Biopharma Strategies

BIO-PATH HOPES TO BLAZE PROFITABLE PATH WITH ANTISENSE DRUGS

Peter Nielsen believes he leads the little biotech company that could. Armed with technology that was licensed from the **University of Texas MD Anderson Cancer Center**, **Bio-Path Holdings Inc.** is trying to become the next company to make it big with antisense drugs, which are designed to inhibit the production of disease-causing proteins. Although long seen as challenging, the field has staged a comeback with **AbbVie Inc.**, **Roche**, **Johnson & Johnson**, **Cyclacel Pharmaceuticals Inc.**, **Isis Pharmaceuticals Inc.** and others pursuing antisense R&D.

Like so many other companies chasing lucrative patient populations, Bio-Path is focusing on various forms of cancer. Recently, the Houston-based biotech released data showing its lead compound BP-1001 may hold promise in treating advanced acute myeloid leukemia, or AML.

In general, "AML is quickly becoming a crowded space, but the highly fragmented market opens several avenues for drug development," wrote Leerink analysts in an investor note while attending the *57th American Society of Hematology Annual Meeting*, held in Orlando, FL, in early December. "The elderly, unfit AML population offers a low bar for success." They noted the current standard of care offers a complete response rate of just 20%, underscoring a lack of treatment alternatives.

Using what it calls *DNAbilize* technology, Bio-Path maintains that its liposomal delivery system can distribute antisense drugs throughout the body by intravenous infusion. Nielsen, who founded the company in 2007, is betting on the ability to apply the proprietary delivery technology to almost any protein target and, eventually, expand to other cancers, such as lymphoma and CML.

At its core, the company's approach is to avoid using a toxic agent to kill cells and, instead, block production of proteins, specifically targeting disease-causing proteins.

A poster presentation at the ASH meeting reported that two of three evaluable patients suffering from advanced AML in a Phase Ib trial achieved complete remission. Those patients were treated with a 60-mg dose.

Of 36 patients in the Phase I and Phase Ib trials, only one experienced a dose-limiting toxicity, and this was attributed to the previous administration of hydroxyurea, a chemotherapy. The company also pointed out that the patients evaluated in its Phase Ib study were refractory and treatment resistant. On average, they had experienced four prior therapies. (The poster included data from the first seven cohorts of the study; the eighth and final cohort is ongoing.)

"We think we've developed, for the first time, an ability to deliver antisense technology and target cells," says Nielsen, who is Bio-Path's CEO. "We were able to show that, at the highest dose, we could reduce target protein levels in patients by over 50%. And we demonstrated we could efficiently deliver the molecule through an IV infusion," as opposed to injections.

"We don't feel that anybody has a delivery technology that can deliver antisense molecules for cancer therapy as we do," he says. "If we pre-treat AML cells with our drug, which is called Liposomal GRB-2, with cytarabine [an older chemotherapy] at a low dose, we can get a significantly greater killing of cells than when patients are treated with just cytarabine." The dosing, by the way, ranged from 5 mg to 90 mg.

"They're trying to stop cancer on a basic genetic level – by knocking out the RNA part. But the antisense is a slightly unusual twist," says Steve Brozak, managing partner at WBB Securities, who tracks the biopharmaceutical industry for the investment management and banking firm.

"It's got sophistication to it, certainly, compared with blasting someone with toxic drugs, by which I mean chemotherapy. But this is a small-cap player among many other biotech companies that continuously need funding. The science has promise, but the path toward a successful treatment is always a winding road," he states.

Indeed, another analyst notes that the results – while encouraging – are from an early-stage trial and the testing was conducted, naturally, in a small patient population. This, of course, means that more rigorous and extensive testing is needed to take the product from the lab to the hospital or physician's office.

"This seems pretty early," says Les Funtleyder, a former securities analyst who tracked the pharmaceutical industry and is now health care portfolio manager at ESquared Asset Management. "And also, liposomes have been around forever. I am not seeing the novelty. But I guess if they show great later-stage efficacy data that would be something else."

Just the same, investor reaction has been upbeat much of the year. In the weeks leading to the ASH meeting, shares climbed. They were $1.41 on November 5 and reached $1.99 on December 7, just before the company presented its poster at the meeting. The stock settled back to $1.69 the following day.

For his part, Nielsen argues that Bio-Path "isn't just a lipid delivery company. We have the antisense [patents and product] to go with that."

Having demonstrated proof-of-principle for the compound, which was given orphan drug designation by the Food and Drug Administration, Bio-Path now plans a Phase II trial that will test the 90-mg dose on 54 patients at up to eight locations around the US.

"We think antisense can target individual genes that disrupt cells," says Ulrich Mueller, Bio-Path's chief operating officer, who was previously a vice president at the Fred Hutchinson Center Research Center in Seattle. "You have the prospect of cancer treatments without horrible side effects. … We don't feel that anybody else has a delivery technology that can deliver antisense molecules for cancer therapy. … A lot of other molecules are direct injections that are not designed for cancer."

