

BIOCENTURY Innovations

FROM IDEA TO IND

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EMERGING COMPANY PROFILE

FLEXING AGAINST SUPPRESSION

By Karen Tkach Tuzman, Senior Writer

FLX Bio Inc. is creating small molecules to dim immunosuppressive actors in the tumor microenvironment without the baggage of the antibodies dominating the immuno-oncology space. Armed with \$79 million in series A and B funds, the **Flexus Biosciences Inc.** spinout has preclinical candidates targeting Tregs and MDSCs, and hopes to enter the clinic this year.

SAB member Philip Greenberg told BioCentury Tregs and myeloid-derived suppressor cells (MDSCs) have been a common hurdle for multiple cancer immunotherapies, limiting effective immune responses “at different levels, and at different times.” Greenberg is head of the program in immunology in **Fred Hutchinson Cancer Research Center’s** clinical research division.

The newco was founded after **Bristol-Myers Squibb Co.** acquired Flexus for its **IDO** and **TDO2** programs, and is focused on five new immuno-oncology preclinical programs, with a Treg-targeting **CCR4** antagonist in the lead. It retained Flexus’ investors **Kleiner Perkins Caufield & Byers**, **The Column Group**, **Celgene Corp.** and **Topspin Fund**.

FLX Bio CEO Brian Wong said previous attempts to stop Tregs from suppressing antitumor immunity were hobbled because well-established Treg targets like **IL-2** were also critical for effector T cell function. In contrast, he said, work in the last five years has shown the chemokine receptor **CCR4**, which is key for Treg migration into tumors, is “one of the cleanest ways to selectively inhibit Tregs.”

FLX Bio’s compound blocks the chemokine receptor’s interaction with its ligands **CCL22** and **CCL17**, which are upregulated in tumors compared with healthy tissues.

Wong believes that mechanism will make the compound safer than mAbs like **Poteligeo** mogamulizumab, which trigger depletion of **CCR4**-expressing cells. “Every Treg that expresses **CCR4** throughout the body gets reduced,” he said. “They’ve seen severe toxicity in multiple tissues, including the skin.”

FLX Bio has shown its compound decreased Tregs in a more tumor-selective manner than an anti-**CCR4** mAb.

FLX BIO INC., South San Francisco, Calif.

Technology: Small molecule immuno-oncology agents targeting Tregs and myeloid-derived suppressor cells

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2015 by **Flexus Biosciences Inc.**

University collaborators: None

Corporate partners: None

Number of employees: About 60

Funds raised: \$79 million

Investors: **Kleiner Perkins Caufield & Byers**, **The Column Group**, **Celgene Corp.**, **Topspin Fund**

CEO: Brian Wong

Patents: None

Kyowa Hakko Kirin Co. Ltd. markets **Poteligeo** for T cell lymphoma and has it in Phase I/II testing for solid tumors. It is also in Phase III for HTLV-1 associated myelopathy (HAM). The company did not return BioCentury’s request for comment in time for publication.

Wong and Greenberg noted that small molecules also have the advantages of penetrating tumors better than mAbs, and being able to be developed for both intracellular and extracellular targets. **AstraZeneca plc** also has a small molecule **CCR4** inhibitor, **AZD2098**, in preclinical development for cancer.

FLX Bio plans to test its antagonist in the clinic alone and in combination with checkpoint inhibitors to treat solid tumors, and is investigating biomarker candidates, including **CCL22** and **CCL17**, to predict patient responses.

The company is developing two strategies to decrease the suppressive effects of MDSCs: targeting the cells’ signal transduction pathways, and promoting their conversion to antitumor myeloid cells.

COO Rekha Hemrajani said FLX Bio has almost 20 chemists and strong computational biology expertise in-house, which it is using to mine public and private datasets for new immuno-oncology targets.

FLX Bio terminated development of the Flexus asset **FLX925**, which it retained after the spinout, to focus on immuno-oncology. The compound was in Phase I/II for acute myelogenous leukemia. **■**

COMPANIES AND INSTITUTIONS MENTIONED

American Association for Cancer Research (AACR), Philadelphia, Pa.
AstraZeneca plc (LSE:AZN; NYSE:AZN), London, U.K.
Bristol-Myers Squibb Co. (NYSE: BMY), New York, N.Y.
FLX Bio Inc., South San Francisco, Calif.
Fred Hutchinson Cancer Research Center, Seattle, Wash.
Kyowa Hakko Kirin Co. Ltd. (Tokyo:4151), Tokyo, Japan

TARGETS

CCL17 - Chemokine CC motif ligand 17
CCL22 (MDC) - Chemokine CC motif ligand 22
CCR4 (CD194) - CC chemokine receptor 4
IL-2 - Interleukin-2
IDO (INDO) - Indoleamine 2,3-dioxygenase
TDO2 (TDO) - Tryptophan 2,3-dioxygenase

REFERENCES

Talay, O., et al. "Potent and selective C-C chemokine receptor (CCR4) antagonists potentiate anti-tumor immune responses by inhibiting regulatory T cells (Treg)." *Presented at the annual meeting of the American Association for Cancer Research (2017)*

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