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FDA approves Rituxan Hycela (rituximab and hyaluronidase human) for subcutaneous injection in certain blood cancers

- **Treatment can be administered in five to seven minutes, compared to 1.5 hours or more for intravenous Rituxan^{*}**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the US Food and Drug Administration (FDA) approved Rituxan Hycela™ (rituximab and hyaluronidase human) for subcutaneous (under the skin) injection, for the treatment of adults with the following blood cancers: previously untreated and relapsed or refractory follicular lymphoma, previously untreated diffuse large B-cell lymphoma (DLBCL), and previously untreated and previously treated chronic lymphocytic leukaemia (CLL). This new treatment includes the same monoclonal antibody as intravenous Rituxan® (rituximab) in combination with hyaluronidase human, an enzyme that helps to deliver rituximab under the skin.

“With today’s approval of Rituxan Hycela, people with three of the most common blood cancers now have a new treatment option which provides efficacy comparable with intravenous Rituxan and can be delivered under the skin in minutes instead of hours through IV infusion,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “People who benefit from Rituxan may receive years of repeated treatments for their blood cancer, so an option that reduces the administration time can be important.”

The FDA approval is based on results from clinical studies, which demonstrated that subcutaneous administration of Rituxan Hycela resulted in non-inferior levels of rituximab in the blood (pharmacokinetics) and comparable clinical efficacy outcomes compared to intravenous Rituxan. One of the studies showed the majority (77%) of patients preferred Rituxan Hycela over intravenous Rituxan, with the most common reason being that administration required less time in the clinic. People can only receive Rituxan Hycela after at least one full dose of intravenous Rituxan.

^{*} Rituxan® (rituximab) is marketed as MabThera® (rituximab) outside the United States, Canada and Japan.

With the exception of local skin (cutaneous) reactions, the incidence and profile of adverse reactions for Rituxan Hycela were comparable with those for intravenous Rituxan. The most common ($\geq 20\%$) adverse reactions observed with Rituxan Hycela in people with follicular lymphoma were infections, low white blood cell count (neutropenia), nausea, constipation, cough and fatigue. The most common adverse reactions in people with DLBCL were infections, neutropenia, hair loss (alopecia), nausea and low red blood cell count (anemia). The most common adverse reactions in people with CLL were infections, neutropenia, nausea, low platelet count (thrombocytopenia), fever (pyrexia), vomiting and reddening of the skin (erythema) at the injection site.

Rituxan Hycela will be available to people in the United States within one to two weeks, and intravenous Rituxan will continue to be available.

About the Rituxan Hycela Clinical Development Program

The approval of Rituxan Hycela is based on results from clinical studies that together represented nearly 2,000 people. The studies were the following:

- SABRINA (NCT01200758): Phase III combination with chemotherapy and maintenance study in previously untreated follicular lymphoma
- SAWYER (NCT01292603): Phase Ib study in previously untreated chronic lymphocytic leukaemia (CLL)
- MabEase (NCT01649856): Phase III study in previously untreated diffuse large B-cell lymphoma (DLBCL)
- PrefMab (NCT01724021): Phase III patient preference study in previously untreated follicular lymphoma and DLBCL

About MabThera®/Rituxan (rituximab)

MabThera/Rituxan is a therapeutic monoclonal antibody that binds to a particular protein – the CD20 antigen – on the surface of normal and malignant B-cells. It then recruits the body's natural defenses to attack and kill the marked B-cells. Stem cells (B-cell progenitors) in bone marrow lack the CD20 antigen, allowing healthy B-cells to regenerate after treatment and return to normal levels within several months.

Rituxan first received FDA approval for the treatment of relapsed indolent non-Hodgkin Lymphoma (NHL) in 1997 and was the first targeted cancer medicine approved by the U.S. Food and Drug Administration (FDA). MabThera was approved in the EU in June 1998, and has since been used to treat more than 2.7 million people with specific blood cancers. For more than 15 years, the efficacy and safety of MabThera/Rituxan has been documented in more than 300 phase II/III clinical studies. MabThera/Rituxan has been approved for the treatment of several blood cancers, specifically, certain types of NHL and for chronic lymphocytic leukaemia (CLL). It continues to be studied in other types of blood cancers and disease areas where CD20-positive cells are believed to play a role.

MabThera is known as Rituxan in the United States, Japan and Canada. Genentech, a member of the Roche Group, and Biogen collaborate on Rituxan in the United States, and Roche markets MabThera in the rest of the world, except Japan, where MabThera is co-marketed by Chugai and Zenyaku Kogyo Co. Ltd.

About Rituxan Hycela

Rituxan Hycela is a co-formulation of the same monoclonal antibody as intravenous MabThera/Rituxan and Halozyme Therapeutics' proprietary hyaluronidase human, an FDA-approved enzyme that facilitates the delivery of a large volume of medicine under the skin. Rituxan Hycela can be administered in five to seven minutes, compared to 1.5 to four hours for intravenous MabThera/Rituxan. It is known as the subcutaneous (SC) formulation of MabThera (rituximab) in the European Union.

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 NHL¹. It is considered incurable and relapse is common. Every day, more than 50 people in Europe are diagnosed this type of NHL². It is estimated that each year, more than 75,000 people are diagnosed with follicular lymphoma worldwide².

About Diffuse Large B-Cell Lymphoma (DLBCL)

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL), accounting for about one in three cases of NHL³. DLBCL is an aggressive (fast-growing) type of NHL, which is generally responsive to treatment in the frontline⁴. However, as many as 40% of patients will relapse, at which time salvage therapy options are limited and survival is short⁴. Approximately 123,000 people worldwide are estimated to be diagnosed with DLBCL each year⁵.

About Chronic Lymphocytic Leukaemia (CLL)

Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia in the Western world⁶. CLL mainly affects men and the median age at diagnosis is about 70 years⁷. Worldwide, the incidence of all leukaemias is estimated to be over 350,000⁶ and CLL is estimated to affect around one-third of all people newly diagnosed with leukaemia⁸.

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.

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 eight 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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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/old/summary_table_pop.html.asp?selection=224900&title=World&sex=0&type=0&window=1&sort=0&submit=%C2%A0Execute (accessed on 29/05/2017).

³ Lyon, France: IARC Press; 2008. World Health Organization Classification of Tumors of Haematopoietic and Lymphoid Tissues.

⁴ Maurer, JM et al. (2014). 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 32: 1066-73.

⁵ Numbers derived from GLOBOCAN 2012: Estimated cancer incidence, mortality and prevalence worldwide in 2012. <http://globocan.iarc.fr>. Accessed May 2017.

⁶ Chronic lymphocytic leukemia. Union for International Cancer Control. 2014 Review of Cancer Medicines on the WHO List of Essential Medicines. http://www.who.int/selection_medicines/committees/expert/20/applications/CLL.pdf?ua=1 (accessed May 2017).

⁷ SEER Stat Fact Sheets: Chronic Lymphocytic Leukemia (CLL). <http://seer.cancer.gov/statfacts/html/clyl.html> (accessed May 2017).

⁸ Wendtner CM, et al. Chronic lymphocytic leukemia. Onkopedia guidelines 2012. <https://www.onkopedia-guidelines.info/en/onkopedia/guidelines/chronic-lymphocytic-leukemia-cll/@@view/html/index.html> (accessed May 2017).