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With Antisense Rx Already in Phase I, Bio-Path Eyes RNAi Rx Market

WITH AN ANTISENSE-BASED DRUG already in a small phase I study, Bio-Path Holdings has begun eyeing the RNAi space with the hope that the ongoing clinical trial will confirm the efficacy of its proprietary delivery technology and help it secure capital to advance an siRNA therapeutic into the clinic.

Bio-Path was founded in 2007 to commercialize a drug-delivery approach developed at MD Anderson Cancer Center that involves the use of neutral lipids to carry oligonucleotide payloads.

According to President and CEO Peter Nielson, most other lipid-delivery vehicles being tested with antisense and RNAi drugs are cationic, which often causes toxicity at therapeutically relevant levels.

By comparison, Bio-Path's dioleoylphosphatidylcholine lipids have a neutral charge and "basically form liposomes based on their hydrophilic/hydrophobic properties," Nielson said.

The company's lead drug candidate, BP-100-1.01, is a lyophilized powder that, when reconstituted with saline and injected intravenously, "causes the lipids in the drug powder to self-organize into liposome structures with … the hydrophobic antisense incorporating into the interiors of those liposomes."

BP-100-1.01 comprises antisense oligos targeting growth factor receptor-bound protein-2, an adaptor protein that links tyrosine kinases with downstream signaling molecules, according to the company. In 2007, researchers at MD Anderson reported this agent could boost the survival of mice bearing leukemia xenografts, suggesting utility as a cancer therapy.

Having acquired the rights to the delivery technology for use with nucleic-acid drugs, last July Houston-based Bio-Path moved the drug into a phase I trial.

That study, which is ongoing, is designed to evaluate five doses of BP-100-1.01 in up to 30 patients with various leukemias who had relapsed or become refractory to standard therapies. Nielson noted that enrollment was initially difficult given the variety of other treatment options available.

At the same time, a number of patients dropped out of the study before completing treatment because of the severity of their disease.

Nielson said that the trial has enrolled 14 patients, but only six were evaluable. Of those, five completed the full four-week treatment regimen.

Importantly, two of five patients appear to have experienced some therapeutic benefit from BP-100-1.01, a result the company said in a recent filing with the US Securities and Exchange Commission is expected to "help in recruiting new patients into the clinical trial."

Nielson said that the study's lead investigator is aiming to present initial data at the American Society of Hematology meeting in San Diego in December, which could help Bio-Path meet its goal of raising interest in its drug-delivery technology so that it can attract new investors and potentially industry partners.

Noting that Bio-Path is a small company with limited resources, Nielson said that the firm's strategy of first moving an antisense drug into the clinic is meant to

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help establish the safety and efficacy of the delivery system.

Once that had been done, the company could then begin thinking about advancing other of its programs, including a preclinical RNAi cancer therapy.

"For our size and resources … we can't spread ourselves too thin or we won't be able to complete anything," he said. "The prudent path for us was to take a very good antisense drug and put it into the clinic … [to get] a demonstration of proof-of-concept with the delivery technology.

Should the data on BP-100-1.01 be compelling, the publicly traded company aims to raise new capital from institutional investors, Nielson said. This would provide it with the financial resources to continue developing the drug and move forward with its siRNA-based candidate.

At the same time, he said the company hopes to be able to attract big pharmas that might be interested in licensing the delivery technology for applications outside of Bio-Path's focus.

"They will find us as we demonstrate the delivery technology," Nielson said of potential licensees. "We have a platform technology and we can't do everything, so we'd very much be open" to deals.

Once the company does secure these funds, which would enable the required toxicology testing for the siRNA candidate, Bio-Path expects it could have the drug in phase I testing within 12 months, he added.