

FDA grants Priority Review to Roche's polatuzumab vedotin in previously treated aggressive lymphoma

- **Diffuse large B-cell lymphoma is an aggressive type of blood cancer that typically becomes harder to treat each time it returns**
- **Polatuzumab vedotin has shown significant potential to improve outcomes in people living with this disease**

Basel, 19 February 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has accepted the company's Biologics License Application (BLA) and granted Priority Review for polatuzumab vedotin in combination with bendamustine plus Rituxan® (rituximab) (BR) for the treatment of people with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL). The FDA is expected to make a decision on approval by 19 August 2019.

“Polatuzumab vedotin, a potential first-in-class antibody drug conjugate, in combination with bendamustine and Rituxan, improved clinical outcomes including survival in some people with relapsed or refractory diffuse large B-cell lymphoma compared to bendamustine and Rituxan alone,” said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. “We are working with the FDA to bring this important new option to patients with this aggressive disease as quickly as possible.”

The BLA is based on results of the GO29365 study, which showed that polatuzumab vedotin plus BR improved median overall survival compared to BR alone (12.4 vs. 4.7 months, HR=0.42; 95% CI 0.24-0.75; exploratory endpoint), in people with R/R DLBCL not eligible for a haematopoietic stem cell transplant. The study also showed that 40% of people treated with polatuzumab vedotin plus BR achieved a complete response (CR), while only 18% of people treated with BR alone achieved a CR (primary endpoint, as measured by positron emission tomography; CR rates assessed by independent review committee). A CR means no cancer could be detected at that time.

Priority Review designation is granted to medicines that the FDA considers to have the potential to provide significant improvements in the safety and effectiveness of the treatment, prevention or diagnosis of a serious disease. Polatuzumab vedotin was also granted Breakthrough Therapy Designation by the FDA and PRIME (PRIority MEdicines) designation by the European Medicines Agency for the treatment of people with R/R DLBCL in 2017. Breakthrough Therapy Designation is designed to expedite the development and review of medicines intended to treat a serious condition with preliminary evidence that indicates they may demonstrate substantial improvement over existing therapies.

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 bendamustine and Rituxan (rituximab) or Gazyva (obinutuzumab) 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 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).

- 40% of people treated with polatuzumab vedotin plus BR achieved a CR while only 18% of people treated with BR alone achieved a CR (primary endpoint, as measured by PET; CR rates assessed by IRC). A CR means no cancer could be detected at that time.
- Polatuzumab vedotin in combination with BR showed a median OS of over one year compared to the BR arm (12.4 vs. 4.7 months, HR=0.42; 95% CI 0.24-0.75), in people with R/R DLBCL not eligible for a hematopoietic stem cell transplant. OS was an exploratory endpoint.
- Polatuzumab vedotin plus BR increased median PFS and led to a 66% reduction in risk of disease worsening or death compared to BR alone (median PFS: 7.6 months vs. 2.0 months; HR=0.34; 95% CI 0.20-0.57).
- Patients treated with polatuzumab vedotin plus BR showed a longer time between first response to treatment and disease worsening than those receiving BR alone (investigator assessed median DOR: 10.3 months vs. 4.1 months; HR=0.44).
- Updated safety results are similar to those previously described, with infections and cytopenias remaining the most common Grade 3–4 adverse events (AEs). Polatuzumab vedotin plus BR had higher rates of Grade 3–4 cytopenias compared to BR, however, infection and transfusion rates remained similar between arms.

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.^{1,2} Polatuzumab vedotin binds to CD79b and destroys these B-cells through a targeted approach, which is thought to minimise the effects on normal cells while maximising tumour cell death.^{3,4} 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.⁵ DLBCL is an aggressive (fast-growing) type of NHL, which is generally responsive to treatment in the frontline.⁶ However, as many as 40% of patients will relapse, at which time salvage therapy options are limited and survival is short.^{1,4} Approximately 150,000 people worldwide are estimated to be diagnosed with DLBCL each year.⁷

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 which inhibits the interaction of MDM2 with p53 (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. Moreover, for the tenth consecutive year, Roche has been recognised as the most sustainable company in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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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References

- [1] Dornan D, et al. Therapeutic potential of an anti-CD79b antibody-drug conjugate, anti-CD79b-vc-MMAE, for the treatment of non-Hodgkin lymphoma. *Blood* 2009; 114:2721–2729.
- [2] Pfeifer M, et al. Anti-CD22 and anti-CD79B antibody drug conjugates are active in different molecular diffuse large B-cell lymphoma subtypes. *Leukemia* 2015; 29:1578-1586
- [3] Ducry L, Stump B. Antibody-drug conjugates: linking cytotoxic payloads to monoclonal antibodies. *Bioconjug Chem.* 2010; 21:5 - 13.
- [4] ADC Review. What are antibody-drug conjugates? [Internet; cited February 2019]. Available from: <https://adcreview.com/adc-university/adcs-101/antibody-drug-conjugates-adcs/>
- [5] Lyon, France. World Health Organization Classification of Tumors of Haematopoietic and Lymphoid Tissues. IARC Press; 2008.
- [6] Maurer, JM et al. Event-free survival at 24 months is a robust end point for disease-related outcome in diffuse large B-cell lymphoma treated with immunochemotherapy. *J Clin Oncol* 2014; 32:1066-73.
- [7] Numbers derived from GLOBOCAN 2018: Estimated cancer incidence, mortality and prevalence worldwide in 2018. [Internet; cited 2018 May]. Available from: <http://globocan.iarc.fr>.

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