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FDA approves Zelboraf (vemurafenib) for Erdheim-Chester disease with BRAF V600 mutation

- **Zelboraf is the first FDA-approved treatment for Erdheim-Chester disease (ECD), a rare blood disease**
- **Approval based on data from a basket study, which enrolls participants across multiple diseases based predominantly on genetic profile**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the US Food and Drug Administration (FDA) has approved Zelboraf® (vemurafenib) for Erdheim-Chester disease (ECD) with BRAF V600 mutation. ECD is a rare, serious blood disease characterized by the abnormal multiplication of certain white blood cells called histiocytes, which can invade normal tissues and organs in the body.¹

The approval is based on data from the Phase II VE-BASKET study. Basket studies use an innovative clinical trial design that helps collect data faster and may accelerate the development of medicines for diseases with high unmet need. Instead of enrolling people based primarily on their disease or its location, basket studies match a disease's underlying genetic profile to the mechanism of action of the medicine.

“This FDA decision means people living with Erdheim-Chester disease will now, for the first time, have an FDA-approved treatment option,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We are committed to finding new ways to bring medicines to patients with high unmet need, and we are pleased that this innovative clinical trial helped identify Zelboraf for treatment of this rare disease.”

Final results of VE-BASKET for the 22 people with ECD showed a best overall response rate of 54.5 percent. The most common Grade 3 or higher adverse events were new skin cancers, high blood pressure, rash and joint pain. The most common adverse events were joint pain, rash, hair loss, fatigue, change in heart rhythm and skin tags.

Zelboraf monotherapy was approved for the treatment of people with unresectable or metastatic melanoma with BRAF V600E mutation in 2011.² The FDA previously granted Priority Review and Breakthrough Therapy Designation to Zelboraf for ECD with BRAF V600 mutation.³

About the VE-BASKET Study

VE-BASKET is an open-label, Phase II, non-randomized, basket study investigating the use of Zelboraf for people with BRAF V600 mutation-positive cancers and other diseases, including ECD. Final results for the 22 people with ECD showed a best overall response rate of 54.5 percent by RECIST v1.1. The median duration of response was not estimated at a median follow-up time of 26.6 months. The most common Grade 3 or higher adverse events (≥ 10 percent) were new skin cancers, high blood pressure, rash and joint pain. The most common adverse events (≥ 50 percent) were joint pain, rash, hair loss, fatigue, change in heart rhythm and skin tags. Initial study results were published in the *New England Journal of Medicine* in August 2015.⁴

About Erdheim-Chester Disease

Erdheim-Chester disease (ECD) is an extremely rare non-Langerhans cell histiocytosis. The exact prevalence and incidence of ECD are difficult to ascertain given the disease is so rare. Based on available published data, it's estimated there are fewer than 500 cases of ECD in the United States.⁵ More than 50 percent of people with ECD have BRAF V600 mutation-positive disease.⁶

About Zelboraf

Zelboraf is designed to inhibit some mutated forms of BRAF, which cause abnormal signaling inside cancer cells leading to tumor growth. BRAF is a protein in a cell signaling pathway that helps control cell growth and survival. Zelboraf was the first approved product in its class. Zelboraf was co-developed under a 2006 license and collaboration agreement between Roche and Plexxikon, now a member of the Daiichi Sankyo Group.

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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¹ Adawi M, Bisharat B, Bowirrat A. Erdheim-Chester disease (ECD): Case report, clinical and basic investigations, and review of literature. *Medicine (Baltimore)*. 2016;95:e5167.

² Zelboraf prescribing information, April 2017. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/202429s012lbl.pdf

³ Genentech. FDA grants priority review and breakthrough therapy designation for Zelboraf (vemurafenib) in Erdheim-Chester disease with BRAFV600 mutation. Press release August 7, 2017. Available from: <https://www.gene.com/media/press-releases/14676/2017-08-07/fda-grants-priority-review-and-breakthro>

⁴ Hyman DM, Puzanov I, Subbiah V, et al. Vemurafenib in multiple nonmelanoma cancers with BRAF V600 mutations. *N Engl J Med*. 2015;373:726-36.

⁵ Data on file.

⁶ Abdelfattah AM, Arnaout K, Tabbara IA. Erdheim-Chester disease: a comprehensive review. *Anticancer Res*. 2014;34:3257-61.