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Shkreli's Retrophin Eyes Public Markets to Fund Rare Diseases

By Trista Morrison
Staff Writer

Martin Shkreli has never been one to go with the flow. The hedge fund manager at MSMB Capital Management is known for activism: He helped derail the proposed merger between AMAG Pharmaceuticals Inc. and Allos Therapeutics Inc., fought Pfizer Inc.'s decision to replace CEO Jeff Kindler with an insider and has pushed out several health care CEOs he felt weren't doing their jobs.

So it stands to reason that when Shkreli decided to start a biotech company, the approach would be far from conventional.

Retrophin LLC burst onto the rare disease stage last month, announcing that it had licensed a DARA (dual-acting receptor antagonist of angiotensin and endothelin receptors) program from Ligand Pharmaceuticals Inc. In exchange for $1 million up front, $75 million in potential milestone payments and 9 percent royalties, the start-up got rights to a compound that had already completed a Phase IIb trial for hypertension.

But while the hypertension market is "not lucrative anymore," Shkreli pointed out, Retrophin sees DARA as a great potential option for focal segmental glomerulosclerosis (FSGS), a rare kidney disease with no approved treatments.

Shkreli explained that endothelin receptor antagonists Tracleer (bosentan, Actelion Ltd.) and Letairis (ambrisentan, Gilead Sciences Inc.) have proved effective in pulmonary arterial hypertension because they dilate the blood vessels, preventing consistent high blood pressure from degrading the heart and lungs. In FSGS, scar tissue prevents the kidney from effectively filtering blood, eventually degrading the kidney and often resulting in high blood pressure.

"We think we can slow the progression of the disease," Shkreli said. Phase II trials with DARA – now dubbed RE021 – are slated to start soon, and Retrophin is aiming to concurrently start a randomized Phase III trial that could potentially serve as the basis for approval.

It is rare, although certainly not unheard of, for a biotech start-up to come out of stealth mode with a compound poised to enter pivotal trials – but that's not all Retrophin has in its pipeline. The New York-based biotech was founded after Shkreli met a young patient who soon died from a rare condition related to muscular dystrophy. Shkreli said he was inspired to seek out a treatment for Duchenne's muscular dystrophy (DMD), a disease in which a reduction in the protein dystrophin leads to a chronic loss of muscle function.

"We thought it would make sense to replace the missing protein – that's been a good strategy since the dawn of biotechnology," he said. The trick was to get the protein inside the cells; Shkreli explained that most proteins cannot get through the cell membrane. Genzyme Corp. overcame that hurdle by using mannose 6-phosphate, but Retrophin's approach involves using a small, noninfectious piece of HIV.

The resulting compound, RE001, which Shkreli himself wrote the sequence for, caused

a doubling of survival in preclinical DMD models, he said. Retrophin hopes to file an investigational new drug application within the next 12 months.

DMD has proved to be a tough indication: PTC Therapeutics Inc.'s ataluren missed its primary endpoint in a Phase II trial and subsequently was dropped by Genzyme, following that firm's acquisition by Sanofi SA, despite generating other promising data. Prosensa Therapeutics BV and partner GlaxoSmithKline plc have an exon-skipping approach in Phase III, but Shkreli said no one has tried straightforward protein replacement. (See *BioWorld Today*, Sept. 6, 2011.)

He noted that Retrophin's platform technology for delivering proteins into cells could be applicable in a host of diseases like spinal muscular atrophy and cystic fibrosis. "There are probably 50 or 60 intracellular monogenic diseases," Shkreli said. "We think we can definitely open up a new area of medicine."

Retrophin's funding to date also has been somewhat unconventional. The biotech raised $3 million in a Series A round led by MSMB Capital, with participation by private investors, including former Schering-Plough Corp. CEO Fred Hassan, now chairman of Bausch & Lomb, and former president of Schering-Plough's Global Consumer Healthcare unit Brent Saunders, now CEO of Bausch & Lomb. No venture capitalists were included in the round.

Now that Retrophin has in-licensed a pivotal program, expenses will increase, so Shkreli said continuing to fund the firm as needed with investments from private individuals is "probably off the table."

Instead, Retrophin, might do a large fundraising, which would likely be backed by private equity or hedge funds rather than venture capitalists, he said. But the firm is more likely to pursue a public-related transaction, such as a reverse merger or initial public offering, according to Shkreli. ■

Retrophin

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