

BIO WORLD[®] TODAY

MONDAY
JULY 13, 2009

THE DAILY BIOTECHNOLOGY NEWSPAPER

VOLUME 20, No. 132
SPECIAL REPRINT

Presidio Gets \$27M B-Extension for Preclinical HCV Programs

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Presidio Pharmaceuticals Inc. raised \$27 million in a Series B extension to drive clinical trials of PPI-461, a preclinical small-molecule NS5A inhibitor for hepatitis C.

The new round follows a \$26 million Series B financing completed in 2007 and a \$1.4 million Series A financing completed in 2006. Omar Haffar, president and CEO of Presidio, said the San Francisco-based company now has enough money to carry it into 2011.

The Series B extension was triggered by Presidio's recent selection of PPI-461 as its lead clinical candidate. Existing investors Panorama Capital, Baker Brothers Investments, Ventures West Capital, Bay City Capital, Nexus Medical Partners and Sagamore BioVentures re-upped in the round, but new investor New Leaf Venture Partners also joined.

New Leaf's interest in Presidio was driven by managing director Srinivas Akkaraju, who previously worked for Panorama and held a seat on Presidio's board of directors. Akkaraju said that even after leaving Panorama, he stayed on Presidio's board as an independent director in the hope that he could "stay involved in the company." That hope became reality as New Leaf completed its due diligence and joined the syndicate. Most of the funding is dedicated to advancing PPI-461, which Presidio developed internally based on an NS5A inhibitor program licensed from XTL Biopharmaceuticals Ltd. (See *BioWorld Today*, March 21, 2008.)

Preclinical studies have shown that PPI-461 exhibits picomolar potency in the in vitro replicon assay, provides coverage against all seven HCV genotypes, has a high resistance barrier, is well tolerated and has the potential for once-daily dosing. Haffar added that the compound is synergistic with all other classes of HCV drugs, including protease inhibitors, polymerase inhibitors and interferon.

The current standard of care for HCV, ribavirin plus pegylated interferon, often comes under fire for its 40 percent to 50 percent cure rate and significant side effects. Yet the treatment landscape is poised for a paradigm shift, as protease inhibitors like Schering-Plough Corp.'s boceprevir and Vertex Pharmaceuticals Inc.'s telaprevir advance through Phase III. Polymerase inhibitors also are moving through the clinic, and the latest craze is to combine the two direct antiviral approaches and phase out the old standards altogether.

At the annual meeting of the European Association for the Study of the Liver (EASL) in April, data from the first-ever clinical study to combine two direct antivirals garnered plenty of attention. Adding the protease inhibitor R7227 (InterMune Inc. and F. Hoffmann-La Roche Ltd.) to the polymerase inhibitor R7128 (Pharmasset Inc. and F. Hoffmann-La Roche Ltd.) resulted in median viral load reductions between 3.9 log₁₀ and 5.2 log₁₀ after 14 days of dosing in treatment-naïve HCV patients. (See *BioWorld Today*, April 28, 2009.)

Other combinations are likely to move into the clinic as well: Vertex recently acquired ViroChem Pharma Inc. for its polymerase inhibitor VCH-222, which could be combined with telaprevir. (See *BioWorld Today*, March 5, 2009.)

"We all understand the value of combination therapy in antiviral management – the paradigm has been laid down by the management of HIV," Haffar said. He noted that Presidio is taking combination strategies "into consideration" as it determines its clinical development plan. Investigational new drug application-enabling studies of PPI-461 are under way, and clinical trials are slated to begin in the first half of next year.

Meanwhile, interest is picking up in NS5A and other nonstructural proteins involved in HCV replication. Bristol-Myers Squibb Co. has an NS5A program in the clinic, and start-up Eiger BioPharmaceuticals Inc. is working on NS4B and NS5A as well. Presidio, too, has a second program targeting NS4B and a different region of NS5A than PPI-461. The technology was licensed from Stanford University and is still in the discovery stage.

Akkaraju noted that although the NS5A field isn't crowded yet, it will be in the future. He predicted that the ultimate HCV combination therapy will include an NS5A inhibitor and said there may be room for two or three potent NS5A inhibitors on the market.

Presidio's pipeline includes other assets as well. The nucleoside reverse transcriptase inhibitor PPI-802, licensed from Medivir AB, is in preclinical for HIV, and a nuclear exclusion technology platform licensed from Cytokine PharmaSciences is in early discovery for HIV. Yet Haffar noted that, like many other small biotechs, Presidio has had to make some tough decisions and prioritize, so for now most of the emphasis is on reaching clinical proof of concept with PPI-461 for HCV. ■

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