Media Release

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FDA approves Zelboraf (vemurafenib) and companion diagnostic for BRAF mutation-positive metastatic melanoma, a deadly form of skin cancer

First and Only Personalized Medicine Shown to Help People With BRAF V600E Mutation-Positive Metastatic Melanoma, Found in Half of Melanoma Patients, Live Longer

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) approved Zelboraf (vemurafenib) for the treatment of BRAF V600E mutation-positive, inoperable or metastatic melanoma, as determined by an FDA-approved test. The FDA today also approved the cobas 4800 BRAF V600 Mutation Test, a diagnostic test developed by Roche to identify patients eligible for treatment. Zelboraf is the first and only FDA-approved personalized medicine shown to improve survival in people with BRAF V600E mutation-positive metastatic melanoma, demonstrating the benefits of Roche's personalized healthcare approach. It is designed to target and inhibit some mutated forms of the BRAF protein found in about half of all cases of melanoma, the deadliest and most aggressive form of skin cancer.

"The FDA approval of Zelboraf marks a major step forward in personalizing the treatment of metastatic melanoma, a devastating disease that until this year had limited approved treatment options," said Hal Barron, M.D., chief medical officer and head, Global Product Development. "We will continue to study this medicine with a goal of further improving outcomes for people with melanoma and other cancers that are driven by BRAF mutations."

Zelboraf should be used only in people whose inoperable or metastatic melanoma carries a BRAF V600E mutation, which can be determined by the FDA-approved cobas BRAF Mutation Test.

"The cobas BRAF Mutation Test has improved sensitivity, accuracy and speed compared to other commonly used, unapproved detection methods," said Paul Brown, head of Roche Molecular Systems. "With a personalized medicine now available, all people diagnosed with inoperable or metastatic melanoma should be tested to help determine the best options for treatment."

F. Hoffmann-La Roche Ltd 4070 Basel Switzerland
Group Communications Roche Group Media Relations
Tel. +41 61 688 88 88 Fax +41 61 688 27 75 www.roche.com

Zelboraf will be available in the United States within two weeks of approval. Roche has also submitted new drug applications for Zelboraf in the EU, Switzerland, Australia, New Zealand, Brazil, India, Mexico and Canada. While Roche seeks regulatory approval of Zelboraf in other countries, a global Expanded Access Program (EAP) is available for people with previously treated or untreated BRAF V600 mutation-positive metastatic melanoma.

Zelboraf Efficacy in BRAF V600E Mutation-Positive Metastatic Melanoma

The FDA approval of Zelboraf is based on results from two clinical studies (BRIM3 and BRIM2) in people with BRAF V600E mutation-positive, inoperable or metastatic melanoma as determined by the cobas BRAF Mutation Test.

BRIM3 is a global, randomized, open-label, controlled, multicenter, Phase III study that compared Zelboraf to dacarbazine chemotherapy, a standard of care, in 675 patients with previously untreated BRAF V600E mutation-positive, unresectable (inoperable) or metastatic melanoma. The endpoints of BRIM3 were overall survival (OS) and investigator-assessed progression-free survival (PFS). Other endpoints included confirmed investigator-assessed overall response rate. BRIM2 is a global, single-arm, multicenter, open-label Phase II study that enrolled 132 patients with previously treated BRAF V600E mutation-positive, unresectable or metastatic melanoma. The primary endpoint of BRIM2 was confirmed overall response rate as assessed by independent review.

BRIM3: Previously Untreated BRAF V600E Mutation-Positive Unresectable or Metastatic Melanoma

- In BRIM3, the risk of death was reduced by 56 percent for people who received Zelboraf compared to those who received chemotherapy (hazard ratio [HR] =0.44, $p<0.0001$). At the time of the analysis, median overall survival of patients receiving Zelboraf had not been reached and was 7.9 months for those receiving chemotherapy.
- People who received Zelboraf also had a 74 percent reduced risk of the disease getting worse or dying (PFS) compared to those who received chemotherapy (HR=0.26, $p<0.0001$). Median PFS was 5.3 months for those who received Zelboraf compared to 1.6 months for those who received chemotherapy.
- The confirmed investigator-assessed response rate (those who experienced tumor shrinkage) in people who received Zelboraf was 48.4 percent (1 percent complete responses and 47.4 percent partial responses) compared to 5.5 percent (partial responses) for those who received chemotherapy ($p<0.0001$).

