

## BioVex's \$70M Series F to Fund Pivotal OncoVex Melanoma Trial

The terms "cancer vaccine" and "gene therapy" don't tend to inspire investor confidence, given the history of high-profile failures in both fields. Nor does "melanoma," for that matter.

But none of that stopped BioVex Inc. from raising \$70 million in a Series F financing to support its ongoing Phase III melanoma trial of OncoVex GM-CSF, a modified herpes simplex virus that carries the gene for granulocyte macrophage colony-stimulating factor (GM-CSF).

BioVex has raised upward of \$150 million since spinning out of University College London in 1999. Many existing investors like GeneChem Management, Avalon Ventures and Forbion Capital Partners have remained true along the way: Forbion and others ponied up \$40 million for the first close of BioVex's Series F round in March. (See *BioWorld Today*, March 31, 2009.)

Yet BioVex also has been able to attract new money - no easy feat in the current economy. The Woburn, Mass.-based company just completed an oversubscribed \$30 million second close to the Series F round backed entirely by new investors. Morningside Venture, Ventech and MVM Life Science Partners co-led the second close, while Sectoral Asset Management and Ysios Capital Partners also participated.

The investor interest may have to do with what BioVex president and CEO Philip Astley-Sparke calls OncoVex's "paradigm-shifting" dual mechanism of action.

The drug primarily works through direct tumor cell lysis: the herpes simplex virus, which has undergone a single gene deletion to render it harmless to normal cells, targets and destroys tumor cells. Yet the added gene for GM-CSF triggers an immune response, giving OncoVex a gene therapy and cancer vaccine flavor.

A single-arm Phase II trial of 50 late-stage melanoma patients treated with OncoVex as a monotherapy resulted in 14 objective responses, including 10 complete responses, some of which have been maintained for nearly four years.

Ninety two percent of the responses lasted at least six months, and many are ongoing. Astley-Sparke called the data "unprecedented," particularly given the difficulty in

treating melanoma.

Only 16 percent of late-stage melanoma patients are expected to survive five years, and there is no standard of care, Astley-Sparke said.

He noted that treatment guidelines recommend seeking out a clinical trial, but those are growing fewer and farther between.

Clinical failures have included Genta Inc.'s Genasense (oblimersen sodium), Synta Pharmaceuticals Corp.'s elesclomol, Onyx Pharmaceuticals Inc. and Bayer AG's Nexavar (sorafenib), CancerVax Corp.'s Canvaxin and many others.

Some metastatic melanoma patients currently are treated with the immunotherapy interleukin-2, and patients who respond usually go into durable remission.

Although side effects make the regimen too harsh for widespread use, Astley-Sparke said it provides validation for the immune-stimulating approach.

Now BioVex's challenge is to replicate its single-arm Phase II efficacy in a controlled Phase III setting.

The company's ongoing pivotal trial is enrolling 360 patients to receive either OncoVex or subcutaneously administered GM-CSF, which has been shown to delay melanoma recurrence in an adjuvant setting.

The primary endpoint of BioVex's pivotal study is durable response, defined as a 50 percent decrease in disease burden maintained for at least six months. It's an interesting choice, given the FDA's emphasis on overall survival as the gold standard in oncology trials. But the trial was designed under an FDA special protocol assessment, which implies that the FDA is on board. (See *BioWorld Today*, April 23, 2008.)

Astley-Sparke declined to speculate as to the FDA's thinking, but he noted that the lack of recognized therapies in the U.S. for most melanoma patients may have factored into the outcome.

Data from the study are expected in late 2010, and the Series F financing will carry BioVex to that point as well as into 2011 and toward an approval filing. That puts the company in the "luxurious" position of not needing a partner immediately, Astley-Sparke said - yet he added that partnership discussions are ongoing.

BioVex also has a special protocol assessment in place for a Phase III trial of OncoVex in head and neck cancer, but Astley-Sparke said the company is "looking for alternative ways to fund" that study.

A second product, the ImmunoVex HSV2 vaccine for genital herpes, is poised to begin clinical trials.

Additional funding for those programs also could come from the public markets.

BioVex made plans to go public back in 2006 but never completed the deal.

Astley-Sparke said the company has "no plans" for an initial public offering at the moment but is keeping an eye on developments in the IPO markets.