Obinutuzumab (GA101) significantly improved progression-free survival in people with chronic lymphocytic leukemia (CLL)

First stage of phase III study met its primary endpoint and an additional futility analysis suggested that GA101 could show superiority compared to MabThera/Rituxan in first line CLL

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from stage 1 of CLL11, a phase III randomised study to investigate the efficacy and safety profile of the investigational medicine obinutuzumab (GA101) plus chlorambucil, a chemotherapy, compared with chlorambucil alone in people with previously untreated chronic lymphocytic leukemia (CLL). An improvement in progression-free survival (PFS) was achieved: GA101 plus chlorambucil significantly reduced the risk of disease worsening or death compared to chlorambucil alone.

“The improvement in progression-free survival seen with GA101 is encouraging for people with CLL, a chronic illness of older people for which new treatment options are needed,” said Hal Barron, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “GA101 demonstrates our ongoing commitment to the research and development of new medicines for this disease.”

GA101 has been specifically designed as the first glycoengineered, type 2 anti-CD20 monoclonal antibody in development for B cell malignancies. In preclinical development GA101 has shown evidence of increased direct cell killing and antibody-dependant cellular cytotoxicity (ADCC). As a result, GA101’s clinical development program is designed to show superiority to MabThera/Rituxan in CLL and non-Hodgkin’s lymphoma (NHL).

CLL11 is a three-arm study that compares GA101 plus chlorambucil to MabThera/Rituxan plus chlorambucil or chlorambucil alone. The study includes two separate stages. Stage 1 evaluated GA101 plus chlorambucil compared to chlorambucil alone and included a pre-planned PFS futility analysis comparing GA101 plus chlorambucil to MabThera/Rituxan plus chlorambucil. The goal of this futility analysis was to evaluate the
likelihood that the study would meet its pre-specified endpoint criteria during stage 2 analysis – improved efficacy (PFS) in the direct comparison of GA101 plus chlorambucil versus MabThera/Rituxan plus chlorambucil. The independent Data and Safety Monitoring Board (DSMB) assessment concluded that stage 2 of the study should continue until its final analysis. No new safety events were reported for the GA101 or MabThera/Rituxan containing arms in the study up to the time of this analysis.

Data from CLL11 will be submitted for presentation at an upcoming medical meeting and submitted to European and other regulatory authorities as well as the US Food and Drug Administration (FDA) for potential marketing approval.

**About CLL11 (BO21004)**

CLL11 is a phase III, multicenter, open-label, randomised three-arm study to investigate the safety and efficacy profile of GA101 plus chlorambucil compared to MabThera plus chlorambucil or chlorambucil alone in nearly 800 previously untreated people with CLL and coexisting medical conditions. The study is conducted in close collaboration with the German CLL Study Group (DCLLSG). The primary endpoint of the study is PFS with secondary endpoints including overall response rate (ORR), overall survival (OS), disease free survival (DFS), molecular remission and safety profile.

**About hematological malignancies**

Hematological malignancies are cancers of the blood and include chronic lymphocytic leukemia (CLL), indolent non-Hodgkin’s lymphoma (NHL) and diffuse large B-cell lymphoma (DLBCL). By 2015 it is expected that there will be nearly 225,000 annual deaths worldwide from NHL and nearly 250,000 from leukemia.

The current standard of care in CD20+ hematological malignancies is MabThera/Rituxan (rituximab) in combination with chemotherapy or as a single agent. On 4 December 2012 Roche submitted a line-extension marketing application to the European Medicines Agency (EMA) for a subcutaneous formulation of MabThera which may shorten treatment time significantly, enabling administration over approximately five minutes compared with 2.5 hours for IV infusion.

In addition to GA101, Roche’s pipeline of potential hematologic compounds includes two antibody-drug conjugates (anti-CD79b [RG7596] and anti-CD22 [RG7593]), a small molecule BCL-2 inhibitor (RG7601) and a small molecule antagonist of MDM2 (RG7112).
About obinutuzumab (GA101)

GA101 is Roche’s most advanced drug in development for the treatment of hematological malignancies (cancers which affect the blood, bone marrow and lymph nodes). Like standard of care MabThera/Rituxan (rituximab), GA101 targets CD20 proteins found on healthy and malignant B lymphocytes (B cells). These cells die as a result. Once the cancerous cells are destroyed, the immune system is repopulated with healthy B cells.

GA101 is the first glycoengineered, type 2 anti-CD20 monoclonal antibody in development for B cell malignancies. As GA101 and MabThera/Rituxan bind to different (though overlapping) parts of CD20, it is believed that GA101 causes more direct cell death. Glycoengineering, or specific modifications which are made to the structure of GA101, increases its ability to recruit the body's immune cells to assist in attacking the cancerous cells.

GA101 therefore has the potential to be more effective than MabThera/Rituxan for the treatment of non-Hodgkin’s lymphoma and chronic lymphocytic leukemia, the most common CD20+ B cell malignancies.

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, infectious diseases, inflammation, metabolism 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 diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2012 Roche had over 82,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 45.5 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.

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