## Roche announces FDA grants Venclexta accelerated approval for people with newly-diagnosed acute myeloid leukaemia or those who are ineligible for intensive induction chemotherapy

- **Approval based on two studies that showed durable remissions in people with newly-diagnosed acute myeloid leukaemia, who are age 75 years or older, or for those ineligible for intensive induction chemotherapy**
- **Venclexta represents a new treatment option for people with acute myeloid leukaemia regardless of subtypes**

Basel, 21 November 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has granted accelerated approval to Venclexta® (venetoclax), in combination with a hypomethylating agent (azacitidine or decitabine), or low-dose cytarabine (LDAC), for the treatment of people with newly-diagnosed acute myeloid leukaemia (AML), who are age 75 years or older, or for those ineligible for intensive induction chemotherapy due to coexisting medical conditions. AML is the most common type of aggressive leukaemia in adults and has the lowest survival rate for all types of leukaemia.

"Today's approval marks a significant advance for people with acute myeloid leukaemia, a highly aggressive and difficult-to-treat blood cancer," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "Many people with acute myeloid leukaemia are unable to tolerate standard intensive chemotherapy, and the Venclexta combination regimens represent important new options for these patients."

This accelerated approval was based on results from the M14-358 study and the M14-387 study in people newly-diagnosed with AML including those who were ineligible for intensive induction chemotherapy. In M14-358, the rate of complete remission (CR) was 37% (n=25/67) and the rate of complete remission with partial blood count recovery (CRh) was 24% (n=16/67) for those who received Venclexta plus azacitidine. For those who received Venclexta plus decitabine, the rate of CR was 54% (n=7/13) and the rate of CRh was 8% (n=1/13). M14-387 showed a CR rate of 21% (n=13/61) and a CRh rate of 21% (n=13/61) for those who received Venclexta in combination with LDAC.

The most common serious side effects of these regimens (occurring in at least 5% of patients) were low white blood cell count with fever, pneumonia, bacteria in the blood, inflammation of tissue under the skin, device-related infection, diarrhoea, fatigue, bleeding, localized infection, multiple organ dysfunction syndrome, and respiratory failure.

The FDA's Accelerated Approval Program allows conditional approval of a medicine that fills an unmet medical need for a serious condition. This approval of Venclexta is based on surrogate endpoints that are reasonably likely to predict clinical benefit, including CR and CRh. Continued approval for this indication may be contingent upon verification and description of clinical benefit observed in confirmatory trials.

The supplemental New Drug Application (sNDA) was granted Priority Review, a designation given to medicines that the FDA has determined to have the potential to provide significant improvements in the treatment, prevention or diagnosis of a disease. In addition, the FDA previously granted two Breakthrough

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Therapy Designations for Venclexta in people with previously untreated AML ineligible for intensive chemotherapy, either in combination with a hypomethylating agent or LDAC, based on results from these two studies. With this approval, Venclexta is available in the US for two forms of blood cancer.

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 outside of the US.

**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 in combination with hypomethylating agents, azacitidine or decitabine, in newly-diagnosed people with AML who were 60 years or older, or ineligible to receive intensive induction chemotherapy due to coexisting medical conditions. Study endpoints included complete remission rates, overall survival and safety.

- In M14-358, the rate of CR was 37% and the rate of CRh was 24% for those who received Venclexta plus azacitidine. The median follow-up for this group was 7.9 months (0.4-36 months). At the time of analysis, for patients who achieved a CR, the median observed time in remission was 5.5 months (0.4-30 months).
- For those who received Venclexta plus decitabine, the rate of CR was 54% and the rate of CRh was 8%. The median follow-up for this group was 11 months (0.7-21 months). At the time of analysis, for patients who achieved a CR, the median observed time in remission was 4.7 months (1.0-18 months).
- The observed time in remission for these regimens was defined as the time from the start of CR to the time of the data cut-off date or relapse from CR.
- The most common adverse reactions with Venclexta plus azacitidine were nausea, diarrhoea, constipation, low white blood cell count with or without fever, low platelet count, bleeding, swelling in the arms, legs, hands and feet, vomiting, fatigue, rash and low red blood cell count.
- The most common adverse reactions with Venclexta plus decitabine were low white blood cell count with or without fever, constipation, fatigue, low platelet count, stomach (abdominal) pain, dizziness, bleeding, nausea, pneumonia, infection in the blood, cough, diarrhoea, low blood pressure, pain in muscles or back, sore throat, swelling in the arms, legs hand and feet, fever and rash.

**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 in combination with LDAC in newly-diagnosed people with AML who were 60 years or older, or ineligible to receive intensive induction chemotherapy due to coexisting medical conditions. Study endpoints included complete remission rates, overall survival and safety.

- The study showed the rate of CR and CRh was 21% for those who received Venclexta plus LDAC. The median follow-up for this group was 6.5 months (0.3-34 months). At the time of analysis, for patients who achieved a CR, the median observed time in remission was 6.05 months (0.3-25 months). The observed time in remission for this regimen was defined as the time from the start of CR to the time of the data cut-off date or relapse from CR.
- The most common adverse reactions with Venclexta in combination with LDAC were nausea, low platelet count, bleeding, low white blood cell count with or without fever, diarrhoea, fatigue, constipation and difficulty breathing.

**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 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 by AbbVie outside of the US. Together, the companies are committed to research with Venclexta, 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.

Venclexta is approved in more than 50 countries. Roche and AbbVie are currently working with regulatory agencies around the world to bring this medicine to additional eligible patients in need.

**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. It has the lowest survival rates 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 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.

## References

[1] 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
[2] 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.
[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 2018]. Available from: http://www.cancerresearchuk.org/about-cancer/acute-myeloid-leukaemia-aml/survival?_ga=2.239561667.1384102361.1500450925-993068745.1500450925
[5] 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.
[6] Visser O, et al. (RARECARE Working Group). Incidence, survival and prevalence of myeloid malignancies in Europe. Eur J Cancer. 2012;48:3257-3266.

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