Oncternal Announces Publication of Data from Phase 1 Trial of Cirmtuzumab in CLL in Cell Stem Cell

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ROR1 antibody found to inhibit the ability of chronic lymphocytic leukemiacells

to self-renew and differentiate

SAN DIEGO, June 1, 2018 – Oncternal Therapeutics, Inc., a clinical-stage biotechnology company developing first-in-class therapies for rare and common malignancies, today announced that data from a Phase 1 clinical trial of humanized IgG1 monoclonal antibody, cirmtuzumab, in 26 patients with relapsed/refractory chronic lymphocytic leukemia (CLL), were published in the journal *Cell Stem Cell*. In the manuscript, entitled "Phase I trial: Cirmtuzumab inhibits ROR1-signaling and stemness signatures in patients with chronic lymphocytic leukemia," authors Michael Choi, M.D., hematologist and oncologist at UC San Diego Moores Cancer Center, Thomas Kipps, M.D., Ph.D., distinguished professor of medicine and deputy director of research at UC San Diego Moores Cancer Center, and colleagues, summarize the Phase 1 results. Cirmtuzumab was found to be well tolerated and to measurably inhibit the ability of CLL cells to self-renew and differentiate. The article published online today and will be included in a future print edition of *Cell Stem Cell*.

Oncternal licensed cirmtuzumab from the University of California San Diego (UC San Diego), where Dr. Kipps and colleagues initially developed the antibody with funding through the California Institute for Regenerative Medicine (CIRM). Cirmtuzumab is designed and developed to bind with high affinity to a biologically important epitope on the extracellular domain of Receptor-tyrosine kinase-like Orphan Receptor 1 (ROR1). When cirmtuzumab binds to ROR1, it blocks Wnt5a activation and inhibits tumor-cell proliferation, migration and survival.

The first in human, Phase 1 dose escalation trial was designed to evaluate the safety and tolerability of bi-weekly infusions of cirmtuzumab in CLL patients. Study findings highlighted by the publication authors were as follows:

- Cirmtuzumab targets ROR1 signaling on CLL and reduces activation of RhoA and HS1, a pair of gene-signaling proteins that promote cancer cell reproduction and tumor growth
- Cirmtuzumab inhibits expression of stemness gene expression signature of CLL cells, or their ability to self-renew and differentiate
- Cirmtuzumab was well tolerated in CLL patients, with no dose-limiting toxicities observed
- Higher doses of cirmtuzumab were associated with greater reduction in cancer cell activity
- Cirmtuzumab treatment appeared to prolong time required to next treatment

According to Dr. Choi, first author on the paper, "The patients who enrolled on the trial had leukemia that was getting worse and disrupting normal blood production or causing other symptoms. For most patients, after receiving four doses of cirmtuzumab, the disease stopped progressing, and stayed under control without needing any other treatment for approximately 8 months."

"We are thrilled that the results from the Phase 1 study of cirmtuzumab were published in *Cell Stem Cell*, a prestigious, peer-reviewed journal in the field," said James Breitmeyer, M.D., Ph.D., Oncternal's President and CEO. "These important data formed the basis of our Phase 2 development program, including the Phase 1b/2 CIRLL trial that is now underway in collaboration with UC San Diego and CIRM to evaluate cirmtuzumab in combination with ibrutinib in the treatment of CLL and other B-cell malignancies. We are encouraged that cirmtuzumab may have the potential to bring deeper, more durable responses to these patients who are in urgent need of new treatment options."

CLL is the most common form of blood cancer in adults, resulting in a progressive and deadly overabundance of white blood cells called lymphocytes. The disease accounts for roughly one-quarter of new cases of leukemia (21,000) annually and roughly 4,500 deaths each year.

About Cirmtuzumab

Cirmtuzumab is a first-in-class humanized monoclonal antibody that binds with high affinity to a biologically important epitope on ROR1 (Receptor-tyrosine kinase-like Orphan Receptor 1). ROR1 is a type 1 transmembrane protein expressed on the plasma membrane with an extracellular domain that is essential for ligand binding and signal transduction. Cirmtuzumab binds to many different types of cancer cells, but does not recognize normal human tissues. Tumor cells that express ROR1 have stem-cell like features that are associated with the dedifferentiated oncogenic state. When expressed by hematologic malignancies such as mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), and small lymphocytic leukemia (SLL), ROR1 acts as a receptor for the tumor growth factor Wnt5a. When cirmtuzumab binds to ROR1, it blocks Wnt5a activation and inhibits tumor-cell proliferation, migration and survival.

About Oncternal Therapeutics

Oncternal Therapeutics is a clinical-stage oncology company developing first-in-class and novel therapies for both rare and common cancers by focusing on targets that are differentially expressed by cancer cells. The company is leveraging its scientific and development expertise, as well as academic collaborations, to rapidly advance its two pipeline products, cirmtuzumab, an anti-ROR1 monoclonal antibody, and TK216 , a small molecule that inhibits the biological activity of ets-family transcription factor oncoproteins. In a collaboration with UC San Diego, Oncternal is developing a chimeric antigen receptor expressing T cell (CAR-T) targeting ROR1.

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