Roche announces submission of supplemental New Drug Application for Venclexta for people with previously untreated acute myeloid leukaemia who are ineligible for intensive chemotherapy

- **Venclexta represents a potential new way of treating AML, the most common type of aggressive leukaemia in adults [1]**

Basel, 12 July 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced submission of a supplemental New Drug Application (sNDA) to the United States (U.S.) Food and Drug Administration (FDA) for Venclexta® (venetoclax), in combination with a hypomethylating agent or in combination with low dose cytarabine (LDAC), for treatment of people with previously untreated acute myeloid leukaemia (AML) who are ineligible for intensive chemotherapy. The submission is based on the results of two phase Ib/II studies that evaluated Venclexta in combination with azacitidine or decitabine (M14-358 study) or LDAC (M14-387 study) in this patient population. Venclexta is being developed by AbbVie and Roche. It is jointly commercialised by AbbVie and Genentech, a member of the Roche Group, in the U.S. and commercialised by AbbVie outside of the U.S.

"Nearly 20,000 people will be diagnosed with AML in the U.S. this year, and many of them are not eligible to receive standard intensive chemotherapy," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "AML is an aggressive disease with the lowest survival rate of all leukaemias, and we look forward to working closely with the FDA to bring this potential option to patients with this very difficult-to-treat blood cancer as soon as possible."

Data recently presented from the phase Ib M14-358 study showed Venclexta in combination with azacitidine or decitabine resulted in a complete remission rate (with or without full recovery of normal blood cell count; CR/CRi) of 73% in patients treated with Venclexta at a dose of 400 mg.[2] After more than a year of follow-up, the observed median overall survival (OS) across all Venclexta dose groups in the study was 17.5 months (95% CI: 12.3-not reached).[2] The most common Grade 3-4 adverse events (occurring in 10% or more patients) were low white blood cell count with fever, low white blood cell count, anaemia, low platelet count and decreased potassium levels.[2]

Additionally, results from the phase Ib/II M14-387 study of Venclexta in combination with LDAC showed a CR/CRi rate of 62% in patients treated with Venclexta at a dose of 600 mg.[3] After more than a year of follow-up, the observed median OS was 11.4 months (95% CI: 5.7-15.7).[3] The most common Grade 3-4 adverse events (occurring in 10% or more patients) were low white blood cell count with fever, decreased potassium levels, pneumonia, disease progression, decreased phosphate levels, high blood pressure and sepsis (blood infection).[3]

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The FDA previously granted two breakthrough therapy designations for Venclexta in previously untreated AML ineligible for intensive chemotherapy, either in combination with hypomethylating agents or LDAC, based on results from these two studies. Recently, the FDA approved Venclexta in combination with Rituxan® (rituximab) for the treatment of people with chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy. A robust clinical development programme is ongoing in several other cancer types.

About the M14-358 study
The M14-358 study (NCT02203773) is an open-label, phase Ib dose escalation and expansion study evaluating the safety and efficacy of Venclexta in combination with hypomethylating agents, azacitidine or decitabine, in 212 patients who are 60 years or older with previously untreated AML unfit to receive intensive chemotherapy. Study endpoints included CR/CRi, OS and safety.

About the M14-387 study
The M14-387 study (NCT02287233) is an open-label, phase Ib/II dose escalation and expansion study evaluating the safety and efficacy of Venclexta in combination with LDAC in 94 patients who are 60 years or older with previously untreated AML unfit to receive intensive chemotherapy. Study endpoints included CR/CRi, objective response rate (ORR), OS and safety.

About Venclexta
Venclexta 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 AML 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 is being developed by AbbVie and Roche. It is jointly commercialised by AbbVie and Genentech, a member of the Roche Group, in the U.S. and commercialised by AbbVie outside of the U.S.

Together, the companies are committed to further research with Venclexta, which is currently being evaluated in phase III clinical trials for several types of blood cancers. In the U.S., 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 AML ineligible for intensive chemotherapy; and in combination with LDAC for people with untreated AML ineligible for intensive chemotherapy.

About 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.[1] 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 U.S. 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® (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 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.

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