Basel, 7 December 2015

Pivotal Phase II study showed nearly 80 percent of people with hard-to-treat type of chronic lymphocytic leukaemia responded to investigational medicine venetoclax

- Regulatory applications for venetoclax have been submitted to the U.S. Food and Drug Administration and European Medicines Agency
- Additional results in previously treated chronic lymphocytic leukaemia from a separate Phase Ib study published online today in New England Journal of Medicine

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new, positive data from the Phase II M13-982 study of venetoclax, an investigational medicine being developed in partnership with AbbVie. Results of the study showed a clinically meaningful reduction in the number of cancer cells (overall response rate, ORR) in 79.4 percent of people with previously treated (relapsed or refractory) chronic lymphocytic leukaemia (CLL) with 17p deletion. No unexpected safety signals were reported for venetoclax.

“The high response rates, including complete responses, and duration of response demonstrate the potential of venetoclax to help people with this hard-to-treat type of leukaemia,” said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development. “This is a patient population that has very few treatment options, and we are working with AbbVie to bring this new option to people as quickly as possible.”

These pivotal data from the Phase II M13-982 study were featured in the official press program of the 57th American Society of Hematology (ASH) Annual Meeting in Orlando on Sunday, December 6, and will be presented during the Late-Breaking Abstracts Session on Tuesday, December 8, at 7:30 A.M. EST by Dr. Stephan Stilgenbauer, University of Ulm, Germany (Abstract #LBA6). The results show:

- The study met its primary endpoint, with an ORR of 79.4 percent with venetoclax, as assessed by an independent review committee (IRC). In addition, 7.5 percent of people achieved a complete
response with or without complete recovery (complete response without normal blood counts) in the bone marrow (CR/CRi).

- Forty-five people had an assessment for minimal residual disease (MRD) in the blood. Notably 18 people (17 percent of the total, 21 percent of responders) achieved MRD-negativity, meaning no cancer could be detected using a specific test. Ten of these 18 people also had bone marrow assessments and six were MRD-negative.

- At one year, 84.7 percent of all responses and 94.4 percent of MRD-negative responses were maintained. The one-year progression-free survival (PFS) and overall survival (OS) rates were 72 percent and 86.7 percent, respectively.

- No unexpected safety signals were reported. The most common Grade 3-4 adverse events were low white blood cell count (40 percent), low red blood cell count (18 percent), and low platelet count (15 percent). Grade 3 or higher infection occurred in 20 percent of people. Laboratory tumour lysis syndrome was reported in five people; none had clinical consequences.

Data for venetoclax as a monotherapy or in combinations with other medicines across multiple blood cancers, including CLL, non-Hodgkin’s lymphoma (NHL), multiple myeloma (MM) and acute myeloid leukaemia (AML), will also be presented during the ASH Annual Meeting.

Separately, positive results in people with CLL included in the Phase I M12-175 study of venetoclax were published online today in the *New England Journal of Medicine*. The findings support the potential of venetoclax monotherapy for people with relapsed or refractory CLL, including those with 17p deletion.

AbbVie has submitted a New Drug Application (NDA) for venetoclax to the U.S. Food and Drug Administration (FDA) under breakthrough therapy designation (BTD), based in part on results of the M13-982 study. Venetoclax received BTD from the FDA earlier this year for the treatment of people with relapsed or refractory chronic lymphocytic leukaemia harbouring the 17p deletion. AbbVie has also submitted a marketing authorization application (MAA) to the European Medicines Agency (EMA). Submissions to other regulatory authorities around the world are planned in 2016.

**About Study M13-982**

M13-982 (NCT01889186) is a Phase II, open label, single arm, multi-centre study evaluating the efficacy and safety of venetoclax in patients with relapsed, refractory or previously untreated CLL harbouring the 17p deletion. The main study cohort included 107 patients with relapsed or refractory disease (all patients except
for one had 17p deletion) and approximately 50 patients with relapsed, refractory or previously untreated disease have been enrolled in the safety expansion cohort. 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), duration of response (DOR), progression-free survival (PFS) and overall survival (OS). The level of minimal residual disease (MRD) in peripheral blood and/or bone marrow was assessed in a subset of people.

**About Study M12-175**

M12-175 (NCT01328626) is a Phase I, open-label, multi-centre study of venetoclax in people with relapsed or refractory chronic lymphocytic leukaemia (CLL), small lymphocytic lymphoma (SLL) or non-Hodgkin’s lymphoma (NHL). The study involved an initial dose-escalation phase, followed by an expanded safety phase. The study enrolled approximately 116 patients with relapsed or refractory CLL or SLL, and approximately 95 patients with relapsed or refractory NHL. The primary endpoints of the study included safety, maximum tolerated dose (MTD) and recommended Phase II dose (RPTD). Secondary endpoints included progression-free survival (PFS), overall response rate (ORR), overall survival (OS) and duration of response. The level of minimal residual disease (MRD) in peripheral blood and/or bone marrow was assessed in people with CLL.

**About Chronic Lymphocytic Leukaemia (CLL)**

CLL is a slow-growing cancer of the blood and bone marrow that is generally considered incurable and is one of the most common adult leukaemias worldwide.¹² Most cases of CLL (95 percent) start in white blood cells called B-cells.¹ In certain cases of CLL, a part of chromosome 17 is lost and along with it an important gene that controls apoptosis called p53.³ The 17p deletion is found in 3 to 10 percent of previously untreated cases and approximately 30 to 50 percent of relapsed or refractory cases.⁴

**About Venetoclax (RG7601, GDC-0199/ABT-199)**

Venetoclax is an investigational 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). It is believed that blocking BCL-2 may restore the signalling system that tells cancer cells to self-destruct. The BCL-2 protein is linked to the development of resistance in certain blood cancers and is expressed in chronic lymphocytic leukaemia (CLL) and non-Hodgkin’s lymphoma (NHL). In collaboration with AbbVie, venetoclax is being evaluated in a robust development program as a single agent or in combination with other medicines. There are ongoing Phase II and III studies for venetoclax in CLL, and Phase I and II studies are also ongoing in...
several other blood cancers, including indolent NHL, diffuse large B-cell lymphoma (DLBCL), acute myeloid leukaemia (AML) and multiple myeloma (MM).

**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) and Gazyva/Gazyvaro (obinutuzumab), Roche’s pipeline of investigational haematology medicines includes an anti-PDL1 antibody (atezolizumab/MPDL3280A), an anti-CD79b antibody drug conjugate (polatuzumab vedotin/RG7596), a small molecule antagonist of MDM2 (idasanutlin/RG7388) and in collaboration with AbbVie, a small molecule BCL-2 inhibitor (venetoclax/RG7601/GDC-0199/ABT-199). 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**

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world’s largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche’s personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. 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 chemotherapy.

In 2014, the Roche Group employed 88,500 people worldwide, invested 8.9 billion Swiss francs in R&D and posted sales of 47.5 billion Swiss francs. 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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References