutropenia; 42% vs. 19%) and low red blood cell count (anaemia; 26% vs. 20%).

The study also met its secondary endpoint of CR and CR with partial haematologic recovery (CR + CRh), with the combination showing a CR + CRh of 64.7% compared to 22.8% with azacitidine alone.

Data from the VIALE-A study has been shared with health authorities globally including the US Food and Drug Administration (FDA). Venclexta has previously been granted accelerated approval by the FDA in combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of people with newly diagnosed AML who are aged 75 years or older, or for those ineligible for intensive induction chemotherapy

due to coexisting medical conditions. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory studies. VIALE-A is part of Venclexta's ongoing development programme to convert the current accelerated approval of Venclexta, granted by the FDA in previously untreated AML, to a full approval. Venclexta has also been granted five Breakthrough Therapy Designations by the FDA, including two for previously untreated AML.

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 multicenter study evaluating the efficacy and safety of Venclexta®/Venclyxto® (venetoclax) plus azacitidine, a hypomethylating agent, compared to placebo plus azacitidine, in 433 people with previously untreated acute myeloid leukaemia who are ineligible for intensive chemotherapy. Two-thirds of patients received 400 mg Venclexta/Venclyxto daily, in combination with azacitidine, and the remaining patients received placebo tablets in combination with azacitidine. Patients enrolled in the study had a range of mutational subtypes, including IDH1/2 and FLT3. The primary endpoints of the study are overall survival (OS) and rate of complete remission (CR) and CR with incomplete blood count recovery (CRi). OS was the sole primary endpoint in the United States (US) and US reference countries, and OS and CR + CRi were co-primary endpoints in China, Japan, the European Union (EU) and EU reference countries. Secondary endpoints include CR and CR with partial haematologic recovery (CRh), event-free survival, transfusion independence and patient-reported outcomes.

	Venclexta/Venclyxto plus azacitidine (n=286)	**Azacitidine plus placebo (n=145)**
Primary endpoints		
Median OS	14.7 months	9.6 months
	Hazard ratio: 0.66, 95% CI: 0.52–0.85, p<0.001	
CR + CRi	66.4%	28.3%
	p<0.001	
Secondary endpoints		
CR + CRh	64.7%	22.8%
	p<0.001	
CR + CRi rates in molecular subgroups		
IDH1/2	75%	11%
	p<0.001	
FLT3	72%	36%
	p=0.021	

NPM1	67%	24%
	p=0.012	
TP53	55%	0%
	p<0.001	

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/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 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 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 idasanutlin, a small molecule which inhibits the interaction of MDM2 with p53; 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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