Roche receives EU approval of Cotellic for use in combination with Zelboraf in advanced melanoma

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the European Commission has approved Cotellic™ (cobimetinib) for use in combination with Zelboraf® (vemurafenib) for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation. The EU approval is based on data that showed Cotellic plus Zelboraf helped people with previously untreated BRAF V600 mutation-positive advanced melanoma live for more than a year without their disease worsening.

“There has been significant progress in the treatment of melanoma, with more medicines being approved in the past five years than in the previous 30,” said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development. "Together, Cotellic plus Zelboraf more strongly suppressed cancer growth than Zelboraf alone. This underscores the critical role of combination medicines in helping melanoma patients live longer without their disease worsening."

Today’s EU approval is based primarily on results of the Phase III coBRIM study, which showed that people with previously untreated BRAF V600 mutation-positive advanced melanoma who were being treated with the MEK inhibitor Cotellic in combination with Zelboraf lived a median of one year (12.3 months) without their disease worsening or death (progression-free survival; PFS) compared to 7.2 months with Zelboraf alone (hazard ratio [HR]=0.58; 95 percent confidence interval [CI] 0.46-0.72). The objective response rate (ORR) with the combination was 70 percent (16 percent complete response [CR], 54 percent partial response [PR]) compared to 50 percent (11 percent CR, 40 percent PR) in the Zelboraf arm. The safety profile of Cotellic plus Zelboraf was consistent with safety data previously reported. The most common adverse events in the combination arm were diarrhea, rash, nausea, fever, sun sensitivity, liver lab abnormalities, elevated creatine phosphokinase (CPK, an enzyme released by muscles) and vomiting.
Additional data were presented on November 21, 2015 at the Society for Melanoma Research congress demonstrating that the combination of Cotellic plus Zelboraf met its secondary endpoint of improving overall survival compared to Zelboraf alone. These data will be submitted to the European Medicines Agency for consideration and inclusion in the label. Cotellic in combination with Zelboraf is now approved in the EU and Switzerland for the treatment of people with BRAF V600 mutation-positive advanced melanoma. In the US, the combination is approved for the treatment of people with BRAF V600E or V600K mutation-positive advanced melanoma. Further country approvals are anticipated in 2016.

About the coBRIM study
CoBRIM is an international, randomised, double-blind, placebo-controlled Phase III study evaluating the safety and efficacy of 60 mg once daily of cobimetinib plus 960 mg twice daily of Zelboraf compared to 960 mg twice daily of Zelboraf alone. 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 randomised to receive Zelboraf every day on a 28-day cycle plus either cobimetinib 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 Cotellic and Zelboraf are right for the patient. Cotellic and Zelboraf are not used to treat melanoma with a normal BRAF gene. It is not known if Cotellic and Zelboraf are safe and effective in children under 18 years of age.

Cotellic is also being investigated in combination with several investigational medicines, including an immunotherapy, in several tumour types such as non-small cell lung cancer and colorectal cancer. Cotellic
was discovered by Exelixis Inc. and is being developed by Roche in collaboration with Exelixis.

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 roche.com.

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References
1. Cotellic Summary of Product Characteristics (SmPC), Roche data on file 2015