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10 Health Care Information Technology: Venture's New Darling?

As traditional venture-like returns are harder to generate from drug development and medtech plays, some frustrated VCs see new opportunities in health care information technology, an area many have traditionally avoided.

BY PAUL BONANOS

16 Drug-Eluting Balloons: Promise Versus Practicalities

Drug-eluting balloons might someday pick up where drug-eluting stents leave off, promising to solve problems not addressed – and even created - by DES. But despite what interventional cardiology companies have learned about device and drug combinations, the drug-eluting balloon markets aren't as simple as they might at first seem.

BY MARY STUART

PROFILES | Novel Respiratory Therapies: Moving Beyond Symptomatic Relief

Start-Ups *Across Health Care*

BIOTECHNOLOGY

Promedior Inc.

Advancing a pentraxin platform against fibrosis

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Contact: Dominick Colangelo, President & CEO
Business: Pentraxin therapeutics for treating fibrosis and inflammation
Founded: April 2006
Founders: Richard H. Gomer, PhD (Texas A&M University); Darrell Pilling, PhD (Texas A&M University)
Employees: 12
Financing to Date: $41 million
Investors: Morgenthaler Ventures; HealthCare Ventures; Polaris Venture Partners; Forbion Capital Partners; Easton Capital Investment Group
Board of Directors: Joseph S. Zakrzewski (Xcellerex); Dominick C. Colangelo; James W. Broderick, MD (Morgenthaler Ventures); Amir Nashat, PhD (Polaris Venture Partners); Harold R. Werner (HealthCare Ventures); Geert-Jan Mulder, MD, (Forbion Capital Partners); John H. Friedman (Easton Capital Investment Group); Paul D. Goldenheim, MD (formerly TransForm Pharmaceuticals)
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Wound healing allows survival of all sorts of grievous injuries, but it has its dark side. Improperly regulated, the complex interplay between scaffolding and new tissue growth can lead to scar tissue and fibrosis. It's not a matter of cosmetics: fibrosis can seriously impede organ function, and it is considered a leading cause of death in the US.

Few treatments exist for fibrosis, and none are currently approved by FDA. In March, **InterMune Inc.** announced that its drug pirfenidone had received marketing clearance in the European Union for the treatment of mild to moderate idiopathic pulmonary fibrosis (IPF), characterized by scarring and thickening of lung tissue. Pirfenidone inhibits the synthesis of TGF-beta, which plays an active role in inflammation. The company has also obtained priority review status for the drug in the US.

Promedior Inc. is developing a biology platform based upon a protein called pentraxin-2 (PTX-2) to combat fibrosis. It is a naturally occurring protein that circulates in the serum, where it binds to DNA, chromatin and cellular debris so that they can be digested and cleared away by phagocytes before they prompt an inappropriate inflammatory response. After binding to cell debris, PTX-2 undergoes a change in shape that allows it to bind to Fc gamma receptors on monocytes, which respond by differentiating into regulatory macrophages.

In normal healing, monocytes differentiate into both regulatory macrophages and profibrotic cells known as M2 macrophages and fibrocytes. During fibrosis, that balance is upset and differentiation favors profibrotic cells.

Promedior researchers believe that PTX-2 could push that equilibrium back to a more normal balance. Recent studies suggest levels of the protein may be low in patients suffering from idiopathic pulmonary fibrosis, and lung function is directly correlated to circulating levels of PTX-2. Similar findings have been noted in kidney disease and kidney function, as well as myelofibrosis, in which scar tissue replaces bone marrow. "There is emerging data correlating low pentraxin-2 levels with fibrotic disease and impaired organ function," says Nick Colangelo, president and CEO of Promedior.

Extensive preclinical studies provided further encouragement. "We saw robust efficacy in more than a dozen validated disease models, in the lung, liver, and kidney, among others. There's a common biology in play here, and we think that's demonstrated by the strong biologic effect we've seen with PTX-2 in all these models of disease," says Colangelo.

