REPRINT FROM JANUARY 30, 2012

BioCentury

THE BERNSTEIN REPORT ON BIOBUSINESS™

Emerging Company Profile

Cantargia: Stemming CML

By Stephen Hansen
Senior Writer

Tyrosine kinase inhibitors have turned chronic myelogenous leukemia into a chronic disease for many patients, but imposes a financial burden on payers. **Cantargia AB** thinks that targeting CML stem cells can provide a cost-effective, curative therapy.

The majority of CML cases are characterized by cells carrying the Philadelphia chromosome, which encodes the oncogenic BCR-ABL fusion protein. The gold standard treatments for CML are TKIs that target BCR-ABL: Gleevec imatinib and Tasigna nilotinib from **Novartis AG** and Sprycel dasatinib from **Bristol-Myers Squibb Co.**

While the TKIs are excellent at killing mature, differentiated CML cells, they are not as effective at killing a small population of self-renewing stem cells that carry the Philadelphia chromosome.

Patients thus must remain on therapy for the rest of their lives. With a $40,000 annual price tag for Gleevec, CML therapy can be very expensive for payers.

"Patients are being treated for 10 years or more and it's costing society quite a lot of money," CEO Agneta Svedberg told BioCentury.

Cantargia believes that targeting the CML stem cells in combination with a TKI that attacks mature CML cells could cure patients and eliminate the need for chronic therapy.

Cantargia AB

Lund, Sweden

Technology: mAbs targeting chronic myelogenous leukemia (CML) stem cells

Disease focus: Cancer

Clinical status: Lead optimization

Founded: 2010 by Thoas Fioretos, Marcus Jaras, Kjell Sjostrom and Lund University Bioscience AB

University collaborators: Lund University

Corporate partners: None

Number of employees: 1

Funds raised: SEK5.8 million ($855,432)

Investors: Lund University Bioscience AB

CEO: Agneta Svedberg

Patents: None issued

Cantargia is based on the work of **Lund University** researchers Thoas Fioretos, a professor and senior consultant of clinical genetics, and Marcus Jaras, a postdoctoral fellow. They discovered that both mature and stem cells that contain the Philadelphia chromosome overexpress the cell surface protein interleukin-1 (IL-1) receptor accessory protein (IL-1RAP). The protein is not expressed on normal hematopoietic stem cells.

Preclinical data published in 2010 in the *Proceedings of the National Academy of Sciences* showed that a polyclonal rabbit antibody against IL-1RAP could induce antibody-dependent cell-mediated cytotoxicity (ADCC) in primary CML stem cells taken from treatment-naïve patients, but not in normal bone marrow cells *(see SciBX: Science-Business eXchange, Sept. 16, 2010)*.

Treating Philadelphia chromosome-positive CML cells with Gleevec resulted in partial down-regulation of IL-1RAP. But Svedberg noted CML stem cells are insensitive to Gleevec and thus should continue to express IL-1RAP despite treatment with a TKI.

Preclinical data on the use of an IL-1RAP mAb in Gleevec-treated CML cells are not yet available from the company.

Svedberg also said there is no evidence that the protein sheds from the cell surface, which is a concern because shedded protein could act as a sink for the thera-

See next page

BioCentury®
THE BERNSTEIN REPORT ON BIOBUSINESS

PO Box 1246
San Carlos CA 94070-1246
Voice: 650-595-5333
Fax: 650-595-5589
www.biocentury.com

DAVID FLORES
President & CEO

KAREN BERNSTEIN, Ph.D.
Chairman & Editor-in-Chief

Emerging Company Profile,
from previous page

peutic antibody and decrease the amount that reaches the target cell.

She did note there are two isoforms of IL-1RAP, one membrane-bound and the other soluble. The latter could act as such a sink. But the soluble form is found in much lower concentration, so the company hopes there will not be enough to sequester an anti-IL-1RAP mAb and affect efficacy.

The company's mAb against IL-1RAP is in lead optimization. Cantargia expects the first mAb candidate to be selected by year end and enter preclinical testing in 2013.

Because TKIs are standard of care, Svedberg said Cantargia will likely develop the mAb first as a follow-on therapy for the 20-35% of patients who develop resistance or intolerance to TKIs. Svedberg said a combination trial with TKIs could be done alongside a follow-on trial in Phase II.

Cantargia also plans to develop the mAb for acute lymphoblastic leukemia (ALL) and acute myelogenous leukemia (AML), where IL-1RAP is similarly overexpressed.

Cantargia has filed patent applications for methods of treatment and diagnosis of hematological malignancies that express IL-1RAP. Svedberg said the company has no plans to develop a diagnostic for IL-1RAP, although a test might be useful in the future.

Svedberg said Cantargia is looking to partner the program, either for the CML setting or all indications, but would like to stay involved at least through Phase I/II trials.

She added the company is focused solely on IL-1RAP, with no plans to do discovery work on other targets or to in-license other projects.

Svedberg said Cantargia has sufficient financial support from its sole investor, **Lund University Bioscience AB**, but would welcome new investors.

COMPANIES AND INSTITUTIONS MENTIONED

Bristol-Myers Squibb Co. (NYSE:BMY), New York, N.Y.
Cantargia AB, Lund, Sweden
Lund University, Lund, Sweden
Lund University Bioscience AB, Lund, Sweden
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland