CELL DESIGN LABS ANNOUNCES PEER-REVIEWED PUBLICATION VALIDATING ABILITY TO PROGRAM IMMUNE CELLS TO TREAT CANCER AND AUTOIMMUNE DISEASE

-- Researchers Show Combining Universal Cell Sensor with T Cells Creates Cellular "Robots" that Search and Precisely Treat Complex Diseases --

-- Preclinical Results Published in *Cell* Illustrate Next Generation of Precision-Designed Immunotherapies –

SAN FRANCISCO, Calif. – September 29, 2016 – Cell Design Labs, Inc. today announced the publication of key preclinical data demonstrating that by engineering immune cells (T cells) with a synthetic Notch receptor (synNotch™), the T cell becomes a programmable living machine able to combat cancer and other diseases.

"In this paper, we demonstrate our ability to easily and flexibly program what an immune cell senses and how it responds," said Wendell Lim, Ph.D., Scientific Founder of Cell Design Labs and Professor and Chair of the Department of Cellular and Molecular Pharmacology at UC San Francisco (UCSF) and an Investigator of the Howard Hughes Medical Institute. "Combining this universal sensor, synNotch, and immune cells gives us the capability to engineer cellular "robots" capable of patrolling the body to detect and precisely treat complex diseases. These robots can be customized with different features and functions, which when triggered by appropriate signals, can deploy diverse weapons against disease."

Dr. Lim continued, "Specifically, we have shown that T cells can be programmed to deliver and produce therapeutic agents at the site of a tumor to treat disease. Importantly, the local production of these molecular therapies by the therapeutic immune cell results in a radically new approach – one that is both more effective and far safer than systemic infusion of therapeutics being used today."

The results of the study, entitled 'Engineering T cells with customized therapeutic response programs using synthetic notch receptors,' were published in the peer-reviewed journal *Cell* online today, and will appear in the October 6, 2016 print edition. In the paper, researchers demonstrated that by integrating immune cells (T cells) with a synthetically created universal molecular sensing system (synNotch receptor), they created, in essence, living programmable micro-devices. The researchers showed that these programmable cells can carry out highly localized actions in the complex environment of the body.

Preclinical testing demonstrated that T cells could be programed to produce and deliver a wide range of therapeutic payloads, including checkpoint inhibitors, bispecific antibodies and custom cytokine programs. The synNotch sensing system directs the production of these molecular therapies only to the tumor site, based on recognition of tumor-specific molecules. These

customized, site-specific immune activities will be instrumental in developing a new generation of more effective and safer therapeutics for cancer, autoimmune and infectious diseases.

For cancer applications, synNotch T cells could be used as standalone therapies, or the synNotch system could be used in combination with Chimeric Antigen Receptors (CARs) to enhance their effectiveness and safety.

"Delivering these powerful therapeutic molecules directly and not systemically, and thus only to the site of disease will not only be more effective, but it will likely prevent the many strong side effects that occur when such agents are delivered indiscriminately everywhere in the body," continued Dr. Lim. "The added precision of synNotch sensors and ability to deliver agents that disable tumor immunosuppression are powerful tools that may allow CAR T cell treatments to expand into the larger arena of solid tumors."

"Cell Design Labs is extremely pleased to be the exclusive licensee of this ground-breaking technology. We believe the logical, bottom-up programming of T cells enabled by synNotch receptors represents a complete frame shift from clinical approaches using CAR-T or TCRs today," commented Brian Atwood, Co-Founder, President and Chief Executive Officer of Cell Design Labs

About the Notch Receptor

Notch, a well-characterized receptor, is found in all multicellular organisms. First discovered in 1914, Notch, which is instrumental in how cells communicate with each other, has both external and internal functionality. It works by first detecting a molecular partner in a neighboring cell using a part of Notch outside the cell. This interaction then "tugs" on the Notch receptor, linking it with the neighbor cell and allowing the internal portion of Notch to move into the nucleus where it activates various genes. Both the external and internal portions of the Notch receptor have been synthetically re-engineered by Dr. Lim's lab in various combinations to instruct immune cells to detect new molecular partners and to turn on new genes. By engineering different aspects of the synNotch scaffold, diverse sensing/response behavior results. This video provides an audiovisual illustration of this novel technology.

By engineering Notch, it is possible to create a programmable immune cell. When this reprogrammed cell binds to its sole intended target (i.e. a cancer cell), it triggers a specific molecular activity. These activities include delivering a checkpoint inhibitor to combat cancer, inducing a customized cytokine profile or encouraging T cells to differentiate into specific subtypes to convey long-term protection against cancer recurrence. The synNotch receptor conveys sensor functionality while the T cell ensures the cell's ability to roam throughout the body to find its target.

Technology in Context of Current Clinical Oncology Approaches

The most direct application for today's publication is CAR T technology. CAR T cells redirect natural T cells to antigens, or molecular markers, found primarily on cancer cells. An unintended consequence of this approach is an immunologic meltdown coupled with collateral damage to related normal tissue. Moreover, CAR T cells have not proved potent enough to attack solid tumors, such as pancreatic, breast and colorectal cancers. In contrast, with this novel technology, a physician will be able to deploy a precise therapeutic response program specifically targeted against the tumor, based on a precision recognition profile. Moreover, by arming T cells with locally delivered therapeutics, physicians can increase the potency of the T cells without increasing side effects. It not only provides the best of current immunotherapy (CAR T cells and checkpoint inhibitors), it offers a highly customized solution that has the potential to be more potent, specific and safe.

About Cell Design Labs, Inc.

Cell Design Labs is a biotherapeutics company pioneering breakthrough science to develop disruptive cell-based therapies for cancer and other devastating diseases. Based on innovative research from Dr. Wendell Lim's lab at the UCSF, Cell Design Labs leverages the power of the body's immune system to develop smart, living therapies with the capability to treat our most challenging diseases with unprecedented power, precision, safety and durability. Using its proprietary technology platform for custom cell engineering, Cell Design Labs will develop its own portfolio of anticancer therapies as well as create partnerships with leading oncology companies. Initially focused on cancer, including both hematologic and solid tumors, this broad technology may also have applications in other complex diseases such as autoimmune and degenerative disorders. To learn more about Cell Design Labs, please visit our web site at: www.celldesignlabs.com.

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