BioCentury
REPRINT FROM NOVEMBER 6, 2017

EMERGING COMPANY PROFILE

TWO FACES OF MYELOID

BY VIRGINIA LI, STAFF WRITER

Pionyr Immunotherapeutics Inc. has a pipeline of preclinical antibodies that could enable it to selectively deplete immunosuppressive myeloid cells from tumors without harming immune-stimulating myeloid cells.

Myeloid cells such as tumor-associated macrophages (TAMs) and myeloid-derived suppressor cells (MDSCs) can weaken antitumor immunity and limit efficacy of checkpoint therapies.

However, a 2014 *Cancer Cell* paper by founder Max Krummel and his colleagues at University of California San Francisco demonstrated that at least one subtype of intratumoral myeloid cell — the CD103+ dendritic cell — stimulates CD8+ T cells. Krummel is a professor of pathology and co-inventor of CTLA-4 inhibitor Yervoy ipilimumab.

In addition, Executive Chairman and CEO Steven James told BioCentury Pionyr has unpublished data from melanoma patients showing high numbers of intratumoral CD103+ dendritic cells correlate with an increased likelihood of responding to anti-PD-1 therapy.

James said Pionyr's pipeline includes four antibodies against undisclosed targets that are expressed by undisclosed subtypes of immunosuppressive myeloid cells but not CD103+ dendritic cells. All are in development for solid tumors.

James said Pionyr is looking to deplete both individual myeloid cell subsets and combinations of subsets. TAMs and MDSCs are among its target cell types.

It also is profiling subpopulations of myeloid cells in tumor biopsies looking for additional subpopulations of immune-stimulating and immunosuppressive cells. "The number of myeloid subpopulations is evolving as more precise technologies are used to characterize the tumor immune infiltrate," said James.

The company hunts for targets on the suppressive cells that could be used to deplete them, then screens phage-displayed libraries of antibodies against the targets using its CellectSeq platform. It also holds an option to license undisclosed antibodies from Adimab LLC, and has non-exclusive rights to undisclosed antibodies from the University of Toronto, where its second scientific co-founder Sachdev Sidhu is a professor.

PIONYR IMMUNOTHERAPEUTICS INC.
San Francisco, Calif.

Technology: Antibodies targeting immunosuppressive myeloid cells

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2015 by Max Krummel and Sachdev Sidhu

University collaborators: University of California San Francisco, University of Toronto

Corporate partners: Adimab LLC

Number of employees: 14

Funds raised: $10 million

Investors: OrbiMed Advisors, SV Health Investors, Osage University Partners, Mission Bay Ventures, angel investors

CEO: Steven James

Patents: Undisclosed

Even if other stimulatory myeloid cell types are found that its existing antibodies inadvertently deplete, James still thinks that because the antibodies avoid CD103+ dendritic cells they will produce stronger antitumor immunity than antibodies that indiscriminately target myeloid cells.

James said Pionyr has unpublished data from multiple mouse models showing its antibodies can convert tumors from resistant to PD-1 inhibitors to sensitive, as well as data from syngeneic mouse models of solid tumors showing the antibodies are effective as single agents.

James expects at least one of Pionyr's programs to enter the clinic in the next two years but declined to disclose indications the company plans to test. He said additional preclinical studies will determine whether its initial clinical trials will evaluate the antibodies as monotherapies or in combination with checkpoint inhibitors.

Several clinical cancer therapies target myeloid cells, including 11 that inhibit colony-stimulating factor 1 receptor (CSF1R; C-FMS; CD115), eight against CXC chemokine receptor 4 (CXCR4; NPY3R) and three against CC chemokine receptor 2 (CCR2; CD192).

According to James, all three of those targets are broadly expressed across myeloid cell types, and compounds against them do not discriminate suppressive from stimulatory cells.

However, at least one company, FLX Bio Inc., is developing small molecules specifically targeting MDSCs or Tregs, a type of immunosuppressive lymphoid cell in tumors. Its most advanced agent, FLX475, is a small molecule inhibitor of CCR4 on Tregs that is slated to enter the clinic this year.

James declined to compare Pionyr's myeloid-targeting strategy to FLX's.

Pionyr raised $8 million in a series A-1 round in January. James told BioCentury the company plans to raise another venture round of undisclosed size and timing to bring its antibodies through Phase I testing. bc

COMPANY AND INSTITUTIONS MENTIONED

Adimab LLC, Lebanon, N.H.
FLX Bio Inc., South San Francisco, Calif.
Pionyr Immunotherapeutics Inc., San Francisco, Calif.
University of California San Francisco, San Francisco, Calif.
University of Toronto, Toronto, Ontario

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