WEEK OF SEPTEMBER 6, 2010

BioCentury

THE BERNSTEIN REPORT ON BIOBUSINESS

Volume 18 • Number 39 • Page A1 of 21

Strategy

Laying siege

By Karen Bernstein
& Aaron Bouchie
Senior Writers

sanofi-aventis Group made clear in its conference call last week that it's in no hurry to complete its proposed acquisition of **Genzyme Corp.** — with the obvious implication that time is on its side. If so, the lull provides time to consider alternative scenarios. These range from the emergence of a white knight for Genzyme to acquisitions by sanofi of other companies in the rare disease space.

Assuming Genzyme is going to be taken out, the only question is whether shareholders will get more than the $69 per share on offer, or $18.5 billion. The answer depends on whether sanofi thinks it has alternatives and whether Genzyme can find another bidder.

sanofi clearly needs a boost to its P&L. The company posted €25.8 billion ($37.2 billion) in pharmaceutical sales last year, but all five of its top drugs — which account for nearly half of its sales — face generic competition in 2010-14.

sanofi has a few alternatives if it wants to buy a company like Genzyme, especially if it is focusing on rare disease plays,

See next page

BioCentury This Week

Cover Story

Laying Siege — Assuming Genzyme is going to be acquired, the only question is whether shareholders will get more than the $18.5 billion on offer from sanofi-aventis. The pharma's body language suggests it doubts there's a white knight in the wings, so that time is on its side.

Strategy

A Fatter Deal Wasn't Needed — In partnering Contrave with Takeda, Orexigen decided having a launch engine now was more important than hoping to win richer terms after the obesity drug's FDA panel meeting in December./*A8*

Product Discovery & Development

Anti-Scarring Antisense — Excaliard thinks statistical significance from a small Phase II trial of EXC 001 will translate into a robust treatment effect to prevent scars when the data are final./*A10*

Avoiding Redundancy — Promedior is launching a Phase IIa study of PMR-151 to reduce postsurgical scarring in glaucoma, which it expects will demonstrate its strategy of targeting monocytes to prevent fibrosis./*A11*

Emerging Company Profile

Scaffolds with a Twist — Complix believes its Alphabody technology provides greater stability and diversity than other protein scaffolds, plus multiple routes of administration, and is applying it first in infectious and autoimmune settings./*A12*

Ebb & Flow

Double Duty — Forbion closes twice. FoldRx fold 'em. PDL's royalties. Celator's investable data. IPOs: Zogenix, BG Medicine, Pharmsynthez. VCs: Index. Also: Alimera; Biofrontera; Dendreon; Forest; Cepheid; ThromboGenics; Celldex; Emergent, Santhera, et al./*A13*

BioCentury 100™ Indicators

Week ended 9/3/10

PRICES	VOLUME
1864.85	561.9M shrs
up 4%	up 4%

Back-to-School

BioCentury's 18th Annual Back-to-School edition is coming next week.

This Week in *SciBX*

Kinase Race in PD — An undisclosed company has optioned LRRK2 inhibitors that a Johns Hopkins team has shown to be neuroprotective in Parkinson's, putting it in competition with LRRK2 inhibitors from two biotechs: Zenobia Therapeutics and TauTaTis. Please see Table of Contents on A9.

China SEED Tour

Announcing BioCentury's tour for the 2010 China SEED Business Plan Competition award winners. Please see announcement following A21.

NewsMakers Update

Register now to see the expanding list of presenting companies at the 17th annual NewsMakers in the Biotech Industry from BioCentury and Thomson Reuters. Please see announcement following A21.

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.

> ***"Fibrosis involves a very complex pathophysiology made up of multiple redundant systems."***
>
> **Dominick Colangelo, Promedior Inc.**

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 potently 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."

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

See page A18