FLEXUS BIOSCIENCES

**Corporate Fact Sheet | December 2014**

**At A Glance**
**Founded:** 2013
**Location:** San Carlos, CA
**Employees:** 30+ and growing
**Investors:** Kleiner Perkins Caufield & Byers, The Column Group, Celgene

## VISION
Disrupt the field of cancer therapeutics

## MISSION
Create cancer therapeutics through the innovative application of unexploited insights in immunology

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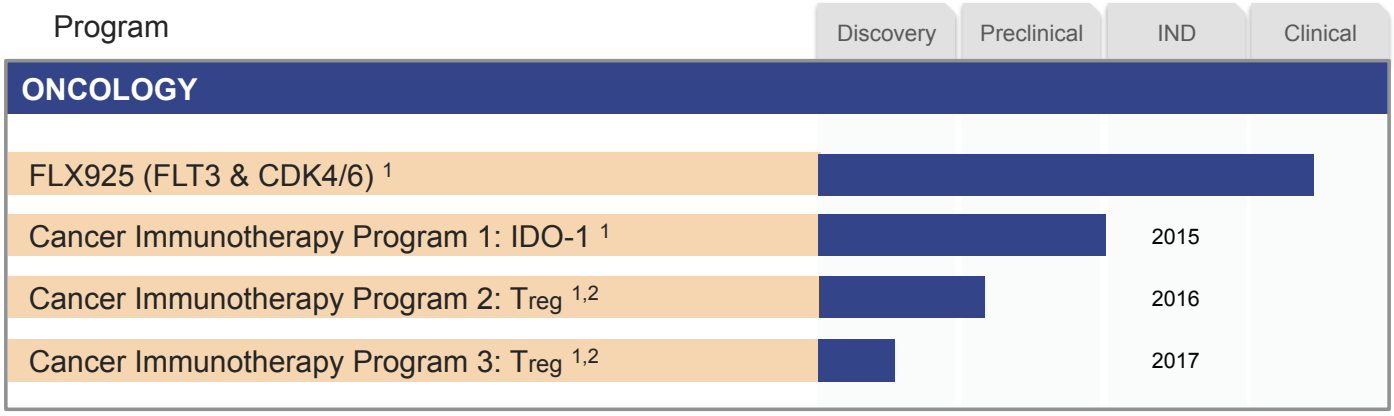
### ABOUT FLEXUS

Founded in 2013, Flexus is a biotechnology company focused on the discovery, development, and commercialization of small-molecule cancer immunotherapies targeting regulatory T cells. The company is leveraging unexploited insights in immunology to discover Agents for Reversal of Tumor Immunosuppression (ARTIS). This disruptive approach to cancer therapy targets that which is common to all tumors, the host immune system.

Flexus, located in San Carlos, CA, has raised $38M in funding from blue-chip investors Kleiner Perkins Caufield & Byers (KPCB), The Column Group (TCG), and Celgene. Flexus has assembled a management and R&D leadership team with a proven track record of success and an advisory group and team of scientists with unparalleled knowledge and expertise in drug discovery and translational sciences essential to execution of the ARTIS approach.

### PIPELINE




1. Worldwide Rights, Flexus Biosciences, Inc. 2. $T_{reg}$ targets not disclosed.

## RESEARCH AND DEVELOPMENT

Under the leadership of seasoned R&D executives and the guidance of world-class scientific advisors, Flexus has built an industry leading internal R&D engine focused on discovering and developing innovative cancer immunotherapies, with the goal of delivering one IND per year.

The research programs are focused on discovering and developing small molecule inhibitors against novel regulatory T cell targets, and we anticipate filing an IND on the first of three internal programs in 2015. This compound is a potent and selective IDO-1 inhibitor. Flexus has also advanced into the clinic a dual-inhibitor that targets FLT-3 (including FLT-3 mutations) and CDK4/6 for the treatment of acute myeloid leukemia.

## REGULATORY T CELLS

Regulatory T cells ($T_{reg}$) have evolved to keep immune responses to foreign antigens (e.g., viruses, commensal bacteria) in check. This allows the protective but transient inflammation and tissue repair cycle to be appropriately curtailed and the system reset (i.e., homeostasis), thus preserving self-tolerance.

Cancers – with their many genetic alterations – frequently present themselves to the immune system as 'foreign' and, as such, tumors are capable of "adapting" and co-opt immune suppressive mechanisms to evade eradication by the immune system.

Numerous studies of human cancers have found $T_{reg}$ cell accumulation in and around tumors; this observation repeatedly correlates with poor patient prognosis in many cancer types, including, amongst others, melanoma, lung and breast cancers. Such data have resulted in the concept of manipulating Treg cells, in an effort to provoke a therapeutic anti-tumor immune response to put an end to the 'immune privileged' state, under which many cancers thrive.

Strategies to suppress $T_{reg}$ cells have included modulating cytokine signaling, depletion with antibodies or treatment with cytotoxic agents. However, these approaches frequently also impact the cell populations required for a robust immune response. Novel approaches to selectively interfere with tumor-associated Treg cells are therefore of interest. A particularly important mechanism by which tumors stimulate the generation of Treg is through an enzyme called indoleamine-2,3-dioxygenase-1 (IDO-1), which is upregulated in tumors and lymph nodes.

$T_{reg}$ cells are characterized by the expression of the forkhead transcription factor (FOXP3) which was shown by the Rudensky and Sakaguchi laboratories to be both necessary and sufficient for these cells to repress inflammatory immune cells. These cells also express a number of other cell surface proteins such as the high affinity interleukin-2 (IL-2) receptor (IL-2Rα/CD25) and cytotoxic T lymphocyte antigen 4 (CTLA4), an important inhibitor of effector T cell function. While the system is intricate, interfering with FOXP3 function represents an attractive and perhaps specific approach to unleashing a therapeutic anti-tumor immune response.