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## Intellikine Moves into Busy P13K Space with Tricks Up Its Sleeve

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Start-up Intellikine Inc. came out from under the radar earlier this month with a \$51 million Series B financing to tackle one of the hottest pathways in biotech: PI3K.

Data indicate big potential for phosphoinositide-3 kinase inhibitors in cancer and other diseases, and pharma is taking notice. Sanofi-Aventis Group agreed to pay Exelixis Inc. a whopping \$140 million up front in a potential billion-dollar PI3K deal, and F. Hoffmann-La Roche Ltd. forked over \$175 million to acquire Piramed Ltd. for its PI3K programs.

Other biotechs with PI3K programs in the clinic include Semafore Pharmaceuticals Inc., Calistoga Pharmaceuticals Inc. and Oncothyreon Inc. At least another half-dozen biotechs are in preclinical, and pharma has its own programs under way as well. It is the crowded space in which Intellikine intends to play, but the start-up has a few tricks up its sleeves.

Troy Wilson, co-founder, president and CEO of the La Jolla, Calif.-based company, explained that most of the PI3K work currently under way involves pan-inhibitors. "The challenge has been to inhibit one protein or enzyme and not everything. You really want isoform-selective inhibitors," Wilson noted.

The PI3K family includes alpha, beta, delta and gamma isoforms. PI3K-alpha is one of the most frequently mutated kinases in cancer, and inhibitors selective for alpha or possibly alpha and beta are expected to provide better efficacy and safety in solid tumors than pan-inhibitors.

Meanwhile, delta and gamma are more common in hematologic cancers such as lymphoma, leukemia and myeloma and also may play a role in asthma, allergy and autoimmune diseases. One of the only companies pursuing isoform-selective PI3K inhibitors is Calistoga. Its CAL-101 is specific for delta, while CAL-120 is specific for beta.

But interest in isoforms is growing: Sanofi and Exelixis' deal included a discovery agreement aimed at isoform-selective PI3K inhibitors. Intellikine has preclinical programs targeting alpha/beta for oncology, delta/gamma for oncology, delta/gamma for inflammatory disease and delta/gamma for respiratory disease. One of the oncology programs is expected to move into the clinic in 2010. Yet Intellikine's lead program targets the mammalian target of rapamycin, or mTOR, a popular cancer target in the PI3K pathway. Again, selectivity is the key. While most inhibitors developed to date focus on mTOR com-

plex 1 (mTORC1), Intellikine's compound inhibits both mTORC1 and mTOR complex 2 (mTORC2). Intellikine's mTORC1/2 program is expected to enter the clinic within a year.

Wilson said Intellikine is "in the midst" of business development discussions with potential partners and has plenty of programs available to license. The company's scientific team has an "unbelievable" ability to generate isoform-selective inhibitors, he added. That team includes kinase pioneer Kevan Shokat, professor at the University of California in San Francisco and in Berkeley and Howard Hughes Medical Institute investigator.

Shokat co-founded Intellikine in 2007 along with Zachary Knight, of Rockefeller University, as well as Yi Liu and Pingda Ren, both of whom formerly worked for the Genomics Institute of the Novartis Research Foundation and now hold management positions at Intellikine. After raising a \$12.5 million Series A round in 2007, Intellikine hired Chief Scientific Officer Christian Rommel, who headed target research at Merck-Serono, a division of Merck KGaA. "If Kevan Shokat was the academic heavyweight in PI3K, Christian Rommel was his industry counterpart," Wilson explained.

In addition to the team, Wilson attributed Intellikine's edge to an academic collaboration that provides privileged access to crystal structures of the PI3K isoforms. Additionally, the company has a fast cycle time thanks to outsourcing chemistry operations to China, Wilson said.

And now, with a \$51 million Series B financing in place, Intellikine is set through at least 2012. The company already received a \$28.5 million first tranche, and the remaining \$22.5 million will be delivered subject to the achievement of undisclosed milestones. Novartis Bioventures Ltd. led the financing, which also included new investors U.S. Venture Partners, Biogen Idec and FinTech Global Capital. Existing investors Abingworth, CMEA Capital and Sofinnova Ventures also participated.

Wilson said the Series B attracted so much interest that "we have additional investors who have approached us and want us to take more money, and the board is evaluating what to do." Investors are banking on PI3K remaining a hot target, and although Wilson said Intellikine worked hard on the financing, he admitted the company was "very much in the right place at the right time." ■

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