Media Release

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Phase II data showed Roche's investigational polatuzumab vedotin plus bendamustine and MabThera/Rituxan (BR) increased complete response rates compared to BR alone in previously treated aggressive lymphoma

- **Polatuzumab vedotin combination demonstrated improvements across multiple efficacy measures compared to BR alone in relapsed or refractory diffuse large B-cell lymphoma**
- **These data led to FDA Breakthrough Therapy and EMA PRIME (PRIority MEdicines) designations**
- **Results will be presented at the 59th American Society of Hematology Annual Meeting**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the randomised phase II GO29365 study that compared polatuzumab vedotin in combination with bendamustine plus MabThera®/Rituxan® (rituximab) (BR) against BR alone in people with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant. The study met its primary endpoint, demonstrating that the addition of polatuzumab vedotin to BR increased complete response (CR) rates from 15% to 40% (p=0.012) at the end of treatment, as measured by positron emission tomography (PET) and assessed by an independent review committee (IRC). No unexpected safety signals were observed with the addition of polatuzumab vedotin to BR.

"As many as forty percent of people with diffuse large B-cell lymphoma do not respond to initial therapy or experience the return of their disease, at which point their treatment options are limited and the prognosis is poor," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "The promising efficacy observed for polatuzumab vedotin in this study supports its potential as a new treatment option for people previously treated for this aggressive blood cancer, and we look forward to discussing the results with health authorities."

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The data will be presented in a poster session on Sunday, 10 December at the 59th American Society of Hematology (ASH) Annual Meeting by Laurie Sehn, MD, British Columbia Cancer Agency/University of British Columbia.

The results showed:

- Polatuzumab vedotin plus BR significantly improved CR rates from 15% with BR alone to 40% (p=0.012), as measured by PET and assessed by IRC. A CR means no cancer could be detected at that time.
- The benefit observed was consistent across secondary endpoints, including improvements in investigator-assessed best objective response (OR; CR and partial response, PR) and CR with polatuzumab vedotin plus BR (70.0% OR, 57.5% CR) compared to BR alone (32.5% OR, CR 20.0%).
- Exploratory endpoints also improved with the addition of polatuzumab vedotin to BR:
  - Patients treated with polatuzumab vedotin plus BR lived longer than those receiving BR alone (median overall survival; 11.8 months vs. 4.7 months; HR 0.35; 95% CI 0.19-0.67; p=0.0008).
  - The addition of polatuzumab vedotin also increased the time until disease worsening or death (median progression-free survival: 6.7 months vs. 2.0 months; HR 0.31; 95% CI 0.18-0.55; p<0. 0001), and the time between first response to treatment and disease worsening (duration of response: 8.8 months vs. 3.7 months).
- No unexpected safety signals were observed with the addition of polatuzumab vedotin to BR. The most common Grade 3-4 adverse events with polatuzumab vedotin plus BR compared to BR alone, respectively, were low white blood cell count (46.2% vs. 35.9%), low white blood cell count with fever (10.3% vs. 5.1%), low platelet count (33.3% vs. 20.5%), anaemia (25.6% vs. 12.8%) and infections (17.9% vs. 17.9%).

Based on results from this study, polatuzumab vedotin was recently granted Breakthrough Therapy Designation by the US Food and Drug Administration and PRIME (PRIority MEdicines) designation by the European Medicines Agency for the treatment of people with relapsed or refractory DLBCL. There are a number of ongoing studies evaluating the efficacy and safety of polatuzumab vedotin for several types of non-Hodgkin lymphoma, including combinations with Gazyva® /Gazyvaro® (obinutuzumab), MabThera/Rituxan, Venclexta™/Venclyxto™ (venetoclax) and Tecentriq® (atezolizumab).

About the GO29365 study

GO29365 is a global, phase Ib/II randomised study evaluating the safety, tolerability and activity of polatuzumab vedotin in combination with MabThera /Rituxan (rituximab) or Gazyva /Gazyvaro (obinutuzumab) plus bendamustine in relapsed or refractory (R/R) follicular lymphoma or diffuse large B-cell lymphoma (DLBCL). The phase II stage randomised 80 patients with heavily pre-treated R/R DLBCL to receive either bendamustine plus MabThera/Rituxan (BR), or BR in combination with polatuzumab vedotin. Patients enrolled had received a median of two prior therapies (a range of 1-7 prior therapies in the polatuzumab vedotin arm and range of 1-5 prior therapies in the BR alone arm). The primary endpoint was complete response (CR) at the end of treatment, as measured by positron emission tomography (PET) and assessed by an independent review committee (IRC). Secondary endpoints included objective response (OR; CR and partial response, PR) by investigator assessment and best objective response at the end of treatment by investigator and IRC assessment. Exploratory endpoints included duration of response (DOR), progression-free survival (PFS), event-free survival (EFS) and overall survival (OS).

About polatuzumab vedotin

Polatuzumab vedotin is a first-in-class anti-CD79b antibody drug conjugate (ADC) currently being investigated for the treatment of several types of non-Hodgkin lymphoma (NHL). The CD79b protein is highly specific and expressed in the majority of types of B-cell NHL, making it a promising target for the development of new therapies.[1] Polatuzumab vedotin binds to CD79b and destroys these B-cells via a targeted approach, which is thought to minimise the effects on normal cells while maximising tumour cell death. Polatuzumab vedotin is being developed by Roche utilising Seattle Genetics ADC technology.

About diffuse large B-cell lymphoma

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL), accounting for about one in three cases of NHL.[2] DLBCL is an aggressive (fast-growing) type of NHL, which is generally responsive to treatment in the frontline.[3] However, as many as 40% of patients will relapse, at which time salvage therapy options are limited and survival is short.[3] Approximately 123,000 people worldwide are estimated to be diagnosed with DLBCL each year.[4]

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 Hemlibra (emicizumab), a bispecific monoclonal antibody for the treatment of haemophilia A.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. 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.

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. Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. Thirty 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 nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 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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