

Basel, 5 December 2016

## **Roche's Gazyva/Gazyvaro Helped People With Previously Untreated Follicular Lymphoma Live Significantly Longer Without Their Disease Worsening Compared to MabThera/Rituxan**

- **First Phase III study to show superior progression-free survival compared to MabThera/Rituxan-based standard of care treatment for most common slow-growing form of non-Hodgkin lymphoma**
- **Results were presented during the Plenary Scientific Session at 58<sup>th</sup> American Society of Hematology Annual Meeting**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced data from the positive, pivotal Phase III GALLIUM study that compared Gazyva®/Gazyvaro® (obinutuzumab) plus chemotherapy followed by Gazyva/Gazyvaro alone head-to-head against MabThera®/Rituxan® (rituximab) plus chemotherapy followed by MabThera/Rituxan alone for people with previously untreated follicular lymphoma. At a pre-planned interim analysis in May 2016, an independent data monitoring committee determined that the study met its primary endpoint early. The results showed Gazyva/Gazyvaro-based treatment reduced the risk of disease worsening or death (progression-free survival; PFS, as assessed by investigator) by 34 percent compared to MabThera/Rituxan-based treatment (HR=0.66; 95% CI 0.51-0.85, p=0.0012). Median PFS was not yet reached. Adverse events with either Gazyva/Gazyvaro or MabThera/Rituxan were consistent with those seen in previous studies.

“Follicular lymphoma, the most common slow-growing form of non-Hodgkin lymphoma, is an incurable blood cancer characterized by cycles of remission and disease progression, and becomes harder to treat with every relapse,” said Sandra Horning, M.D., Roche's Chief Medical Officer and Head of Global Product Development. “This study of Gazyva/Gazyvaro-based treatment is the first and only Phase III trial to date to show superior progression-free survival compared to MabThera/Rituxan-based treatment, the current standard of care, in previously untreated follicular lymphoma.”

The primary results from the GALLIUM study (Abstract #6) were presented during the Plenary Scientific Session of the 58th American Society of Hematology (ASH) Annual Meeting in San Diego by Dr. Robert

Marcus, King's College Hospital, London and the National Cancer Research Institute (NCRI), on Sunday, December 4 at 2:00 P.M. PST. Additionally, an analysis of minimal residual disease (MRD) status in the GALLIUM study (Abstract #613) was presented in a separate oral session by Dr. Christiane Pott, University Hospital Schleswig-Holstein, Kiel, Germany, and the German Low Grade Lymphoma Study Group (GLSG) on Monday, December 5 at 7:00 A.M. PST.

GALLIUM is the third positive Phase III study for Gazyva/Gazyvaro, following the CLL11 study in patients with previously untreated chronic lymphocytic leukaemia (CLL) and the GADOLIN study in patients with indolent (slow-growing) non-Hodgkin lymphoma whose disease progressed during or within six months of prior MabThera/Rituxan-based therapy. The results of the GALLIUM study will be submitted to health authorities around the world for approval consideration.

### **About the GALLIUM study**

GALLIUM (NCT01332968) is a global Phase III open-label, multi-centre, randomised two-arm study examining the efficacy and safety of Gazyva/Gazyvaro plus chemotherapy followed by Gazyva/Gazyvaro alone for up to two years, as compared head-to-head against MabThera/Rituxan plus chemotherapy followed by MabThera/Rituxan alone for up to two years. Chemotherapies used were CHOP, CVP or bendamustine and were selected by each participating study site prior to beginning enrolment. GALLIUM included 1401 patients with previously untreated indolent non-Hodgkin lymphoma (iNHL), of which 1202 patients had follicular lymphoma. The primary endpoint of the study was investigator-assessed PFS in patients with follicular lymphoma, with secondary endpoints including PFS assessed by independent review committee (IRC), PFS in the overall study population (iNHL), response rate (overall response, ORR; and complete response, CR), overall survival (OS), and safety. The GALLIUM study is being conducted in cooperation with the GLSG (Germany), the East German Study Group Hematology and Oncology (OSHO; Germany) and the NCRI (United Kingdom).

A summary of the GALLIUM study results presented at ASH is included below.

