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## Plexxikon, Servier In Potential \$100M CV Drug Discovery Deal

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In its third major collaboration to date, Plexxikon Inc. signed a deal potentially worth more than \$100 million with French firm Servier to discover non-peptidic renin inhibitors aimed at cardiovascular disease, particularly hypertension.

An enzyme related to hypertension, renal failure and vascular disease, renin is a member of the aspartyl protease family, a class of proteins that Plexxikon scientists have been investigating using the company's Scaffold-Based Drug Discovery platform. The company will use that platform to identify potential candidates that Servier will take forward into development and possible commercialization.

With about three-fourths of their business dedicated to developing therapies for the cardiovascular space, Servier "was quite interested in pursuing this target," said Kathleen Sereda Glaub, president of Berkeley, Calif.-based Plexxikon. "Knowing the competitive landscape out there, they felt they needed a competitive advantage to accessing novel compounds, and that led to" this collaboration.

Under the terms, privately held Plexxikon will receive an up-front payment, research funding and potential milestone payments that could end up totaling more than \$100 million. The specific figures were not broken down, but Glaub described the deal as "very attractive relative to other discovery stage deals."

On top of that, Plexxikon could receive royalties on potential product sales, while Servier would hold exclusive worldwide rights to any renin inhibitors emerging from the collaboration in the cardiovascular field.

Meanwhile, the Servier deal allows Plexxikon to "work in new target areas," Glaub told *BioWorld Today*, while "really starting to develop a broader discovery effort" in the aspartyl protease family, which has been linked to other indications beyond cardiovascular, such as digestion, maturation of the HIV virus and Alzheimer's disease.

The aspartyl protease renin is an enzyme that has been shown to initiate the signaling cascade that up-regulates angiotensin II causing vasoconstriction. Though other hypertension products, namely angiotensin receptor blockers (ARBs) and ACE inhibitors, are on the market, Plexxikon said data suggest that renin inhibitors provide an added benefit to ARBs and ACE inhibitors and also might show promise in congestive heart failure and chronic renal disease.

Plexxikon's discovery platform is designed to screen for compounds using a biochemical screening process followed by co-crystallography filtering to identify compounds with binding sites. That technology "is really able to explore a different part of the chemical universe," Glaub said, compared to high-throughput screening techniques that employ potency as a filter and often end up with repetitive hits.

Compounds identified by Plexxikon "are small to start with, usually in the range of 150 to 300 in molecular weight," she said, and their straightforward structures "allow us to identify a potential development candidate and get it to the clinic much faster."

Glaub said it's too early to provide any sort of timeline for the development of a cardiovascular drug candidate for the Servier collaboration.

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In its pipeline, the company has a lead product, PLX204, in Phase II testing with partner Wyeth, of Madison, N.J. That compound is a peroxisome proliferators-activated receptor (PPAR), designed with a "pan activity" in the hope of targeting Type II diabetes, as well as lipid disorders often associated with Type II diabetes, Glaub said.

Plexxikon and Wyeth entered the deal, worth up to \$372 million to Plexxikon, two years ago to develop drugs for metabolic disorders. (See *BioWorld Today*, Nov. 1, 2004.)

The company also has a collaboration signed in May 2003 with South San Francisco-based Genentech Inc. to use its discovery platform to identify and develop protein lead compounds against a target in the kinase family. (See *BioWorld Today*, May 21, 2003.)

Additional partnerships are expected to follow, Glaub said, adding that "we're in active partnering mode right now," though the company intends to seek those future collaborations after identifying a development stage compound.

Not yet partnered is the firm's lead oncology program, PLX4032, a B-Raf inhibitor aimed at targeting a mutation found in 70 percent of skin cancers as well as a significant number of colorectal, ovarian and thyroid cancers.

That product is completing preclinical work, and "we hope to be filing an IND on that shortly," Glaub said. ■