Media Release

Basel, 7 December 2015

New data from pivotal study showed Roche's Gazyva/Gazyvaro induced deep remissions and provided meaningful quality of life improvements in people with difficult-to-treat indolent non-Hodgkin lymphoma

- **Minimal residual disease-negativity rates were almost double for people receiving Gazyva/Gazyvaro plus bendamustine versus bendamustine alone in patients with follicular lymphoma**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced follow-up results from the pivotal phase III GADOLIN study in people with indolent non-Hodgkin lymphoma (iNHL) who relapsed during or within six months after treatment with a MabThera®/Rituxan® (rituximab)-based regimen. In a subgroup analysis of people with follicular lymphoma, the most common type of iNHL, treatment with Gazyva®/Gazyvaro® (obinutuzumab) plus bendamustine provided significantly greater depth of remission at end of induction compared to bendamustine alone, as measured by minimal residual disease (MRD)-negativity (82% vs 43%, respectively; $p<0.0001$)[1]. MRD assessment was an exploratory analysis.

"Building on the significant progression-free survival benefit previously reported in the GADOLIN study, these follow-up data show that Gazyva/Gazyvaro-based treatment achieves significant rates of deep remission, known as minimal residual disease negativity, at the end of induction treatment," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "This achievement is particularly impressive in this difficult-to-treat patient population with follicular lymphoma, for whom treatment options are limited."

An additional analysis of the overall study population in the GADOLIN trial showed that a greater proportion of patients in the Gazyva/Gazyvaro arm reported a meaningful improvement in health-related quality of life (HRQoL) compared to those treated with bendamustine alone. HRQoL was a secondary endpoint in the study. This finding suggests that increased progression-free survival (PFS) does not appear to come at the expense of an increase in treatment-related toxicity that adversely impacts a patient's quality of life.

F. Hoffmann-La Roche Ltd 4070 Basel Switzerland
Group Communications Roche Group Media Relations
Tel. +41 61 688 88 88 Fax +41 61 688 27 75 www.roche.com

Data from the GADOLIN MRD subgroup analysis will be presented in a poster session today, Monday December 7 by Dr. Kirsten Mundt, Senior Scientist, Roche at the 57th American Society of Hematology (ASH), in Orlando, Florida. Data from the GADOLIN HRQoL analysis was also presented on Saturday, December 5, during a poster session by Dr. Peter Trask, Principal Scientist, Genentech and Professor Bruce Cheson from the Georgetown University Hospital, Washington DC, USA.

The FDA has accepted for priority review a supplemental Biologics License Application (sBLA) for Gazyva/Gazyvaro in the treatment of people with follicular lymphoma who relapsed after or are refractory to a MabThera/Rituxan-containing regimen. Marketing applications have also been submitted to other global regulatory authorities, including the EMA, for approval consideration in the treatment of people with follicular lymphoma who did not respond or who progressed during or up to six months after treatment with MabThera/Rituxan or a MabThera/Rituxan-containing regimen.

About the GADOLIN study

GADOLIN is a phase III open-label, multicentre, randomised two-arm study evaluating Gazyva/Gazyvaro plus bendamustine followed by Gazyva/Gazyvaro alone for up to two years, compared to bendamustine alone. GADOLIN included 413 patients with iNHL 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, response rate (RR), best response and overall survival (OS). GADOLIN data presented at the annual meeting of the American Society of Clinical Oncology (ASCO) in June this year showed the median PFS (mPFS) was not reached in the Gazyva/Gazyvaro-based treatment group versus 14.9 months with bendamustine alone (HR=0.55, p=0.0001) as assessed by IRC. The median PFS with Gazyva/Gazyvaro-based treatment was more than double that with bendamustine alone (29.2 months versus 14.0 months (HR=0.52, p<0.0001) as assessed by investigator review. No unexpected safety signals were identified in the Gazyva/Gazyvaro-based treatment arm. Grade 3-4 adverse events that occurred in at least two percent of patients in the Gazyva/Gazyvaro-treated group or bendamustine alone group included low white blood cell count (33% versus 26.3%), low blood platelet count (10.8% versus 16.2%), infusion-related reactions (10.8% versus 5.6%), low red blood cell count (7.7% versus 10.1%), low white blood cell count with fever (4.6% versus 3.5%), nausea (1% versus 3%), fatigue (1.5% versus 2.5%), diarrhoea (1% versus 2.5%), vomiting (2.1% versus 1%), respectively.

The MRD data from the subgroup analysis of people with follicular lymphoma will be presented at a poster

presentation today, Monday 7 December, from 6:00-8:00 PM ET *[Abstract #3978]*.

Patients	**Follicular Lymphoma (N= 321/396 total)**	
Evaluable Patients	93*	
Study Groups	**G plus B, followed by G alone (n=51 evaluable)**	**B alone (N=42 evaluable)**
Minimal Residual Disease (MRD) Negative		
End of Induction (EOI)	82% (42/51)	43% (18/42)
	p<0.0001	
Response Rates by MRD Status		
CR rate	6% (2/33) of MRD-positive patients 28% (17/60) of MRD-negative patients	
PFS by MRD Status		
PFS at 24 months post-EOI for MRD-neg patients	74% (mPFS not reached)	21% (mPFS 7.6 months)
PFS at 24 months post-EOI for MRD non-responders (MRD-pos)	0% (mPFS 5.4 months)	0% (mPFS 3.0 months)

* Induction treatment completed at the clinical cut-off date; samples available at baseline and end of treatment

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 non-Hodgkin lymphoma

There are two main types of lymphoma: Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). NHL represents approximately 85 percent of all lymphomas diagnosed[2]. Approximately 200,000 people die each year from NHL worldwide and approximately one person is newly diagnosed every 90 seconds[2]. There are more than 60 different types of NHL that fall under two subsets, aggressive and indolent (slow growing). The most common type of indolent NHL is follicular lymphoma (FL), found in about 25 percent of all NHL patients[3]. Most cases of NHL start in B-lymphocytes, cells that are part of the body's immune system and help to defend the body against infections. B-cell lymphoma develops when these cells become cancerous and begin to multiply and collect in the lymphatic system such as in lymph nodes, lymphatic tissues or the spleen.

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

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

In 2014, the Roche Group employed 88,500 people worldwide, invested 8.9 billion Swiss francs in R&D and posted sales of 47.5 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**.

Roche Group Media Relations

Phone: +41 -61 688 8888 / e-mail: roche.mediarelations@roche.com

- Nicolas Dunant (Head)
- Ulrike Engels-Lange
- Nicole Rüppel
- Claudia Schmitt

References

[1]Pott et al. Analysis of Minimal Residual Disease in Follicular Lymphoma Patients in GADOLIN, a phase III Study of Obinutuzumab plus Bendamustine versus Bendamustine in Refractory Indolent Non-Hodgkin Lymphoma. *[Abstract #3978]*.

[2] 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 09/11/2015).

[3] Salles, GA. Clinical features, prognosis and treatment of follicular lymphoma. Hematology Am Soc Hematol Educ Program. 2007: 216–225.