Media Release

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FDA approves Roche's Gazyva (obinutuzumab) for certain people with previously treated follicular lymphoma

- **This is the second FDA approval for Gazyva based on a positive Phase III study**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) approved Gazyva® (obinutuzumab) plus bendamustine chemotherapy followed by Gazyva alone as a new treatment for people with follicular lymphoma who did not respond to a Rituxan® (rituximab)-containing regimen, or had their follicular lymphoma return after such treatment. Follicular lymphoma is the most common type of indolent (slow-growing) non-Hodgkin lymphoma (NHL) and accounts for approximately one in five cases of NHL.[1]

"People with follicular lymphoma whose disease returns or worsens despite treatment with a Rituxan-containing regimen need more options because the disease becomes more difficult to treat each time it comes back," said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. "Gazyva plus bendamustine provides a new treatment option that can be used after relapse to significantly reduce the risk of progression or death."

The approval is based on results from the Phase III GADOLIN study, which showed that, in people with follicular lymphoma whose disease progressed during or within six months of prior MabThera®/Rituxan-based therapy, Gazyva/Gazyvaro® plus bendamustine followed by Gazyva/Gazyvaro alone demonstrated 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 assessed by an independent review committee (IRC). The supplemental Biologics License Application based on these data was granted Priority Review, a designation granted to medicines that the FDA has determined to have the potential to provide significant improvements in the treatment, prevention or diagnosis of a disease.

The safety of Gazyva/Gazyvaro was evaluated based on 392 people in the GADOLIN study with indolent NHL of whom 81 percent had follicular lymphoma. The most common Grade 3-4 side effects of this

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Gazyva/Gazyvaro regimen were low white blood cell counts, infusion reactions and low platelet counts. The most common side effects of this Gazyva/Gazyvaro regimen were infusion reactions, low white blood cell counts, nausea, fatigue, cough, diarrhoea, constipation, fever, low platelet counts, vomiting, upper respiratory tract infection, decreased appetite, joint or muscle pain, sinus infection, low red blood cell counts, general weakness and urinary tract infection.

With this approval, Gazyva is approved in the United States to treat two common types of blood cancer. Gazyva is also approved in combination with chlorambucil for people with previously untreated chronic lymphocytic leukemia (CLL) based on data from the pivotal CLL11 study, which compared Gazyva/Gazyvaro plus chlorambucil head-to-head with MabThera/Rituxan plus chlorambucil.

Marketing applications for Gazyva/Gazyvaro based on the GADOLIN study results have also been submitted to other regulatory authorities, including the European Medicines Agency (EMA), for approval consideration.

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 413 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 an independent review committee (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).

- In addition, BOR for those receiving the Gazyva/Gazyvaro regimen was 78.7 percent (15.5 percent CR, 63.2 percent PR) compared to 74.7 percent for those receiving bendamustine alone (18.7 percent CR, 56 percent PR), as assessed by IRC.
- The median duration of response was not reached for those receiving the Gazyva/Gazyvaro regimen and was 11.6 months for those receiving bendamustine alone.
- 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 regimen compared to those receiving bendamustine alone were low white blood cell count (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 60 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. Gazyva is marketed as Gazyvaro in 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. It is considered incurable and relapse is common. In the United States, it was estimated that more than 14,000 new cases of follicular lymphoma would be diagnosed in 2015. It is estimated that more than 75,000 people are diagnosed with follicular lymphoma annually worldwide.[1,2]

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) 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

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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