In the absence of anything to bind to, pentraxin-2 is inert, which makes it quite safe, according to Colangelo. It is also attractive from a therapeutic standpoint because it acts as an agonist, encouraging cells to differentiate in a helpful direction. As a result, the effect can be long-lasting because the descendant cells remain active for weeks after the drug has cleared. Some other anti-fibrosis approaches rely on inhibitors of processes such as collagen synthesis or cross-linking, where the effect is likely to disappear with the drug, leading to more frequent and perhaps higher dosing and potentially more side effects.

PRM-151, a fully recombinant version of PTX-2, is the subject of two ongoing clinical studies, including a Phase II study for the prevention of postsurgical scarring in order to maintain improved drainage and reduced intraocular pressure following glaucoma filtration surgery. A common side effect of the procedure is postsurgical scarring. Colangelo expects initial data from the trial to be available by the middle of next year.

The study will allow researchers to gain histological insight into scarring following treatment. "It's a nice proof-of-concept. You can't do that with pulmonary fibrosis without doing biopsies, so it's a nice way to track the anti-fibrotic activity of the drug," says Colangelo.

The company also recently completed a Phase I study of PRM-151 in IPF patients, with a Phase Ib trial ongoing. Preclinical and early clinical data on IPF are promising, says Colangelo. PRM-151 showed good safety and tolerability and had some encouraging effects, including reductions of circulating fibrocytes and interleukin-6 levels – both of which are elevated in IPF patients – and a durability of effect in suppressing fibrocytes out to 21 days. That's a reflection of the drug's agonistic action and the lasting effect of the regulatory macrophages that it promotes.

A second product, PRM-167, is a variant of PTX-2 that is being developed for retinal diseases. It differs only slightly

from PRM-151 – Promedior researchers swapped out a single amino acid to improve its properties for retinal applications. The company plans to begin a Phase Ib study in a retinal disease like age-related macular degeneration or diabetic retinopathy next year.

In addition to injectable formulations, the company is working on various delivery methods, including localized injection, subcutaneous, and even inhaled forms for potential use in the lung.

The company has come a long way quickly, and Colangelo believes it has demonstrated it can perform drug discovery efficiently. "We think we've brought the platform forward in a very capital- and time-efficient manner. The company was formed in 2006. We began our first clinical studies with a recombinant human protein in 2009. In three years, for about $20 million, we were able to move into the clinic, which I think is an excellent performance," he says.

Premedior has lots of flexibility when deciding how to proceed with development of its lead candidates. "Depending on our partnering and financial strategy, the ophthalmology indications could be developed and commercialized internally," Colangelo says. Systemic indications such as IPF would involve larger and more expensive trials that would necessitate partnering or additional financing.

Colangelo believes that the company's drugs have strong market potential. "In a disease like IPF, survival rates are two to five years, and there's a huge economic burden with cost of care in the $60,000 to $75,000 per year range. It provides a pretty good pharmacoeconomic case for strong pricing."

IPF, glaucoma surgery, age-related macular degeneration, diabetic retinopathy, kidney and liver fibrosis, and myelofibrosis are all potential indications. "There is strong commercial potential given the severity and economic costs of these diseases, and many of them are orphan indications," says Colangelo.

Other companies in the field are developing antagonists of the TGF-beta signaling pathway, which affects fibroblast activation that accompanies wound healing and scar formation. "That's by far one of the pathways that has been most extensively studied by other companies," notes Colangelo.

Other approaches include inhibition of macrophage activation and inhibition of IL-13. All of these approaches seek to influence biological healing cascades once they've already been triggered. But these processes are complex and sometimes redundant, which could undermine a therapy if other processes make up for a pathway inhibited by a drug. "We believe that targeting a single pathway is not going to be effective," Colangelo says.

To date, Promedior has raised $41 million from Morgenthaler Ventures, HealthCare Ventures, Polaris Venture Partners, Forbion Capital Partners and Easton Capital Investment Group.

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– Jim Kling