<b>Study Group</b>	Patients with previously untreated follicular lymphoma	
<b>Treatment Group</b>	Gazyva/Gazyvaro + chemotherapy, followed by Gazyva/Gazyvaro alone	MabThera/Rituxan + chemotherapy, followed by MabThera/Rituxan alone
<b>N=</b>	601	601
<b>PFS (primary and secondary endpoints)<sup>1</sup></b>		
<b>PFS</b>	Investigator: HR=0.66 (0.51, 0.85), p=0.0012 Independent: HR=0.71 (0.54, 0.93), p=0.0138	
<b>PFS Rate at 3 Years</b>	Investigator: 80.0% Independent: 81.9%	Investigator: 73.3% Independent: 77.9%
<b>OS (secondary endpoint)</b>		
<b>OS</b>	HR = 0.75 (0.49, 1.17), p=0.21	
<b>OS Rate at 3 Years</b>	94.0%	92.1%
<b>Time to Next Treatment (TTNT; secondary endpoint)</b>		
<b>TTNT</b>	HR = 0.68 (0.51, 0.91), p=0.0094	
<b>TTNT at 3 Years</b>	87.1%	81.2%
<b>Response Rates (at end of induction; secondary endpoints)<sup>2</sup></b>		
<b>ORR</b>	88.5%	86.9%
<b>CR</b>	19.5%	23.8%
<b>Partial Response (PR)</b>	69.1%	63.1%
<b>Minimal Residual Disease (MRD; exploratory endpoint) [Pott et al.]</b>		
<b>N =</b>	351	345
<b>MRD-Negativity<sup>3</sup> (in blood and/or bone marrow at end of treatment with Gazyva/Gazyvaro or MabThera/Rituxan plus chemotherapy)</b>	92.0%	84.9%
	p=0.0041	
<b>Safety (secondary endpoint)</b>		
<b>N=</b>	595	597
<b>Adverse Events (AEs)</b>	<ul style="list-style-type: none"> <li>• AEs observed with Gazyva/Gazyvaro and MabThera/Rituxan were consistent with those seen in previous clinical trials when each was combined with various chemotherapies.</li> <li>• The overall rate of Grade 3 or higher AEs occurring in the Gazyva/Gazyvaro and MabThera/Rituxan arms was 74.6% and 67.8%, respectively.</li> <li>• The most common Grade 3 or higher AEs that occurred more often in the Gazyva/Gazyvaro versus MabThera/Rituxan arm were low white blood cell counts (neutropenia, 43.9% vs. 37.9%; leukopenia, 8.6% vs.</li> </ul>	

	<p>8.4%), low white blood cell count with fever (febrile neutropenia, 6.9% vs. 4.9%), infusion-related reactions<sup>4</sup> (12.4% vs. 6.7%), low platelet count (thrombocytopenia, 6.1% vs. 2.7%), infections (20.0% vs. 15.6%) and second neoplasms (4.7% vs. 2.7%).</p> <ul style="list-style-type: none"> <li>• Fatal AEs occurred in 4.0% of people in the Gazyva/Gazyvaro arm compared to 3.4% of people in the MabThera/Rituxan arm.</li> </ul>
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<sup>1</sup> Primary endpoint is PFS as assessed by investigator; median follow-up of 34.5 months

<sup>2</sup> Measured by computerized tomography (CT) scans

<sup>3</sup> MRD-negativity means no cancer can be detected in the blood or bone marrow using a specific highly sensitive test

<sup>4</sup> Defined as any AE occurring during or within 24 hours of infusion of Gazyva/Gazyvaro or MabThera/Rituxan and considered drug-related

### **About Gazyva/Gazyvaro (obinutuzumab)**

Gazyva/Gazyvaro is an engineered monoclonal antibody designed to attach to CD20, a protein expressed on certain B-cells, but not on stem cells or plasma 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 80 countries in combination with chlorambucil, for people with previously untreated chronic lymphocytic leukaemia. The approvals were 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.

In February 2016, Gazyva was approved by the US Food and Drug Administration in combination with bendamustine followed by Gazyva alone for people with follicular lymphoma who did not respond to a Rituxan-containing regimen, or whose follicular lymphoma returned after such treatment. In June 2016, Gazyvaro was approved by the European Commission in combination with bendamustine followed by Gazyvaro maintenance in people with follicular lymphoma who did not respond or who progressed during or up to six months after treatment with MabThera or a MabThera-containing regimen. Both approvals were based on the phase III GADOLIN study, showing a significant improvement in progression-free survival with Gazyva/Gazyvaro-based therapy compared to bendamustine alone. Gazyva is marketed as Gazyvaro in the EU and Switzerland.

Additional combination studies investigating Gazyva/Gazyvaro with other approved or investigational medicines, including cancer immunotherapies and small molecule inhibitors, are 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.<sup>2</sup> It is considered incurable and relapse is common. It is estimated that more than 75,000 people are diagnosed with follicular lymphoma each year worldwide.<sup>3</sup>

### **About Roche in haematology**

For more than 20 years, Roche has been developing medicines that redefine treatment in haematology. Today, we are 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 Venclexta™/Venclyxto™(venetoclax) in collaboration with AbbVie, Roche’s pipeline of investigational haematology medicines includes Tecentriq®(atezolizumab), 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 malignancy, 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 eight 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](http://www.roche.com).

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### **References**

1. GAZYVA full Prescribing Information. South San Francisco, CA: Genentech USA, Inc.; February 2016.
2. Shankland KR, et al: Non-Hodgkin lymphoma. Lancet 380 (9844): 848-57, 2012.
3. Ferlay J, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr> (accessed on 19/05/2016).