

Basel, 12 April 2016

## **Roche announces FDA grants Venclexta(venetoclax) accelerated approval for people with hard-to-treat type of chronic lymphocytic leukemia**

- **Venclexta is designed to help restore a cell's ability to self-destruct and is the first medicine of its kind to be approved**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the U.S. Food and Drug Administration (FDA) granted accelerated approval to Venclexta™ (venetoclax) for the treatment of people with chronic lymphocytic leukemia (CLL) with 17p deletion, as detected by an FDA approved test, who have received at least one prior therapy. The pivotal study showed a clinically meaningful improvement (overall response rate, ORR) in 80.2 percent of people (95 percent CI 71.3-87.3). Venclexta is the first approved medicine designed to help restore a process in which cells self-destruct (apoptosis) by selectively blocking the BCL-2 protein and is Roche's tenth new medicine approved in the past seven years. Venclexta is being developed by AbbVie and Roche. It is jointly commercialised by AbbVie and Genentech, a member of the Roche Group, in the United States and commercialised by AbbVie outside of the United States.

“Up to half of people whose CLL progressed have 17p deletion, a genetic marker that makes the disease difficult-to-treat,” said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development. “Venclexta is the first approved medicine designed to trigger a natural process that helps cells self-destruct, and is a new way to help people who have been previously treated and have this high-risk form of the disease.”

Possible serious side effects with Venclexta include pneumonia, low white blood cell count with fever, fever, abnormal immune response that results in low red blood cell count, low red blood cell count and tumor lysis syndrome (TLS). The most common side effects of Venclexta include low white blood cell count, diarrhea, nausea, low red blood cell count, upper respiratory tract infection, low platelet count and tiredness.

The FDA's Accelerated Approval Program allows conditional approval of a medicine that fills an unmet medical need for a serious condition based on early evidence suggesting clinical benefit. This indication is approved under accelerated approval based on ORR. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Venclexta will be available to people in the United States within approximately one week. For those who qualify, Genentech and AbbVie plan to offer patient assistance programs for people taking Venclexta.

Venclexta was granted Breakthrough Therapy Designation by the FDA for the treatment of people with previously treated (relapsed or refractory) CLL with 17p deletion. Breakthrough Therapy Designation is designed to expedite the development and review of medicines intended to treat serious or life-threatening diseases and to help ensure people have access to them through FDA approval as soon as possible. The New Drug Application for Venclexta was granted Priority Review, a designation for medicines that the FDA has determined to have the potential to provide significant improvements in the treatment, prevention or diagnosis of a disease.

A Marketing Authorization Application (MAA) has also been validated by the European Medicines Agency (EMA).

#### **About the M13-982 Study**

M13-982 (NCT01889186) is a Phase II, open-label, single arm, multicenter study evaluating the safety and efficacy of Venclexta (400 mg orally once daily following a weekly ramp-up schedule for the first five weeks) in patients with relapsed, refractory or previously untreated chronic lymphocytic leukemia (CLL) with 17p deletion. The study included 106 patients with relapsed or refractory disease with 17p deletion. In the study, 17p deletion was confirmed in blood samples from patients using the Vysis CLL FISH Probe Kit, which is FDA-approved for selection of patients for Venclexta treatment. The primary endpoint of the study is overall response rate (ORR) as determined by an independent review committee (IRC), and secondary endpoints include complete response (CR), partial response (PR) and duration of response (DOR). The level of minimal residual disease (MRD) in peripheral blood and bone marrow was assessed in a subset of patients. Results showed:

- The study met its primary endpoint, with an ORR of 80.2 percent with Venclexta,
  - as assessed by IRC (95 percent CI 71.3-87.3).

- In addition, 7.5 percent of patients achieved a complete response with complete or incomplete recovery of blood counts in the bone marrow (5.7 percent CR, 1.9 percent CRi, respectively).
- Median DOR has not been reached with approximately 12 months median follow-up (DOR range: 2.9 to more than 19.0 months).
- MRD was evaluated in the blood and bone marrow for those who achieved a CR or CRi following treatment with Venclexta. Three percent (3/106) were MRD-negative, meaning no cancer could be detected using a specific test.

A pooled safety analysis of 240 patients with previously treated CLL from three clinical trials showed serious side effects were reported in 43.8 percent of patients. The most frequent serious side effects (occurring in at least 2 percent of patients) were pneumonia, low white blood cell count with fever, fever, abnormal immune response that results in low red blood cell count, low red blood cell count and tumor lysis syndrome (TLS). The most common Grade 3 or 4 side effects were low white blood cell count (41 percent), low red blood cell count (18 percent) and low platelet count (15 percent).

#### **About Chronic Lymphocytic Leukemia (CLL)**

CLL is the most common type of adult leukemia, and in 2016, there will be an estimated 4,660 deaths from the disease in the United States. Although signs of CLL may disappear for a period of time after initial treatment, the disease is considered incurable and many people will require additional treatment due to the return of cancerous cells.

In certain cases of CLL, a part of chromosome 17 is lost and along with it an important gene that controls apoptosis (programmed cell death) called p53. The 17p deletion is found in 3 to 10 percent of previously untreated cases and up to 30 to 50 percent of relapsed or refractory cases.

#### **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 chronic lymphocytic leukemia (CLL) has been associated with resistance to certain therapies. It is believed that blocking BCL-2 may restore the signaling system that tells cells, including cancer cells, to self-destruct. Venclexta is being developed by AbbVie and Roche. Together, the companies are committed to research with Venclexta, which is currently being evaluated in Phase III clinical trials for the treatment of relapsed, refractory and previously untreated CLL, along with studies in several other cancers. Venclexta is jointly

commercialised by AbbVie and Genentech, a member of the Roche Group, in the United States and commercialised by AbbVie outside of the United States.

### **About Roche in haematology**

For more than 20 years, Roche has been developing medicines that redefine treatment in haematology. Today, we're 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 in collaboration with AbbVie, Venclexta (venetoclax), Roche's pipeline of investigational haematology medicines includes an anti-PDL1 antibody (atezolizumab/MPDL3280A), 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 oncology, with the development of the investigational haemophilia A treatment emicizumab (ACE910).

### **About Roche**

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives.

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. 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.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. Twenty-nine 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 seven years in a row by the Dow Jones Sustainability Indices.

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2015 employed more than 91,700 people worldwide. In 2015, Roche invested CHF 9.3 billion in R&D and posted sales of

CHF 48.1 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](http://www.roche.com).

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