Emerging Company Profile

Merganser: Hip to hep

By Michael Flanagan
Senior Writer

Merganser Biotech Inc. is working on a treatment for beta thalassemia that can reduce the toxic accumulation of iron. The company expects using peptide mimetics to regulate iron absorption will be more effective than mopping excess iron up after the fact, as marketed chelators do.

Beta thalassemia is an Orphan genetic blood disorder caused by aberrant synthesis of hemoglobin beta chains resulting in continuous overproduction of defective proteins, many of which are broken down and release a glut of iron.

Patients with moderate to severe thalassemia are treated with blood transfusions, iron chelation and vitamin supplements.

CEO Brian MacDonald said the iron chelator Exjade deferasirox "gets a lot of use in thalassemia."

Novartis AG reported $870 million in 2012 sales of Exjade.

Merganser is developing peptides that mimic hepcidin, an endogenous hormone that regulates iron absorption.

Hepcidin "acts as a key regulator of iron transfer and metabolism in the body, and it sounded as though it could be applied in a variety of rare or specialist-treated diseases," MacDonald said.

The hormone itself has not been developed, he said, perhaps owing to its complex structure that would make purification very difficult. However, researchers at the **University of California, Los Angeles** identified peptides that mimic its ability to regulate iron absorption in animals.

Merganser received an exclusive option to license the program contingent upon the company's ability to show biologic activity in a relevant animal model and secure financing.

After obtaining the option, Merganser received $300,000 from BioAdvance, a Southeastern Pennsylvania preseed and seed investor, and Stateside Developments LLC. This investment did not satisfy the requirements of the option, but it did fund the necessary animal studies.

Merganser identified several lead candidates in partnership with the lab of Stefano Rivella, an associate professor of genetic medicine at the **Weill Cornell Medical College** whom MacDonald said is an expert in hepcidin biology and conditions of iron overload and deficiency.

According to MacDonald, "Stefano's group has a lot of expertise with a validated animal model of thalassemia, which we tested our peptide in and got back pretty compelling data."

The data showed a rapid increase in hemoglobin that lasted for at least 24 hours, and a reduction in the disease burden in mice. The results have been submitted for presentation at a conference this year.

"We will see if higher doses might be able to sustain the therapeutic effect out to even weekly dosing," MacDonald said.

MacDonald has now turned to the financing requirement of the deal with UCLA.

Merganser hopes to raise $10 million in a series A round, which he believes will be enough to file an IND and conduct both a Phase I trial and a Phase IIa proof-of-concept study. The company hopes to enter the clinic in mid-2015 and achieve proof of concept (POC) in 2017.

Merganser will remain virtual and rely on academic and third-party groups to conduct the IND-enabling work and, when the time comes, clinical studies.

Other companies are targeting the same pathway as Merganser with antisense products that silence genes that reduce hepcidin levels: **Alnylam Pharmaceuticals Inc.** and partners **Xenon Pharmaceuticals Inc.** and **Isis Pharmaceuticals Inc.** have preclinical antisense programs focused on hepcidin.

MacDonald thinks the peptide mimetics will have advantages.

"The antisense approaches are only as good as the biological effect of the targeted gene will allow, whereas we can give as much hepcidin activity as is needed. I think that these factors might be advantages of our approach," he said.

In addition, MacDonald said having a peptide that has a relatively short duration of effect might be an advantage because dosing could be adjusted to optimize efficacy, and if safety problems occur, it could be withdrawn more quickly.

Aside from iron chelators, the most advanced thalassemia programs include a pair of Phase II agents from partners **Acceleron Pharma Inc.** and **Celgene Corp.** Sotatercept (ACE-011) is an activin receptor type 2A (ACVR2A) antagonist and ACE-536 is a modified ACVR2B-Fc fusion protein.

Merganser Biotech Inc.

Newtown Square, Pa.
Technology: Peptide mimetics of the iron regulatory hormone hepcidin
Disease focus: Hematology
Clinical status: Preclinical
Founded: 2011 by Brian MacDonald and Gene Merutka
University collaborators: University of California, Los Angeles, and Weill Cornell Medical College
Corporate partners: None
Number of employees: Two
Funds raised: $300,000
Investors: BioAdvance and Stateside Developments LLC
CEO: Brian MacDonald
Patents: None issued

COMPANIES AND INSTITUTIONS MENTIONED

Acceleron Pharma Inc., Cambridge, Mass.
Alnylam Pharmaceuticals Inc. (NASDAQ: ALNY), Cambridge, Mass.
Celgene Corp. (NASDAQ:CELG), Summit, N.J.
Isis Pharmaceuticals Inc. (NASDAQ:ISIS), Carlsbad, Calif.
Merganser Biotech Inc., Newtown Square, Pa.
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
University of California, Los Angeles, Los Angeles, Calif.
Weill Cornell Medical College, New York, N.Y.
Xenon Pharmaceuticals Inc., Burnaby, B.C.