

BIOCENTURY Innovations

FROM IDEA TO IND

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EMERGING COMPANY PROFILE

TWO LEASES ON LIF

By Mark Zipkin, Staff Writer

While most immuno-oncology products in the clinic target the immunosuppressive factors that help tumors evade an attack, [Northern Biologics Inc.](#)'s anti-LIF antibody takes a step further. By simultaneously blocking both immunosuppression and self-renewal of cancer stem cells the newco expects the antibody to be effective against a wider range of cancers than other immuno-oncology programs.

Northern was launched in 2014 by Versant Ventures to develop cancer and fibrosis therapies, but for strategic reasons merged in December 2016 with another Versant start-up, cancer play [Mosaic Biomedicals S.L.](#)

Under a 2015 deal with [Celgene Corp.](#), the revamped Northern received \$70 million to fund clinical development of its lead candidate, the humanized anti-LIF antibody [MSC-1](#) that it inherited from Mosaic, and to support R&D on the three other antibodies in its pipeline. The deal also gives Celgene the option to acquire the newco at an undisclosed milestone event, according to Northern CEO Stefan Larson.

LIF is a soluble cytokine that, outside of cancer, is highly expressed only in pregnant women, where it drives the immunosuppressive environment that allows for embryonic implantation. The protein also promotes self-renewal of mouse embryonic stem cells (ESCs) and early mouse and human neuroprogenitor cells. But a 2009 *Cancer Cell* study led by Joan Seoane, co-founder of Mosaic and the revamped Northern, was the first to elucidate a role for LIF in cancer.

In that study, Seoane's group showed LIF enabled self-renewal of tumor stem cells and prevented their differentiation in patient-derived glioblastoma multiforme (GBM) cells.

Since then, Seoane's groups and others have shown that multiple tumor types secrete high levels of LIF that co-opt the protein's immunosuppressive function to evade host immunity. "LIF is driving a very broad — we think — immunosuppressive program in the tumor microenvironment, as well as very likely supporting self-renewal tumor of initiating cells," Larson said.

He noted LIF mediates immunosuppression via myeloid-derived suppressor cells (MDSCs), whereas "the vast majority

NORTHERN BIOLOGICS INC., Toronto, Ontario

Technology: Antibodies against leukemia inhibitor factor (LIF) and other targets regulating tumor immunosuppression

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2014 by Jose Baselga, Joan Seoane and Ben Neel

University collaborators: Vall d'Hebron Research Institute, Memorial Sloan Kettering Cancer Center, Princess Margaret Cancer Centre

Corporate partners: Celgene Corp.

Number of employees: 30

Funds raised: \$82 million

Investors: Versant Ventures, Celgene Corp., other undisclosed VC firms

CEO: Stefan Larson

Patents: One patent family issued covering LIF in cancer

of I-O clinical trials today are using agents — for example, checkpoint inhibitors of co-stimulatory agonists — that aim to directly modulate the activity of T effector cells."

Seoane added that MSC-1 also targets Tregs, which he said are not well-targeted by other immuno-oncology products in development. Seoane, whose group developed MSC-1, is a professor at the [Catalan Institution for Research and Advanced Studies](#) (ICREA) and Vall d'Hebron University Hospital's Institute of Oncology (VHIO).

Larson said Northern has unpublished data showing the antibody is effective in mouse cancer models and causes no obvious toxicity. The company plans to present those data at meetings and in a paper this fall.

In addition, Northern has unpublished data on LIF expression in patient tumors, and so far has identified LIF-expressing subtypes of 20 different tumors.

Northern is on track to submit an IND in 4Q17 and expects to dose the first patient in a Phase Ia trial of MSC-1 in solid tumors by January, then move into Phase Ib testing in lung, ovarian and prostate cancers by the end of 2018.

Larson said the company chose those three tumor types based on unmet clinical need and the learnings that will come from evaluating MSC-1 in LIF-positive tumors that vary in immune sensitivity: lung tumors, which are typically immune-sensitive; prostate tumors, which typically are not; and ovarian tumor subtypes that may be checkpoint inhibitor-naïve and either immune-insensitive or not.

According to BioCentury's BCIQ database, no other companies have disclosed programs targeting LIF. ■

COMPANIES AND INSTITUTIONS MENTIONED

Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain
Celgene Corp. (NASDAQ:CELG), Summit, N.J.
Northern Biologics Inc., Toronto, Ontario
Vall d'Hebron University Hospital, Barcelona, Spain

TARGETS

LIF- Leukemia inhibitory factor

REFERENCES

Peñuelas, S., et al. "TGF- β increases glioma-initiating cell self-renewal through the induction of LIF in human glioblastoma." *Cancer Cell* (2009)

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