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BIOCENTURY | EMERGING COMPANY PROFILE

DOUBLE THREAT

BY ELIZABETH S. EATON, STAFF WRITER

Boston Immune Technologies & Therapeutics Inc. is developing potentially first-in-class TNFR2 inhibitors that have the dual effect of killing both tumor cells and immunosuppressive Tregs.

President and CEO Russell LaMontagne said tumor necrosis factor receptor 2 (TNFR2; TNFRSF1B) is expressed directly on certain types of tumor cells. "We don't know the extent or exact percentage, but from our screenings of tissue samples, we think it's a high percentage of lymphomas, colon, breast and ovarian cancers," he said.

TNFR2 is also widely expressed on Tregs, but not on healthy cells.

In 2017, BITT co-founder Denise Faustman and colleagues from Massachusetts General Hospital published a paper in *Science Signaling* that demonstrated TNFR2 antagonists killed TNFR2-expressing human ovarian cancer cells *in vitro*.

In the same study, the researchers showed TNFR2 antagonists also inhibited Treg proliferation *in vitro*, enabling T effector cell expansion. Notably, the TNFR2 mAbs inhibited Tregs isolated from ovarian cancer samples more potently than Tregs derived from healthy donor samples, suggesting specificity for the tumor microenvironment.

The study authors also noted that TNFR2-expressing Tregs are more immunosuppressive than other Treg subtypes, and are "abnormally abundant in human and murine tumors."

Faustman is director of the Immunobiology Laboratory at Mass General and an associate professor of medicine at Harvard Medical School.

LaMontagne said the suppressive effect of TNFR2 inhibitors on Tregs is complementary to checkpoint inhibitors. BITT's mAbs adjust the ratio of T effector cells to Tregs, reducing the immunosuppressive populations while allowing the immunostimulatory cells to expand. "Our technology allows for more soldiers to attack the cancer,"

LaMontagne said.

He told BioCentury the company has unpublished interim data suggesting that a TNFR2 inhibitor, as a monotherapy or in combination with a PD-1 antibody, could reduce tumor burden *in vivo*.

In a mouse model of TNFR2-expressing colon cancer, TNFR2 mAb monotherapy decreased tumor size versus placebo.

In a mouse model of colon cancer, regardless of TNFR2 expression, a TNFR2 mAb plus an anti-PD-1 mAb decreased tumor size more than either treatment alone, or placebo.

The company plans to present the data from both ongoing studies this half.

LaMontagne noted that NIH researchers reported similar results in *Science Signaling* in January with a different TNFR2 mAb. In a mouse model of breast cancer, the NIH team showed treatment with their mAb plus an anti-CD25 antibody inhibited tumor growth and increased survival compared with either treatment alone.

BITT has an exclusive license to its preclinical TNFR2 inhibitors from Mass General.

LaMontagne said the company has three mAbs and plans to bring the first to the clinic in two years.

According to BioCentury's BCIQ database, there are no candidates in the clinic targeting TNFR2 for cancer.

There are at least 10 clinical stage cancer therapies aimed at depleting Tregs by targeting TNF receptor superfamily member 4 (OX40; TNFRSF4; CD134) or glucocorticoid-induced tumor necrosis factor receptor (TNFR)-related protein (GITR; TNFRSF18).

LaMontagne said previous studies have shown that Tregs in non-small cell lung cancer (NSCLC) and melanoma tumor microenvironments express higher levels of TNFR2 than OX40 or GITR.

According to LaMontagne, BITT is in discussions with potential partners and plans to close at least one regional deal this year.

"We want to find the fastest path to the clinic and some of those steps might be done faster with a bigger partner," he said.

He declined to disclose how much funding BITT has raised, but noted that the company does not plan to raise another funding round and plans to find a partner "who will help pay for key IND-enabling steps."

COMPANY PROFILE

Boston Immune Technologies & Therapeutics Inc.

Boston, Mass.

Technology: mAbs targeting tumor necrosis factor receptor 2 (TNFR2)

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2014 by Denise Faustman, Russell LaMontagne

University collaborators: Massachusetts General Hospital

Corporate partners: None

Number of employees: 4

Funds raised: Undisclosed

Investors: Hatteras Ventures

CEO: Russell LaMontagne

Patents: Undisclosed number of issued patents covering antibodies, methods and composition of matter claims for TNFR2 epitope

COMPANIES AND INSTITUTIONS MENTIONED

Boston Immune Technologies & Therapeutics Inc. (BITT), Boston, Mass.
Harvard Medical School, Boston, Mass.
Massachusetts General Hospital, Boston, Mass.
National Institutes of Health, Bethesda, Md.

REFERENCES

Nie, Y., et al. **"Blockade of TNFR2 signaling enhances the immunotherapeutic effect of CpG ODN in a mouse model of colon cancer."** *Science Signaling* (2018)
Torrey, H., et al. **"Targeting TNFR2 with antagonistic antibodies inhibits proliferation of ovarian cancer cells and tumor-associated Tregs."** *Science Signaling* (2017)