

Strategy

Plexxing its platform

By Urooj Mujtaba
Staff Writer

Plexxikon Inc., which set out in 2001 to discover and patent as many novel chemical scaffolds as possible, is now vertically integrating into therapeutics. Two deals announced last week will allow the company to develop its BRAF gene in cancer and enter the field of proteases, initially in cardiovascular indications.

“We started from scratch, with no IP or in-licensed compounds,” said CEO Peter Hirth. “We were able to do essential deals in rapid succession due to the compounds we generated

using our platform” (see “Plexxikon Deals”).

Plexxikon partnered with Servier (Neuilly-sur-Seine, France) to discover non-peptidic inhibitors of renin to treat hypertension and other cardiovascular indications. Also last week, the biotech granted Roche (SWX:ROCZ, Basel, Switzerland) an exclusive worldwide license to PLX4032 and follow-on compounds for cancer.

The Servier deal will allow the company to go into the field of proteases. “The problem with protease inhibitors is they are peptidic in nature, making their oral availability difficult to manage,” Hirth said. “But we start with completely nonpeptidic

Plexxikon deals

Selected deals since Plexxikon began operations in 2001, three of which are product-specific. ND = Not disclosed

Date	Company	Terms	Value
10/4/06	Roche	Roche obtains an exclusive worldwide license to develop and commercialize PLX4032, an inhibitor of the oncogenic V600E mutation in the BRAF gene for cancer. Plexxikon has U.S. co-promotion rights. The companies also will develop follow-on compounds against other BRAF mutations. Also, Plexxikon and Roche’s Roche Molecular Diagnostics unit will develop an in vitro assay to screen for the V600E mutation.	\$40M up front; \$6M in research funding over the next 2 years; up to \$660M in milestones; royalties
10/2/06	Servier	Partnered to discover non-peptidic inhibitors of renin to treat hypertension and other cardiovascular indications. Plexxikon will screen compounds from both companies against the aspartyl protease. Servier will be responsible for development and commercialization and will have an exclusive worldwide license to any renin inhibitors discovered for cardiovascular indications.	>\$100M in an upfront payment, research funding, milestones and royalties
4/6/05	Invitrogen	Invitrogen to profile Plexxikon’s kinase inhibitor libraries. The libraries will be screened against therapeutically relevant kinase targets.	ND
12/9/04	Phenomix	Partnered to co-develop PLX647, a dual c-Kit and FMS kinase inhibitor for arthritis. The partners discovered the compound under a 2003 deal.	ND
10/28/04	Wyeth	Partnered to develop Plexxikon’s PLX204 PPAR gamma, alpha and delta agonist to treat Type II diabetes. The deal includes other Plexxikon small molecules that target PPAR nuclear receptors. Wyeth has exclusive rights to PLX204 and other compounds. Plexxikon has an option to co-develop and co-fund clinical-stage compounds. If exercised, Wyeth would provide a loan to fund Plexxikon’s share of clinical expenses.	>\$22M in upfront payments and research funding; \$350M in milestones; royalties
11/20/03	Phenomix	Partners to develop small molecule inhibitors of stem cell factor (SCF) receptor c-Kit (CD117) to treat cancer, inflammatory and other diseases. Plexxikon to develop a series of leads, which Phenomix will evaluate for preclinical development. The companies may jointly or independently develop resulting compounds.	ND
5/20/03	Genentech	Plexxikon to develop a series of small molecule inhibitors against an undisclosed target in the protein kinase family associated with cancer. DNA has an option to commercialize resulting compounds worldwide.	Upfront technology fee; research funding; milestones; royalties
12/4/01	Scynexis	Obtained access to Scynexis’s MedChem-Factory automation and high throughput technology to discover and develop chemical scaffolds and lead compounds.	ND

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molecules. And what we learn from working with renin we can also apply to other protease targets.”

The company’s platform “is not restricted to any one target family or therapeutic area,” noted President Kathleen Sereda Glaub.

Under the deal, Plexxikon will use its platform to screen compounds from both companies against renin, an aspartyl protease. Servier will be responsible for developing and commercializing candidates and will have an exclusive worldwide license to any renin inhibitors discovered for cardiovascular indications.

Plexxikon (Berkeley, Calif.) could receive more than \$100 million from Servier, including an undisclosed upfront payment, research funding and milestones, plus royalties.

The ROCZ deal covers Plexxikon’s inhibitor of the oncogenic V600E mutation in the BRAF gene, PLX4032, which is expected to enter Phase I testing in cancer in November and complete the trial in the first half of 2007. Plexxikon and ROCZ’s Roche Molecular Diagnostic unit also will develop an in vitro assay to screen for the V600E mutation.

In 2002, researchers from The Wellcome Trust Sanger Institute published in *Nature* that the BRAF gene product plays a role in the etiology of melanoma. A screen for BRAF mutations in 530 cancer cell lines showed mutations in 59% (20/34) of melanomas and 18% (7/40) of colorectal cancers.

Under the deal, Plexxikon will receive \$40 million up front plus \$6 million in research funding over the next two years. The company also is eligible for up to \$600 million in milestones, plus royalties. Plexxikon will have a U.S. co-promotion option.