FDA grants Breakthrough Therapy Designation for Venclexta in combination with azacitidine for the treatment of patients with myelodysplastic syndromes

- **Every year in the US, approximately 10,000 people are diagnosed with myelodysplastic syndromes (MDS), and there remains a high unmet need for new treatment options[1]**
- **The designation is based on interim results from the phase Ib M15-531 study investigating Venclexta/Venclyxto plus azacitidine in people with previously untreated higher-risk MDS**
- **This is the 11th Breakthrough Therapy Designation for Roche's haematology medicines and the sixth for Venclexta demonstrating its potential across multiple blood cancers**

Basel, 21 July 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that Venclexta® (venetoclax) in combination with azacitidine has been granted Breakthrough Therapy Designation (BTD) by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with previously untreated intermediate, high- and very high-risk myelodysplastic syndromes (MDS) based on the revised International Prognostic Scoring System (IPSS-R). MDS are a rare group of blood cancers that gradually affect the ability of the bone marrow to produce normal blood cells.[2] This can lead to weakness, frequent infections, anaemia and debilitating fatigue.[3] In some cases, MDS can also progress into acute myeloid leukaemia (AML).[4,5] Every year in the US, approximately 10,000 people are diagnosed with MDS, and the median survival for those with higher-risk MDS is approximately 18 months.[1,3]

"Higher-risk MDS is associated with poor prognosis, reduced quality of life, and limited treatment options," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are pleased that the FDA has granted Venclexta its sixth Breakthrough Therapy Designation in recognition of its potential to improve outcomes for people with MDS in combination with azacitidine."

This designation was granted based on interim results from the phase Ib M15-531 study investigating Venclexta/Venclyxto plus azacitidine in people with previously untreated, higher-risk MDS. BTD is designed to accelerate the development and review of medicines intended to treat serious or life-threatening conditions with preliminary evidence that indicates they may demonstrate a substantial improvement over existing therapies. This is the 38th BTD for Roche's portfolio of medicines, and the 11th designation for its haematology portfolio.

This most recent designation reinforces the potential of Venclexta/Venclyxto-based combinations across several blood cancers, including MDS. In the US, Venclexta has been granted six BTDs by the FDA: one for previously untreated chronic lymphocytic leukaemia (CLL), two for relapsed or refractory CLL, two for previously untreated AML, and one for MDS. Venclexta/Venclyxto is already approved in the US (as Venclexta) 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, and in the EU (as Venclyxto) in combination with hypomethylating agents,

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azacitidine and decitabine, for the treatment of adult patients with newly diagnosed AML who are ineligible for intensive chemotherapy. Venclexta/Venclyxto is also approved in the US and EU in combination with MabThera®/Rituxan® (rituximab) for the treatment of adult patients with 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, under the brand name Venclexta, and commercialised by AbbVie outside of the US.

About myelodysplastic syndrome (MDS)
MDS are a rare group of blood cancers that gradually affect the ability of the bone marrow to produce normal blood cells.[2] This can lead to weakness, frequent infections, anaemia and debilitating fatigue.[3] In some cases, MDS can also progress into acute myeloid leukaemia (AML).[4,5] Every year in the US, approximately 10,000 people are diagnosed with MDS and the median survival for those with higher-risk MDS is approximately 18 months.[1,3]

There are several classifications of MDS – very low-risk to very high-risk – determined by the composition of the bone marrow, blood cell counts, and chromosomal alterations. Higher-risk disease is defined as intermediate, high- or very high-risk based on the revised International Prognostic Scoring System (IPSS-R), which is a risk assessment scale that uses five prognostic indicators to predict the course of a patient's disease.[7] Approximately half (45%) of patients present with higher-risk MDS, which is associated with a poorer prognosis and short life expectancy.[8]

About the M15-531 study
The M15-531 [NCT02942290] study is a phase Ib, open-label, non-randomised, multicentre, dose-finding study evaluating Venclexta®/Venclyxto® (venetoclax) in combination with azacitidine in treatment-naïve patients with higher-risk myelodysplastic syndromes (MDS) comprising a dose-escalation portion and a safety expansion portion. The primary objectives of the study are to assess the safety profile and pharmacokinetics and determine the recommended phase II dose and dosing schedule of Venclexta/Venclyxto in combination with azacitidine. The response criteria specified in the M15-531 study are based on the modified International Working Group 2006 response criteria for MDS.

About Venclexta/Venclyxto
Venclexta®/Venclyxto® (venetoclax) 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 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 cancers.

In the US, Venclexta has been granted six 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, two for previously untreated acute myeloid leukaemia, and one for myelodysplastic syndromes.

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, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

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. In recent years, Roche has invested in genomic profiling and real-world data partnerships and has become an

industry-leading partner for medical insights.

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.

References

[1] Cancer.Net. Myelodysplastic Syndromes - MDS: Statistics. [Internet; cited July 2021]. Available from: https://www.cancer.net/cancer-types/myelodysplastic-syndromes-mds/statistics
[2] American Cancer Society. What Are Myelodysplastic Syndromes? [Internet; cited July 2021]. Available from: https://www.cancer.org/cancer/myelodysplastic-syndrome/about/what-is-mds.html
[3] Steensma DP, Heptinstall KV, Johnson VM, et al. Common troublesome symptoms and their impact on quality of life in patients with myelodysplastic syndromes (MDS): results of a large internet-based survey. Leuk Res. 2008;32(5):691-8.
[4] Catenacci DV, Schiller GJ. Myelodysplastic syndromes: a comprehensive review. Blood Rev. 2005;19(6):301-19.
[5] American Cancer Society. Survival Statistics for Myelodysplastic Syndromes [Internet; cited July 2021]. Available from: https://www.cancer.org/cancer/myelodysplastic-syndrome/detection-diagnosis-staging/survival.html
[6] Center for Drug Evaluation and Research. Medical Review(s): Azacitidine: Application 50-794 (part 2) Silver Spring, MD: FDA; 2004 [Internet; cited July 2021]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2004/50-794_Vidaza_Medr_P2.pdf
[7] Leukemia & Lymphoma Society. The International Prognostic Scoring System. [Internet; cited July 2021]. Available from: https://www.lls.org/myelodysplastic-syndromes/diagnosis/international-prognostic-scoring-system
[8] Kantar Health. Treatment architecture: United States myelodysplastic syndromes. 2015. CancerMPact.

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