BRIM2: Previously Treated BRAF V600E Mutation-Positive, Unresectable or Metastatic Melanoma

- In BRIM2, Zelboraf shrank tumors in 52 percent of trial participants.

Zelboraf safety

The safety profile of Zelboraf in BRIM3 was generally consistent with that previously reported in prior clinical studies. The most common Grade 3 or higher adverse events seen in more people receiving Zelboraf compared to those receiving chemotherapy were a common type of skin cancer, cutaneous squamous cell carcinoma (cSCC) including keratoacanthomas (18 percent vs. <1 percent), rash, liver function abnormalities, joint pain and sensitivity to the sun. In cases of cSCC, the lesions were generally removed and the patients continued with treatment.

The safety profile of Zelboraf in BRIM2 was generally consistent with that observed in the Phase I study. The most common (Grade 3 or greater) adverse events were cSCC (26 percent), abnormal liver function, joint pain/arthritis and rash. In cases of cSCC, the lesions were generally removed and the patients continued with treatment.

About Metastatic Melanoma and BRAF

When melanoma is diagnosed early, it is generally a curable disease. However, when it spreads to other parts of the body, it is the deadliest and most aggressive form of skin cancer. A person with metastatic melanoma typically has on average a short life expectancy that is measured in months. The American Cancer Society estimates there will be more than 70,000 new cases of melanoma and nearly 8,800 melanoma deaths this year in the United States.

The BRAF protein is a key component of the RAS-RAF pathway involved in normal cell growth and survival. Mutations that keep the BRAF protein in an active state may cause excessive signaling in the pathway, leading to uncontrolled cell growth and survival. These mutations of the BRAF protein are thought to occur in an estimated half of all melanomas and eight percent of solid tumors.

About BRAF V600 Mutation Testing

The cobas 4800 BRAF V600 Mutation Test is a polymerase chain reaction-based diagnostic test developed by Roche. This FDA-approved test was clinically validated in the BRIM2 and BRIM3 studies to identify tumors that carry the BRAF V600E mutation. The test has several advantages compared to Sanger sequencing, a commonly used method, including greater sensitivity and reliability for detecting mutations and quicker

results, allowing doctors to know whether a person with metastatic melanoma is eligible for treatment with Zelboraf.

About Zelboraf

Zelboraf is an oral, small molecule, kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. Zelboraf is not recommended for use in melanoma patients who lack the BRAF V600E mutation.

Zelboraf is being co-developed under a 2006 license and collaboration agreement between Roche and Plexxikon, a member of the Daiichi Sankyo Group.

Roche and Genentech are conducting a broad development program with Zelboraf that includes testing combinations with other medicines (both approved and investigational, from Roche/Genentech and other companies), as well as studies in other tumor types. While Roche seeks approval of Zelboraf outside of the United States, Zelboraf is available to eligible patients with BRAF V600 mutation-positive metastatic melanoma through a global EAP. More information about this program or other Zelboraf studies is available at the Roche Clinical Trials Registry at www.roche-trials.com (in the EU) or www.clinicaltrials.gov (in the United States).

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, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2010, Roche had over 80'000 employees worldwide and invested over 9 billion Swiss francs in R&D. The Group posted sales of 47.5 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

Roche Group Media Relations

Phone: +41 -61 688 8888 / e-mail: basel.mediaoffice@roche.com

- Alexander Klauser (Head)
- Silvia Dobry
- Daniel Grotzky
- Claudia Schmitt