Media Release

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CHMP recommends EU approval of Roche's Gazyvaro for people with previously treated follicular lymphoma

- **In the pivotal study, treatment with Gazyvaro plus bendamustine chemotherapy reduced the risk of disease worsening or death by 52 percent compared to bendamustine alone**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the EU Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for Gazyvaro® (obinutuzumab) in combination with bendamustine chemotherapy followed by Gazyvaro maintenance as a new treatment for people with follicular lymphoma who did not respond to, or who progressed during or up to six months after treatment with MabThera® (rituximab) or a MabThera-containing regimen. Each year, approximately 19,000 people in Europe are diagnosed with follicular lymphoma, the most common type of indolent (slow-growing) non-Hodgkin lymphoma.[1,2] Follicular lymphoma is considered incurable, and most people relapse repeatedly.[3]

"Each time a person with follicular lymphoma experiences a progression of their disease, it becomes harder to treat," said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. "Progressive disease is particularly challenging after MabThera-containing therapy, and this CHMP positive opinion for Gazyvaro brings us one step closer to providing a much needed new treatment option for follicular lymphoma patients in Europe."

The CHMP's recommendation is based on results from the phase III GADOLIN study which showed that, in people with follicular lymphoma who did not respond to or who progressed during or within six months of prior MabThera/Rituxan®-based therapy, treatment with Gazyva®/Gazyvaro plus bendamustine followed by Gazyva/Gazyvaro alone resulted in a 52 percent reduction (HR=0.48, 95 percent CI 0.34-0.68, p<0.0001) in the risk of disease worsening or death (progression-free survival, PFS), compared to bendamustine alone, as evaluated by an independent review committee (IRC). The median PFS was not yet reached in those receiving the Gazyva/Gazyvaro regimen, compared with 13.8 months in those receiving bendamustine alone. As assessed by investigator review, median PFS with the Gazyva/Gazyvaro regimen was more than double that with bendamustine alone (29.2 months vs. 13.7 months; HR=0.48, 95 percent CI 0.35-0.67, p<0.0001).

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Based on this positive CHMP recommendation, a final decision regarding the approval of Gazyvaro is expected from the European Commission in the coming months. Gazyvaro is already approved in the EU in combination with chlorambucil for people with previously untreated chronic lymphocytic leukaemia (CLL) and comorbidities that make them unsuitable for full-dose fludarabine based therapy. That approval was based on data from the pivotal CLL11 study, where the combination of Gazyva/Gazyvaro plus chlorambucil showed superior efficacy when compared head-to-head with MabThera/Rituxan plus chlorambucil and chlorambucil alone.

Gazyvaro is marketed as Gazyva outside of the EU and Switzerland. In February 2016, Gazyva received approval by the US Food and Drug Administration in combination with bendamustine followed by Gazyva monotherapy as a treatment for people with follicular lymphoma who did not respond to a Rituxan-containing regimen, or whose follicular lymphoma returned after such treatment, based on the results of the GADOLIN study.

About the GADOLIN study

GADOLIN (NCT01059630; GA04753g) is a phase III open-label, multicentre, randomised two-arm study evaluating Gazyva/Gazyvaro plus bendamustine followed by Gazyva/Gazyvaro alone until disease progression or for up to two years compared to bendamustine alone. GADOLIN included 396 patients with indolent (slow-growing) non-Hodgkin lymphoma (NHL), including 321 patients with follicular lymphoma, whose disease progressed during or within six months of prior MabThera/Rituxan-based therapy. The primary endpoint of the study is progression-free survival (PFS) as assessed by IRC, with secondary endpoints including PFS as assessed by investigator review, best overall response (BOR), complete response (CR), partial response (PR), duration of response, overall survival (OS) and safety profile. Results in follicular lymphoma showed:

- The Gazyva/Gazyvaro regimen improved PFS compared to bendamustine alone, as assessed by IRC (HR=0.48, 95 percent CI 0.34-0.68, p<0.0001). Median PFS was not reached in those receiving the Gazyva/Gazyvaro regimen versus 13.8 months in those receiving bendamustine alone.
- Investigator-assessed PFS was consistent with IRC-assessed PFS. As assessed by investigator review, median PFS with the Gazyva/Gazyvaro regimen was more than double that with bendamustine alone (29.2 months vs. 13.7 months; HR=0.48, 95 percent CI 0.35-0.67, p<0.0001).
- The Gazyva/Gazyvaro regimen reduced the risk of death (OS) by 38 percent compared to bendamustine alone based on a post-hoc analysis eight months after the primary analysis (HR=0.62, 95 percent CI 0.39-0.98). The median OS has not yet been reached in either study arm.

- The most common Grade 3-4 adverse events that occurred more often (at least 2 percent or greater) in those receiving the Gazyva/Gazyvaro plus bendamustine regimen compared to those receiving bendamustine alone were low white blood cell count (neutropenia; 33 percent vs. 26 percent), infusion-related reactions (11 percent vs. 6 percent) and urinary tract infection (3 percent vs. 0 percent), respectively.

About Gazyva/Gazyvaro (obinutuzumab)

Gazyva/Gazyvaro is an engineered monoclonal antibody designed to attach to CD20, a protein found only on B-cells. Gazyva/Gazyvaro is designed to attack and destroy targeted B-cells both directly and together with the body's immune system. Gazyva/Gazyvaro is currently approved in more than 70 countries in combination with chlorambucil, for people with previously untreated chronic lymphocytic leukaemia. The approval was based on the CLL11 study, showing significant improvements with Gazyva/Gazyvaro plus chlorambucil across multiple clinical endpoints, including PFS, overall response rate (ORR), complete response rate (CR), and minimal residual disease (MRD) when compared head-to-head with MabThera/Rituxan plus chlorambucil and chlorambucil alone. Gazyva is approved in the US in combination with bendamustine, for people with follicular lymphoma based on the results of the GADOLIN study. Gazyvaro is marketed as Gazyva outside of the EU and Switzerland.

Gazyva/Gazyvaro is being studied in a large clinical programme, including the phase III GOYA and GALLIUM studies. GOYA is comparing Gazyva/Gazyvaro head-to-head with MabThera/Rituxan plus CHOP chemotherapy in first line diffuse large B-cell lymphoma (DLBCL), and GALLIUM is comparing Gazyva/Gazyvaro plus chemotherapy followed by Gazyva/Gazyvaro maintenance head-to-head with MabThera/Rituxan plus chemotherapy followed by MabThera/Rituxan maintenance in first line indolent non-Hodgkin lymphoma (iNHL). Additional combination studies investigating Gazyva/Gazyvaro with other approved or investigational medicines, including cancer immunotherapies and small molecule inhibitors, are planned or underway across a range of blood cancers.

About Follicular Lymphoma

Follicular lymphoma is the most common indolent (slow-growing) form of non-Hodgkin lymphoma (NHL), accounting for about one in five cases of NHL.[1] It is considered incurable and relapse is common. Every year, approximately 19,000 people in Europe are diagnosed with this type of NHL.[2] It is estimated that each year more than 75,000 people are diagnosed with follicular lymphoma worldwide.[2]

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.

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