

Product Discovery & Development**Promedior avoids redundancy**

By Michael Flanagan
Senior Writer

Promedior Inc. is hoping that blocking monocyte activation will be a better approach for preventing fibrosis than targeting stimulatory cytokines or growth factors, because the cells targeted by its PRM-151 are far enough upstream that they cannot be circumvented by the redundant mechanisms that contribute to fibrosis.

The company was set to report this week that it has started a Phase IIa trial of PRM-151 designed to demonstrate proof of concept in fibrotic disorders by preventing post-surgical scarring in glaucoma patients.

"In the past, companies have focused on trying to inhibit a single stimulatory pathway, but fibrosis involves a very complex pathophysiology made up of multiple redundant systems, meaning that controlling a specific cytokine, growth factor or chemokine" will ultimately prove ineffective, CEO Dominick Colangelo told BioCentury.

"The essence of our platform revolves around targeted regulation of monocytes and monocyte-derived cells, which control the progression of fibrosis across tissue and organ systems," he said.

PRM-151 is a recombinant version of serum amyloid P component (SAP; APCS). Academic studies in *in vitro* and mouse models have shown that SAP, a protein produced in the liver, is capable of blocking production of fibrocytes. These monocyte-derived cells occur at the wound site and are believed to play a critical role in the formation of fibrotic lesions (see *SciBX: Science-Business eXchange*, Dec. 3, 2009).

Specifically, SAP binds to Fc gamma receptors (FCGRs) expressed on the surface of monocytes, which shuts down the natural transition of the cells into fibrocytes.

In one example, researchers from **Baylor College of Medicine** and **Rice University** published a study in the *Proceedings of the National Academy of Science* in 2006 showing that SAP markedly reduced the presence of fibroblasts and fibrosis, and inhibited cardiac dysfunction in a mouse model of ischemic cardiomyopathy. In addition, the protein prevented global ventricular dysfunction and improved fractional shortening ($p < 0.05$).

"There is clearly a common biology at play here with monocyte-derived cells being present" in all tissues and organs in the body, Colangelo said.

Preclinical data have shown PRM-151 is effective in ameliorating fibrosis in models of pulmonary, cardiac, renal and liver fibrosis, as well as dermal wound healing.

The company chose postsurgical scarring in glaucoma patients as its lead indication for several reasons. It involves directly shutting down the natural pro-fibrotic process; PRM-151 can be delivered efficiently to the site of action in the eye; and it is an Orphan indication.

Promedior completed a dose-escalation Phase I trial earlier this year that demonstrated single IV doses were well tolerated. The Phase IIa is a double-blind, placebo-controlled trial in 130 glaucoma patients. The primary endpoints are improvement and maintenance of intraocular pressure and reduction in scarring. Results are expected by YE11. In the meantime, Promedior also plans to start a Phase Ib trial in idiopathic pulmonary fibrosis (IPF) by year end and a Phase Ib trial in a second ophthalmic indication next year.

Promedior also was to announce this week that researchers at the **University of Michigan Medical School** published a study in the *Journal of Allergy and Clinical Immunology* showing that human SAP potentially inhibited macrophage differentiation in both *in vitro* and *in vivo* models of fungal-induced allergic airway disease, a condition associated with increased severity of asthma.

Colangelo noted that tissue remodeling and fibrosis are known to contribute to the decline of lung function in asthma. Mechanistically, the group reported that SAP effectively down-regulated macrophage activation, which blocked the secretion of pro-allergic factors and significantly attenuated disease in mice. The study, for which Promedior provided some research support, first appeared online last month.

"Asthma clearly has more of an inflammatory component to it than some of these other diseases, but it is also characterized by tissue remodeling and also involves fibrosis, particularly in severe asthma," said Colangelo. He said that Promedior could potentially develop PRM-151 all the way to the finish line in certain indications, "but given the breadth of our preclinical efficacy package it might make more sense to partner at some point."

Colangelo noted that tissue remodeling and fibrosis are known to contribute to the decline of lung function in asthma. Mechanistically, the group reported that SAP effectively down-regulated macrophage activation, which blocked the secretion of pro-allergic factors and significantly attenuated disease in mice. The study, for which Promedior provided some research support, first appeared online last month.

"Asthma clearly has more of an inflammatory component to it than some of these other diseases, but it is also characterized by tissue remodeling and also involves fibrosis, particularly in severe asthma," said Colangelo.

He said that Promedior could potentially develop PRM-151 all the way to the finish line in certain indications, "but given the breadth of our preclinical efficacy package it might make more sense to partner at some point."

He said that Promedior could potentially develop PRM-151 all the way to the finish line in certain indications, "but given the breadth of our preclinical efficacy package it might make more sense to partner at some point."

"Fibrosis involves a very complex pathophysiology made up of multiple redundant systems."

Dominick Colangelo, Promedior Inc.

COMPANIES AND INSTITUTIONS MENTIONED

Baylor College of Medicine, Houston, Texas

Promedior Inc., Malvern, Pa.

Rice University, Houston, Texas

University of Michigan Medical School, Ann Arbor, Mich.

Company Index,
from previous page

Arresto B16

Arrowhead (NASDAQ:ARWR) B12

Astellas (Tokyo:4503) A16, A20, B9, B17

AstraZeneca (LSE:AZN; NYSE:AZN) A2, A20, B8, B11

Asuragen B5

Basilea (SIX:BSLN) B5

Bavarian Nordic (CSE:BAVA) B6, B9

Baxter (NYSE:BAX) B5

Bayer (Xetra:BAY) B3, B10, B15

Baylor Coll of Med A11

BG Medicine A17, B20

BioAlliance (Euronext:BIO) B5, B9

BioDelivery (NASDAQ:BD) B9

Biofrontera (Xetra:B8F) A17, B9

Biogen Idec (NASDAQ:BIIB) B9

BioMarin (NASDAQ:BMRN) A6,

B9

Bionor (OSE:BIONOR) B8

Bionovo (NASDAQ:BNVID) B20

BioSpecifics (NASDAQ:BSTC) B17

Biovail (TSX:BVF; NYSE:BVF) A18, B3, B11

BioVex A13

Boehringer B11

See page A18