Roche submits supplemental new drug application to FDA for Venclexta plus Gazyva for previously untreated chronic lymphocytic leukaemia with co-existing medical conditions

- Application is being reviewed under FDA’s Real-Time Oncology Review pilot programme
- Combination was granted Breakthrough Therapy Designation, the fifth for Venclexta

Basel, 7 March 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced the submission of a supplemental New Drug Application to the US Food and Drug Administration (FDA) for Venclexta® (venetoclax) in combination with Gazyva* (obinutuzumab) in people with previously untreated chronic lymphocytic leukaemia (CLL) and co-existing medical conditions. The FDA is reviewing the application under the Real-Time Oncology Review pilot programme, which aims to explore a more efficient review process to ensure safe and effective treatments are available to patients as early as possible.

“More than 20,000 people will be diagnosed with untreated chronic lymphocytic leukaemia in the US this year, and many are ineligible for intensive chemotherapy-based options,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We are encouraged that this chemotherapy-free, fixed-duration combination is being reviewed under the FDA’s Real-Time Oncology Review pilot programme, and we are working closely with the agency to bring this new option to people with previously untreated chronic lymphocytic leukaemia as quickly as possible.”

Breakthrough Therapy Designation was granted based on results of the randomised phase III CLL14 study, evaluating the fixed-duration combination of Venclexta plus Gazyva, compared to Gazyva plus chlorambucil, in people with previously untreated CLL and co-existing medical conditions. The study met its primary endpoint and showed a statistically significant reduction in the risk of disease worsening or death (progression-free survival [PFS] as assessed by investigator) compared to standard-of-care Gazyva plus chlorambucil. Safety for the Venclexta plus Gazyva combination appeared consistent with the known safety profiles of the individual medicines, and no new safety signals were identified with the combination. Data from the CLL14 study will be presented at an upcoming medical meeting. The CLL14 study is being conducted in cooperation with the German CLL Study Group (GCLLSG), headed by Michael Hallek, MD, University of Cologne.

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 CLL14 study
CLL14 (NCT02242942) is a randomised phase III study evaluating the combination of fixed-duration Venclexta plus Gazyva compared to Gazyva plus chlorambucil in patients with previously untreated chronic lymphocytic leukaemia (CLL) and co-existing medical conditions. 432 patients with previously untreated...
CLL were randomly assigned to receive either a 12-month duration of Venclexta alongside six-month duration of Gazyva (Arm A) or six-month duration of Gazyva plus chlorambucil followed by an additional six-month duration of chlorambucil (Arm B). The primary endpoint of the study is investigator-assessed progression-free survival (PFS). Secondary endpoints include PFS assessed by independent review committee (IRC), minimal residual disease (MRD) status, overall response (OR), complete response (with or without complete blood count recovery, CR/CRi), overall survival (OS), duration of response (DOR), event-free survival (EFS), time to next CLL treatment (TTNT), and safety. The CLL14 study is being conducted in cooperation with the German CLL Study Group (GCLLSG), headed by Michael Hallek, MD, University of Cologne.

**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 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, under the brand name Venclyxto, 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 five Breakthrough Therapy Designations by the FDA: in combination with Gazyva for people with previously untreated chronic lymphocytic leukaemia (CLL) and co-existing medical conditions; 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 acute myeloid leukaemia (AML) ineligible for intensive chemotherapy; and in combination with low-dose cytarabine for people with untreated AML ineligible for intensive chemotherapy.

**About Gazyva (obinutuzumab)**

Gazyva is an engineered monoclonal antibody designed to attach to CD20, a protein expressed on certain B cells, but not on stem cells or plasma cells. Gazyva is designed to attack and destroy targeted B-cells both directly and together with the body’s immune system. Gazyva is marketed as Gazyvaro in the EU and Switzerland.

Gazyva/Gazyvaro is currently approved in more than 90 countries in combination with chlorambucil for people with previously untreated chronic lymphocytic leukaemia, in more than 80 countries in combination with bendamustine for people with certain types of previously treated follicular lymphoma and in more than 70 countries in combination with chemotherapy for previously untreated follicular lymphoma.

Additional combination studies investigating Gazyva/Gazyvaro with other approved or investigational medicines, including cancer immunotherapies and small molecule inhibitors, are underway across a range of blood cancers.
About the German CLL Study Group (GCLLSG)
Founded in 1996 and headed by Michael Hallek, MD, the GCLLSG has been running various phase III, phase II and phase I trials in chronic lymphocytic leukaemia (CLL) with the goal to provide optimal treatment to patients suffering from this disease. Among those were landmark trials like the CLL8 and the CLL11 trials which led to the current standard of care in CLL. For many years, GCLLSG has been aiming to improve not just the treatment of younger and physically fit patients, but also that of elderly and less fit patients. These patients are generally underrepresented in clinical trials although they constitute the majority of CLL patients treated by doctors in daily practice. The GCLLSG is an independent non-profit research organisation supported by the German Cancer Aid (Deutsche Krebshilfe) www.dcllsg.de.

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 Venetoclax/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 which inhibits the interaction of MDM2 with p53 (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. 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 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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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