The single-arm study is expected to run two years. And, once again, the company will rely on an MD Anderson researcher – who has yet to be chosen – to run the trial. It will not be Jorge Cortes, MD, who is deputy chair of MD Anderson's Department of Leukemia and was principal investigator for the Phase Ib trial, because he joined the firm's scientific advisory board.

The company got its start in 2007; Bio-Path

was privately held and raised seed capital, which was used to obtain an exclusive license for the delivery technology from MD Anderson. The following year, a reverse merger was engineered with a public shell company. Since then, the biotech has been developing its lead compound.

The licensing deal involved giving MD Anderson about 4 million shares, which makes the institution a sizeable shareholder. There are around 90 million outstanding shares and Bio-Path's market capitalization was roughly $170 million last month. The company is burning approximately $1 million per quarter, not including clinical trial costs. Nielsen notes there is $25 million in ATM financing in place with Cantor Fitzgerald, the investment bank.

In the third quarter ended September 30, Bio-Path reported a net loss of $1.5 million, compared with a net loss of $1.1 million during the same quarter in the previous year. The company attributed the increased loss primarily to additional drug manufacturing and testing, an increase in drug material used and higher clinical trial expenses.

Research and development expenses for the most recent quarter were $1 million, up from $0.4 million, reflecting, in part, additional hiring. As of September 30, 2015, Bio-Path had cash of $9.9 million, compared with $13.9 million as of December 31, 2014. Net cash used for operating activities during the recent quarter was $4 million, compared with $2.7 million for the comparable period in 2014.

Going forward, Bio-Path is eyeing a Phase II trial to test the compound for treating chronic myelogenous leukemia. Nielsen acknowledges that AML and CML are "crowded spaces" and finding suitable patients for studies is challenging.

"But we'll use the same strategy" for CML, he says. "We're going into patients who have re-entered blast crisis, where there aren't a lot of treatment options right now. It's another unmet medical need." The firm expects to complete preparations to start the toxicity portion of a Phase II trial before the end of the year.

The company is also looking to develop additional indications in triple negative and inflammatory breast cancers and in other solid tumors. And Bio-Path is in the process of putting together an Investigational New Drug application to test a second compound in a Phase I trial for combating follicular lymphoma. The IND application is expected to be filed in early 2016.

A third potential candidate is being screened for further development and Bio-Path is touting the possibility of treating a variety of maladies, including diffuse large B-cell lymphoma, non-small cell lung cancer, pancreatic cancer and others diseases, such as autoimmune disorders.

"Where we're at right now, we have plenty of money to fund these programs," says Nielsen. "The game plan is to roll these things out this year and become a fully vested Phase II company with a couple of trials going on. From there, we'd probably look to do another common stock offering. … We could use $30 million to $50 million with everything going on for the following year. But we have plenty to last us through 2016."

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By Ed Silverman

DEALS OF THE MONTH

IN VIVO's editors pick November's top alliance, financing and M&A deals

TOP ALLIANCE:
CELLECTIS, SERVIER, PFIZER ALLY IN CAR-T

Cellectis SA's early November news that its TALEN gene-edited CAR-T immunotherapy UCART19 had put a baby with acute lymphoblastic leukemia into remission no doubt encouraged **Pfizer Inc.** and **Servier SA** to morph their existing deals with the company into an exclusive global license and collaboration agreement. Cellectis' products are allogeneic and therefore can be used "off the shelf" potentially giving the partners an easier path to market than competitors with autologous CAR-T products that will likely face major manufacturing and scale-up challenges.

TOP M&A:
PFIZER AND ALLERGAN SEAL THE DEAL

Pfizer Inc. and **Allergan PLC**'s much-anticipated $160 billion merger is the biggest deal in health care history. Pfizer will own 56% of the new company, and the deal enables it to break free from a US corporate tax regime it has described as excessively punitive and damaging to its competitive position. Minority owner Allergan gets direct access to some 70 geographical markets where it has no presence. And for now at least, leaders from both companies tout the deals' operational synergies and R&D advantages.

TOP FINANCING:
BOSTON PHARMA BRIDGES VALLEY OF DEATH

Gurnet Point Capital, the investment firm that recruited ex- Sanofi CEO Christopher Viehbacher earlier this year, has committed $600 million to **Boston Pharmaceuticals Inc.**, which aims to de-risk and hand off promising early-stage drug candidates to partners. Boston Pharma will build a portfolio of up to 25 Phase I and II drug candidates. The start-up is agnostic about drug types and therapeutic areas, as long as candidates are targeting an unmet or undermet disease, have a validated mechanism of action and a clear path to market.