Basel, 29 July 2014

Roche’s Gazyvaro approved in Europe for patients with the most common type of leukemia

- Gazyvaro, the first type II, glycoengineered anti-CD20 monoclonal antibody is now approved in Europe for patients with previously untreated chronic lymphocytic leukemia (CLL)
- Approval is based on the phase III CLL11 study which showed that Gazyvaro plus chlorambucil chemotherapy significantly extended the amount of time people lived without their disease worsening while increasing the depth of their remissions compared to standard treatments such as chlorambucil or MabThera plus chlorambucil

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Commission has approved Gazyvaro (obinutuzumab) in combination with chlorambucil chemotherapy for the treatment of people with previously untreated chronic lymphocytic leukemia who have comorbidities making them unsuitable for an intensive therapy (full-dose fludarabine based therapy). Outside of the EU and Switzerland, Gazyvaro is marketed as Gazyva.

“We are proud to make Gazyvaro available for CLL patients in Europe,” said Sandra Horning, M.D., Roche’s Chief Medical Officer and Head, Global Product Development. “Gazyvaro is a new option that helps patients achieve deep responses to treatment that translate to longer lasting remissions.”

The European approval was based on the outcomes of the CLL11 study which was conducted in close collaboration with the German CLL Study Group. The study showed that Gazyvaro plus chlorambucil met its primary endpoint by significantly reducing the risk of disease worsening or death by 61% compared to MabThera/Rituxan plus chlorambucil (progression free survival; PFS). For patients in the Gazyvaro arm, median PFS was 26.7 months compared with 15.2 months for those in the MabThera/Rituxan arm (HR 0.39, CI 0.31-0.49, p<0.001).
Additional Gazyvaro data from the CLL11 study showed higher complete response rates (21% compared with 7%) and a ten-fold increase in the percentage of people achieving minimal residual disease (MRD) negativity* (37.7% compared with 3.3%) compared to the MabThera/Rituxan arm of the study.

Gazyvaro plus chlorambucil also increased the time people with previously untreated CLL lived (overall survival, OS) compared to those who received treatment with chlorambucil alone. The most common serious adverse events (AEs) for Gazyvaro were infusion-related reactions (IRRs), infections and low cell count of certain white blood cells (neutropenia). The incidence and severity of IRRs decreased dramatically after the first infusion and no serious IRRs have been reported beyond the first infusion. These data from the CLL11 study were published in the New England Journal of Medicine.¹

For CLL patients in Europe, Roche expects to begin launching Gazyvaro in a number of European countries in 2014. Roche is also studying Gazyvaro in other cancers of the blood where anti-CD20 antibodies have been shown to be effective, and where future combination therapies may reduce or eliminate the need for chemotherapy.

About Chronic Lymphocytic Leukemia (CLL)
CLL is the most common leukemia in Europe, representing 25-30% of all forms of leukemia.¹² Each year it is responsible for approximately 20,000 new cases and 13,000 deaths across Europe."³⁴⁵

About Gazyvaro
Outside of the EU and Switzerland, Gazyvaro is marketed as Gazyva. Gazyvaro is a new, type II, glycoengineered monoclonal antibody designed to attach to CD20, a protein found only on B cells. It attacks targeted cells both directly and together with the body’s immune system.

Gazyvaro was discovered by Roche Glycart AG, a part of the company's Pharma Research and Early Development organization. In November 2013, Gazyva became the first medicine with Breakthrough Therapy Designation approved by the FDA. It was approved in combination with chlorambucil for people with previously untreated chronic lymphocytic leukemia. Globally, Gazyvaro is also being investigated in a large clinical program, including multiple head-to-head phase III studies compared to MabThera/Rituxan in indolent non-Hodgkin lymphoma (NHL) and diffuse large B-cell lymphoma (DLBCL). Additional

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¹ In the CLL11 study, MRD negativity was defined as having less than one CLL cell in 10,000 cells in the blood after at the end of the treatment course.
combination studies with small molecule biologic modifiers are planned or underway across a range of blood cancers.

**Gazyvaro Efficacy in CLL**

CLL11 is a phase III, multicentre, open-label, randomised three-arm study conducted in close collaboration with the German CLL Study Group which is investigating the efficacy and safety profile of Gazyvaro plus chlorambucil, MabThera/Rituxan plus chlorambucil and chlorambucil alone in 781 previously untreated people with CLL and co-existing medical conditions who are in need of therapy. Stage 1 (n=589) compared Gazyvaro plus chlorambucil to chlorambucil alone and MabThera/Rituxan plus chlorambucil to chlorambucil alone. Stage 2 (n=663) compared Gazyvaro plus chlorambucil directly with MabThera/Rituxan plus chlorambucil.

The primary endpoint of the study was PFS with secondary endpoints including overall response rate (ORR), overall survival (OS), disease free survival (DFS), MRD and safety profile.

**About Roche in hematology**

For more than 20 years, Roche has been developing medicines that redefine treatment in hematology. Today, we’re investing more than ever in our effort to bring innovative treatment options to people with cancers of the blood.

In addition to MabThera and Gazyvaro, Roche’s pipeline of potential hematology medicines includes an anti-CD79b antibody drug conjugate (RG7596/polatuzumab vedotin), a small molecule antagonist of MDM2 (RG7112) and in collaboration with AbbVie, a small molecule BCL-2 inhibitor (RG7601/GDC-0199/ABT-199).

**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-
four medicines developed by Roche are included in the World Health Organisation Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy.

In 2013 the Roche Group employed over 85,000 people worldwide, invested 8.7 billion Swiss francs in R&D and posted sales of 46.8 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.

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