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Roche personalized investigational medicine shows survival benefit in advanced skin cancer

**Phase III study shows promising results for RG7204 in BRAF V600 mutation-positive metastatic melanoma**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that BRIM3, a Phase III clinical study of RG7204 (PLX4032), met its co-primary endpoints showing a significant survival benefit in people with previously untreated BRAF V600 mutation-positive metastatic melanoma. Study participants who received RG7204 lived longer (overall survival) and also lived longer without their disease getting worse (progression-free survival) compared to participants who received dacarbazine, the current standard of care. RG7204 is a potential first-in-class medicine designed to selectively inhibit the mutated BRAF protein found in about half of all cases of metastatic melanoma – the most aggressive and deadliest form of skin cancer. The safety profile was generally consistent with previous RG7204 studies.

“For the first time, a personalized investigational medicine, RG7204, has shown a significant survival benefit in metastatic melanoma. This is an important advance for people with the BRAF V600 mutation-positive form of the disease who have had extremely limited treatment options,” said Hal Barron M.D., Chief Medical Officer and Head, Global Product Development.

Based on these interim analysis results, patients on the control arm of the study will have the option to crossover to receive RG7204.

Full data will be presented at a medical meeting later this year.

Roche is now working closely with global health authorities to expand the recently announced RG7204 Early Access Program (EAP). The global EAP will be extended to include people with previously untreated, BRAF V600 mutation-positive metastatic melanoma (first line).

RG7204 exemplifies Roche’s personalized healthcare approach using biomarkers and diagnostic tools to

identify the right medicine for the right patient. RG7204 is being co-developed with an investigational diagnostic test, the cobas 4800 BRAF V600 Mutation Test from Roche Molecular Diagnostics to identify patients whose tumors carry the mutated BRAF V600 gene.

### **About BRIM3**

BRIM3 (Study NO25026) is a global, randomized, open-label, controlled, multicenter, Phase III study evaluating RG7204 compared to dacarbazine (the current chemotherapy standard of care) in patients with previously untreated, BRAF V600 mutation-positive metastatic melanoma. Mutation status of the 675 enrolled patients was determined by the cobas 4800 BRAF V600 Mutation Test (Roche Molecular Diagnostics) a companion diagnostic assay being co-developed with RG7204.

Study participants were randomized to receive either RG7204 960 mg orally twice daily or dacarbazine 1000 mg/m<sup>2</sup> intravenously every 3 weeks. Patients continued dosing until their disease progressed or there was unacceptable toxicity.

The most frequent grade 3 adverse events were skin related and included cutaneous squamous cell carcinoma, a common skin cancer treated by local excision. Additionally, generally mild and reversible increases in liver enzymes (GGT, ALT, AST, alkaline phosphatase, and bilirubin) were observed in some patients. The most common adverse events were rash, photosensitivity, joint pain, hair loss and fatigue.

The BRIM3 study started in Q1 2010 and was carried out at over 100 sites worldwide including the US, UK, France, Germany, Australia, New Zealand, Italy and Spain.

### **About Metastatic Melanoma and BRAF**

Metastatic melanoma is the deadliest and most aggressive form of skin cancer. A person with metastatic melanoma typically has a short life expectancy that is measured in months. Less than one in four people are expected to be alive one year after diagnosis and every year there are an estimated 40,000 deaths worldwide from the disease.<sup>i</sup> The number of people with melanoma in developed countries is predicted to double over the next decade from 138,000 new cases a year to 227,000 new cases by 2019.<sup>ii</sup> Until recently there has been no major advance in treatment for 30 years and patients with metastatic melanoma have had very few treatment options.

The BRAF protein is a key component of the RAS-RAF pathway involved in normal cell growth and survival.

Activating mutations in the BRAF gene cause this pathway to be overactive, which may lead to excessive cell growth and cancer. Mutations in residue 600 of the BRAF protein are found in about 50 percent of melanomas and it is estimated that approximately eight percent of all solid tumors contain BRAF V600 mutations.

### **About RG7204**

RG7204 is an investigational, oral, small molecule that is designed to selectively inhibit a cancer-causing mutated form of the BRAF protein. RG7204 is being co-developed under a 2006 license and collaboration agreement between Roche and Plexxikon. A polymerase chain reaction-based companion diagnostic, the cobas 4800 BRAF V600 Mutation Test, is being co-developed by Roche Molecular Diagnostics and Plexxikon in parallel to identify people whose tumors carry the BRAF V600 mutation.

Information about current clinical trials for RG7204 is available at the Roche Clinical Trials Registry (<http://www.roche-trials.com>).

### **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 almost 10 billion Swiss francs in R&D. The Group posted sales of 49.1 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](http://www.roche.com).

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### **Additional information**

- Seventh International Melanoma Research Congress of the Society for Melanoma Research:  
<http://melanoma2010.com/program-melanoma-research.asp>
- Roche in Oncology: [www.roche.com/pages/downloads/company/pdf/mboncology05e\\_b.pdf](http://www.roche.com/pages/downloads/company/pdf/mboncology05e_b.pdf)

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### **References**

<sup>i</sup> Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005; 55:74–108.

<sup>ii</sup> Data Monitor Report. Stakeholder Opinions: Melanoma - Future treatment will be based on individual tumor gene expression signatures, 2010.