



November 15, 2016

Sleeping Beauty System Used to Co-express CAR with Membrane-Bound IL-15 to Enhance Persistence of CD19-Specific T Cells

BOSTON, Nov. 15, 2016 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIOP), a biopharmaceutical company focused on new immunotherapies, today announced the publication of data demonstrating enhanced persistence of genetically modified T cells targeting leukemia through utilization of its non-viral *Sleeping Beauty* (SB) system to co-express membrane-bound IL-15 (mbIL15) and a CD19-specific chimeric antigen receptor (CAR). The article, titled "Tethered IL-15 augments antitumor activity and promotes a stem-cell memory subset in tumor-specific T cells," was published in the *Proceedings of the National Academy of Sciences (PNAS)* and is available online [here](#).

Using the SB system, researchers generated genetically modified T cells that preserved stem-cell memory (T_{SCM}) by co-expressing the CAR with a fusion variant of IL-15. These engineered T cells were effective in treating established CD19⁺ leukemia in mice by facilitating the long-term persistence of T_{SCM} cells sustained by signaling through mbIL15. These findings provide for a translational pipeline of immunotherapies with improved potential by combining mbIL15 and T cells with diverse specificities.

"The ability to generate CAR-T cells with preserved stem-cell memory is a novel strategy for promoting long-lived persistence and effectiveness of immunotherapies for the treatment of patients with cancers. Producing this rare, but highly desirable, T-cell subset has historically been a challenge," said Laurence Cooper, M.D., Ph.D., Chief Executive Officer of ZIOPHARM and an author of the publication.

"We have demonstrated the ability to incorporate membrane-bound IL-15 via the non-viral *Sleeping Beauty* platform, thereby enhancing T-cell survival and raising our expectations for corresponding therapeutic benefit. The fundamental role that IL-15 plays in T-cell activation and propagation makes it an attractive candidate to incorporate into engineered immunotherapies, and we are advancing CAR-modified T cells co-expressing mbIL15 to testing in humans," added Dr. Cooper.

The SB transposon-transposase is a unique non-viral system for introducing genes into cells and is exclusively licensed by Intrexon Corporation (NYSE:XON) through The University of Texas MD Anderson Cancer Center and accessed as part of ZIOPHARM's collaboration with Intrexon.

About ZIOPHARM Oncology, Inc.:

ZIOPHARM Oncology is a Boston, Massachusetts-based biotechnology company employing novel gene expression, control and cell technologies to deliver safe, effective and scalable cell- and viral-based therapies for the treatment of cancer and graft-versus-host-disease. The Company's immuno-oncology programs, in collaboration with Intrexon Corporation (NYSE:XON) and the MD Anderson Cancer Center, include chimeric antigen receptor T cell (CAR-T) and other adoptive cell-based approaches that use non-viral gene transfer methods for broad scalability. The Company is advancing programs in multiple stages of development together with Intrexon Corporation's RheoSwitch Therapeutic System® technology, a switch to turn on and off, and precisely modulate, gene expression in order to improve therapeutic index. The Company's pipeline includes a number of cell-based therapeutics in both clinical and preclinical testing which are focused on hematologic and solid tumor malignancies.

Forward-Looking Safe-Harbor Statement:

This press release contains certain forward-looking information about ZIOPHARM Oncology, Inc. that is intended to be covered by the safe harbor for "forward-looking statements" provided by the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts, and in some cases can be identified by terms such as "may," "will," "could," "expects," "plans," "anticipates," and "believes." These statements include, but are not limited to, statements regarding the Company's plans and expectations regarding its securities offerings, fundraising activities and financial strategy, the progress, timing and results of preclinical and clinical trials involving the Company's drug candidates, and the progress of the Company's research and development programs. All of such statements are subject to certain risks and uncertainties, many of which are difficult to predict and generally beyond the control of the Company, that could cause actual results to differ materially from those expressed in, or implied by, the

forward-looking statements. These risks and uncertainties include, but are not limited to: our ability to finance our operations and business initiatives and obtain funding for such activities, whether chimeric antigen receptor T cell (CAR T) approaches, Ad-RTS-hIL-12, TCR and NK cell-based therapies, or any of our other therapeutic candidates will advance further in the pre-clinical or clinical trials process and whether and when, if at all, they will receive final approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies and for which indications; whether chimeric antigen receptor T cell (CAR T) approaches, Ad-RTS-hIL-12, TCR and NK cell-based therapies, and our other therapeutic products will be successfully marketed if approved; the strength and enforceability of our intellectual property rights; competition from other pharmaceutical and biotechnology companies; and the other risk factors contained in our periodic and interim SEC reports filed from time to time with the Securities and Exchange Commission, including but not limited to, our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, and our Quarterly Report for the quarter ended June 30, 2016. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events.

Trademarks

RheoSwitch Therapeutic System[®] (RTS[®]) technology is a registered trademark of Intrexon Corporation.

Contact:

Lori Ann Occhiogrosso
ZIOPHARM Oncology, Inc.
617-259-1987
locchiogrosso@ziopharm.com

David Pitts
Argot Partners
212-600-1902
david@argotpartners.com