Basel, 23 November 2015

Updated data showed Cotelllic in combination with Zelboraf helped people with a specific type of advanced melanoma live significantly longer than with Zelboraf alone

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced data from the pivotal coBRIM study, which showed that Cotelllic (cobimetinib) in combination with Zelboraf (vemurafenib) helped people with BRAF V600E and V600K mutation-positive unresectable or metastatic melanoma live significantly longer (overall survival; OS) than with Zelboraf alone.¹ Cotelllic plus Zelboraf reduced the risk of death by 30 percent compared to Zelboraf alone and helped people live a median of nearly two years (median OS 22.3 months vs. 17.4 months, hazard ratio {[HR]}=0.70, 95 percent CI: 0.55–0.90, p=0.005)¹. Ongoing study monitoring did not identify any new safety signals. The final coBRIM OS results were presented during the 12th International Congress of the Society for Melanoma Research (SMR) held in San Francisco, California from 18 – 21 November.

“This with about half of the people taking Cotelllic and Zelboraf alive after two years, these data underscore the progress being made in cancer research towards better patient outcomes.” said Sandra Horning, M.D., Chief Medical Officer and Head of Global Product Development. “Five years ago, the survival rate for BRAF mutation-positive advanced melanoma was measured in months, and now we are measuring it in years.”

This final analysis of the OS data from coBRIM showed that with the combination of Cotelllic and Zelboraf, 74.5 percent of people with BRAF V600 mutation-positive advanced melanoma in the study were alive at one year and 48.3 percent were alive at two years.

The data were presented in an oral session presentation by Dr. Victoria Atkinson, Medical Oncologist at Princess Alexandra Hospital, Queensland, Australia on 21 November.

The announcement follows the U.S. Food and Drug Administration (FDA) approval of Cotelllic for the treatment of people with BRAF V600E or V600K mutation-positive unresectable or metastatic melanoma in
combination with Zelboraf. A decision from the European Commission is expected before the end of 2015. The final OS results are being submitted to both of these health authorities for consideration.

**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 Cotellic 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 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.2

**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 melanomas3, mutated BRAF causes abnormal signaling inside cancer cells leading to tumor growth4,5. Zelboraf is designed to inhibit some mutated forms of BRAF and Cotellic is designed to inhibit some forms of MEK6. Both BRAF and MEK are proteins in a cell signaling pathway that help control cell growth and survivals7. 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.5,9 When melanoma is diagnosed early, it is generally a curable disease,10,11 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 our 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.

All trademarks used or mentioned in this release are protected by law.
Additional information
Roche in Oncology: [www.roche.com/media/media_backgrounder/media_oncology.htm](http://www.roche.com/media/media_backgrounder/media_oncology.htm)

Roche Group Media Relations
Phone: +41 61 688 8888 / e-mail: [roche.mediarelations@roche.com](mailto:roche.mediarelations@roche.com)
- Nicolas Dunant (Head)
- Ulrike Engels-Lange
- Claudia Schmitt
- Nicole Rüppel

References
1. Atkinson V, Larkin J, McArthur GA et al. Improved overall survival with cobimetinib (COCI) and vemurafenib (VEM) in advanced
BRAFV600-mutated melanoma and biomarker correlates of efficacy. Abstract presented at the 12th International Congress of the Society for
Melanoma Research in San Francisco, California, 21 November 2015.
6. Johnston S. XL518, a potent, selective, orally bioavailable MEK1 inhibitor, downregulates the Ras/Raf/MEK/ERK pathway in vivo, resulting
in tumor growth inhibition and regression in preclinical models. Poster presented at: AACR-NCI-EORTC Symposium on Molecular Targets
and Cancer Therapeutics; October 22, 2007; San Francisco, CA. Abstract C209.
Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer;