

Basel, 1 June 2009

Encouraging first data on new targeted treatment for patients with melanoma – the deadliest form of skin cancer

PLX4032 (R7204) phase I results offer hope of first highly effective drug in melanoma along with companion diagnostic

Roche announced today results from a phase I study with PLX4032 (R7204) a new, highly selective and promising treatment for patients with advanced melanoma whose cancer harbours the *BRAF* mutation (known as mutation-positive). Patients treated with PLX4032 lived for a median of at least six months without their disease getting worse and experienced shrinkage of their tumours; this included patients where the cancer had spread to the liver, lung and bone^[1]. Historically, metastatic melanoma patients live less than two months before their disease progresses.

PLX4032 works in a highly innovative way by selectively inhibiting the cancer-causing *BRAF* mutation, and is being developed in parallel with a companion diagnostic to identify mutation-positive patients. These data represent a significant development in the treatment of melanoma for which there are few treatment options.

Following these initial positive findings, Roche and its partner Plexxikon will evaluate the activity of PLX4032 in larger trials to support a potential registration program beginning later this year. If successful, it is expected to launch with a tissue based companion diagnostic test, representing another step forward in personalising cancer treatment. The two companies in their strong partnership are co-developing PLX4032 for potential use in a number of cancers harbouring the *BRAF* mutation. They are also co-developing the diagnostic test to select mutation-positive patients for clinical trials, and ultimately, for treatment with PLX4032.

'PLX4032 has shown both tumour shrinkage and delay in tumour progression in patients whose tumours harbour a *BRAF* mutation, as well as improved quality of life for symptomatic patients,' stated Keith T. Flaherty, M.D., assistant professor at the Abramson Cancer Center of the University of Pennsylvania and principal investigator for the PLX4032 phase I clinical trial. 'Seven years after *BRAF* mutations were first identified we have validation that this mutation is a cancer driver and therapeutic target. In addition to a new

and important chapter in the story of targeted therapy development in cancer, we are especially excited for our melanoma patients for whom there are few treatment options.'

PLX4032 works by targeting and destroying tumour cells carrying the *BRAF* mutation. *BRAF* is an important mediator of cell growth and division, but when mutated is known to cause 60% of melanomas, the most deadly form of skin cancer, and approximately eight percent of all solid tumours. PLX4032's potency and selectivity is expected to result in a treatment that is both effective and well tolerated.

Malignant melanoma is the most serious type of skin cancer, with about 160,000 new cases diagnosed worldwide each year. Melanoma is treatable if caught early but patients who develop metastatic disease are rarely cured with available treatments. Only a small proportion of people (<2%) live more than two years once systemic metastases become evident¹.

About the study

ASCO Abstract #9000: Monday 1 June 2009, 16:30–18:00, EDT Level 4, Valencia Room, W415A

Promising preliminary findings reported in *BRAF* mutation-positive melanoma patients include:

- PLX4032 has been well tolerated at therapeutic doses
- Partial responses in nine mutation-positive melanoma patients and minor responses in four mutation-positive melanoma patients have been observed
- Regression of metastatic lesions in every site to which melanoma commonly spreads, including to the liver, lung and bone
- Disease control lasting up to 14 months with continuous therapy, with many responding patients still receiving treatment
- Interim median progression-free survival of at least six months

By contrast, no treatment response was observed in a small group of patients without the *BRAF* mutation, and progression-free survival was less than two months, consistent with historical data.

Drug-related adverse events, including rash and photosensitivity, have been classified as mild in grade. Serious adverse events, including diagnosis of cutaneous squamous cell carcinoma, were observed in some patients after chronic treatment; however the safety profile has been warranted favourable for this population and the trial authorised to proceed to the next stage of investigation.

The PLX4032 data not only represent an important step forward in understanding and treating malignant melanoma, but also represent a significant advance in the use of biomarkers and diagnostic tools and the potential benefits of tailoring cancer treatment to individual patients.

About Plexikon

Plexikon is a leader in the structure-guided discovery and development of novel small molecule pharmaceuticals to treat human disease. The company's clinical stage programs include PLX4032 for the treatment of melanoma and colorectal cancer, PLX5568 for the treatment of polycystic kidney disease and PLX204 for the treatment of diabetes. Among the company's preclinical development programs, candidates are being developed for the treatment of rheumatoid arthritis, multiple sclerosis and other autoimmune diseases as well as for the treatment of pancreatic and metastatic breast cancer.

Plexikon's proprietary Scaffold-Based Drug Discovery™ platform integrates multiple state-of-the-art technologies, including structural screening as one key component that provides a significant competitive advantage over other drug discovery approaches. To date, the company has discovered a portfolio of clinical and preclinical stage compounds being developed to address significant unmet medical needs in cardio-renal disease, CNS disorders, inflammatory and neuro-inflammatory diseases and oncology. For more information: www.plexikon.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 2008, Roche had over 80'000 employees worldwide and invested almost 9 billion Swiss francs in R&D. The Group posted sales of 45.6 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.

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Further information:

- Backgrounder Oncology: www.roche.com/media_backgrounder/media_oncology.htm
- Roche at ASCO: <http://www.roche.com/media/events/med-asco2009.htm>
- Videoclips, of broadcast standard: www.thenewsmarket.com

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^[1] ASCO 2009, Abstract #9000: "Phase 1 study of PLX4032: Proof-of-concept for V600E BRAF mutation as a therapeutic target in human cancer".

¹ Boyle P, et al. World Cancer report. IARC Press, Lyon, 2008