FDA approves Roche’s Cotellic (cobimetinib) in combination with Zelboraf (vemurafenib) in advanced melanoma

- FDA approval underscores the important role of targeted medicines to help people with BRAF V600 mutation-positive advanced melanoma
- Pivotal coBRIM study showed the combination improved progression-free and overall survival compared to Zelboraf alone

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the U.S. Food and Drug Administration (FDA) approved Cotellic (cobimetinib) for the treatment of people with BRAF V600E or V600K mutation-positive unresectable or metastatic melanoma in combination with Zelboraf (vemurafenib). Cotellic and Zelboraf are not used to treat melanoma with a normal BRAF gene. Cotellic is Roche’s seventh new medicine approved by the FDA in the past five years.

“When used in combination, Cotellic and Zelboraf help delay disease progression and help people live significantly longer than with Zelboraf alone,” said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development. “With this approval, people with this type of deadly and aggressive skin cancer now have a new targeted option.”

Today’s FDA approval is based on results from the Phase III coBRIM study, which showed Cotellic plus Zelboraf reduced the risk of disease worsening or death (progression-free survival; PFS) by about half in people who received the combination [HR=0.56, 95 percent CI (0.45-0.70); p<0.001], with a median PFS of 12.3 months for Cotellic plus Zelboraf compared to 7.2 months with Zelboraf alone. An interim analysis also showed the combination of Cotellic and Zelboraf helped people live significantly longer (overall survival; OS) than Zelboraf alone (HR=0.63, 95 percent CI 0.47-0.85; p=0.0019). The objective response rate (tumor shrinkage) was higher with Cotellic plus Zelboraf compared to Zelboraf alone (70 vs. 50 percent; p<0.001), as was the complete response rate (complete tumor shrinkage, 16 vs. 11 percent).
Possible serious side effects with Cotellic include risk of skin cancers, increased risk of bleeding, heart problems that can lead to inadequate pumping of the blood by the heart, rash, eye problems, abnormal liver test or liver injury, increased levels of an enzyme in the blood, and photosensitivity. The most common side effects of Cotellic include diarrhea, sunburn or sun sensitivity, nausea, fever and vomiting. Cotellic can also cause changes in blood test results.

The final overall survival analysis from the coBRIM study will be presented at the Society for Melanoma Research 2015 International Congress (SMR) held in San Francisco, California from November 18-21.

In September, the Committee for Medicinal Products for Human Use (CHMP) at the European Medicines Agency (EMA) issued a positive opinion for Roche’s marketing authorization application for Cotellic in the European Union. A decision from the European Commission is expected before the end of 2015. Cotellic was approved in Switzerland by Swissmedic in August 2015.

About the coBRIM study
CoBRIM is an international, randomized, double-blind, placebo-controlled Phase III study evaluating the safety and efficacy of 60 mg once daily of Cotellic plus 960 mg twice daily of Zelboraf compared to 960 mg twice daily of Zelboraf plus placebo. In the study, 495 patients with BRAF V600 mutation-positive unresectable locally advanced or metastatic melanoma (detected by the cobas 4800 BRAF Mutation Test) and previously untreated for advanced disease were randomized to receive Zelboraf every day on a 28-day cycle plus either Cotellic or placebo on days 1-21. Treatment was continued until disease progression, unacceptable toxicity or withdrawal of consent. Investigator-assessed PFS is the primary endpoint. Secondary endpoints include PFS by independent review committee, objective response rate, overall survival, duration of response and other safety, pharmacokinetic and quality of life measures.

About Cotellic plus Zelboraf
Cotellic and Zelboraf are prescription medicines used in combination to treat melanoma that has spread to other parts of the body or cannot be removed by surgery, and that has a certain type of abnormal “BRAF” gene. Found in approximately half of melanomas, mutated BRAF causes abnormal signaling inside certain cancer cells leading to tumor growth. Zelboraf is designed to inhibit some mutated forms of BRAF and Cotellic is designed to inhibit some forms of MEK. Both BRAF and MEK are proteins in a cell signaling pathway that help control cell growth and survival. When used in combination, Cotellic and Zelboraf are thought to reduce cancer cell growth longer than with Zelboraf alone. A patient’s healthcare provider will
perform a test to make sure Cotellc and Zelboraf are right for the patient. It is not known if Cotellc and Zelboraf are safe and effective in children under 18 years of age.

**About melanoma**

Melanoma is less common, but more aggressive and deadlier than other forms of skin cancer. BRAF is mutated in approximately half of melanomas. When melanoma is diagnosed early, it is generally a curable disease, but most people with advanced melanoma have a poor prognosis. More than 232,000 people worldwide are currently diagnosed with melanoma each year. In recent years, there have been significant advances in treatment for metastatic melanoma and people with the disease have more options. However, it continues to be a serious health issue with a high unmet need and a steadily increasing incidence over the past 30 years.

**Roche in skin cancer**

The Roche Group is the world’s leading provider of cancer care products, including anti-cancer treatments, supportive care products and diagnostics. In the area of skin cancer, Roche scientists have been studying treatments for nearly 20 years. More than 28,000 patients having been treated worldwide, bringing about medical breakthroughs and new standards of care that include Zelboraf and Erivedge, treatments for two of the most difficult-to-treat skin cancers, metastatic melanoma and basal cell carcinoma. Roche is continuing to study skin cancer medicines as monotherapies and in combination with other investigational medicines, such as cancer immunotherapies, in several cancer types and diseases.

**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.

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References
1. Larkin J et al., Update of progression-free survival and correlative biomarker analysis from coBRIM: cobimetinib plus vemurafenib in advanced BRAF-mutated melanoma. Abstract presented at ASCO, Chicago, IL, USA, 29 May – 2 June 2015; abstract #9006.