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Plexxikon Enters Roche Deal On B-Raf Inhibitors For $706M

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Earlier this week, Plexxikon Inc.'s president Kathleen Sereda Glaub told *BioWorld Today* that the company was in "active partnering mode."

That statement was more than corporate speak, and two days after signing a potential $100 million deal with French firm Servier, Plexxikon announced it has partnered an oncology program with F. Hoffmann-La Roche Ltd. in a deal with a $706 million potential, its largest to date.

The agreement focuses on PLX4032, Plexxikon's targeted cancer therapy designed to selectively inhibit a mutation in the B-Raf kinase gene found in about 70 percent of malignant melanomas, as well as a large number of colorectal and thyroid cancers. In exchange for exclusive worldwide rights to PLX4032 and other compounds targeting the B-Raf mutation, Roche will pay Plexxikon $40 million up front and provide $6 million in research funding over the next two years.

On top of that, Berkeley, Calif.-based Plexxikon could receive up to $660 million in development and commercial milestones "generously sprinkled" throughout the length of the collaboration, as well as royalties, Glaub said.

Basel, Switzerland-based Roche was one of "some very attractive contenders" interested in PLX4032 and its disease target, Glaub said, but it was Roche's financing and commercialization terms, which includes a U.S. co-promotion option for Plexxikon, as well as its expertise in the oncology space, that helped seal the deal.

PLX4032 initially will be pursued in melanoma patients with the B-Raf mutation, a population that is estimated at about 50,000 patients in the U.S., a market size that the company "could definitely handle in a fairly straightforward way," Glaub said.

A day before announcing the Roche deal, Plexxikon said it filed an investigational new drug application for PLX4032, with plans to begin a dose-escalation Phase I study before the end of the year.

The drug has shown promise in preclinical testing, where it demonstrated in both melanoma and colorectal cancer models an ability to reduce tumor size or slow progression of tumors for extended periods of time. It is designed to selectively target B-Raf^{V600E}, a mutated form of the B-Raf kinase gene, which is found only on tumor cells, providing the possibility of a "wide therapeutic window where you can increase the dose without having side effects," Glaub said.

That also means PLX4032 has the potential to be used in combination with other cancer drugs.

Because there is no existing standard of care for melanoma patients, Plexxikon is hoping for an accelerated development process, pending positive Phase I results, such as the potential to enter a Phase II registrational trial, Glaub said.

Now that the compound is partnered with Roche, she added, the company also hopes to quickly expand into other indications beyond melanoma, starting with colorectal cancer.

In a separate agreement, Plexxikon is collaborating with Roche's diagnostics division to co-develop an in vitro assay to detect whether cancer patients carry the particular B-Raf mutation targeted by PLX4032. That assay ideally would be used to accelerate clinical development by identifying those patients who would be the most likely responders to the drug.

The Roche deal is Plexxikon's second collaboration this week. On Monday, the firm announced it had signed a deal potentially worth more than $100 million with Servier to discover non-peptidic renin inhibitors aimed at cardiovascular disease, including hypertension.

Plexxikon has ongoing partnerships with Madison, N.J.-based Wyeth to develop PLX204, a peroxisome proliferator-activated receptor (PPAR) aimed at Type II diabetes, and with South San Francisco-based Genentech Inc. for use of Plexxikon's Scaffold-Based Drug Discovery platform to identify compounds against a kinase target.

The Wyeth deal is worth up to $372 million to Plexxikon. Terms of the Genentech collaboration were not disclosed. (See *BioWorld Today*, May 21, 2003, and Nov. 1, 2004.) ■