



August 4, 2016

First-In-Human Trials using Non-Viral Sleeping Beauty System to Express CD19-Specific CAR in T cells Published in Journal of Clinical Investigation

Favorable Long Term Follow-up in Two Trials with Patients Receiving Autologous CAR-T cells and Allogeneic CAR-T cells

Potential benefits of Sleeping Beauty approach include reduced costs, complexity, and improved tolerability

BOSTON, Aug. 04, 2016 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIOP), a biopharmaceutical company focused on new immunotherapies, today announced the publication of data highlighting the benefits of using the non-viral *Sleeping Beauty* (SB) system to genetically modify T-cells to express a chimeric antigen receptor (CAR) for use against leukemias and lymphomas. The article, titled "Phase I trials using Sleeping Beauty to generate CD19-specific CAR T cells," was published in the *Journal of Clinical Investigation* (doi:10.1172/JCI86721), and is available online [here](#).

In the paper, 26 patients with multiply relapsed B-lineage acute lymphoblastic leukemia (ALL, n=17) or B-cell non-Hodgkin lymphoma, (NHL, n=9) were enrolled in two investigator-initiated clinical trials at the University of Texas MD Anderson Cancer Center infusing SB-modified T cells after autologous (n=7) or allogeneic (n=19) hematopoietic stem-cell transplantation (HSCT).

- ┆ *Autologous CAR-T*: Seven patients with advanced NHL were treated with autologous HSCT followed by administration of patient-derived CAR T cells. Six of the seven patients remain in complete remission (CR) and the 30-month progression-free survival (PFS) and overall survival (OS) rates were 83.3% and 100%, respectively.
- ┆ *Allogeneic CAR-T*: Nineteen patients (ALL n=17, NHL n=2) received donor-derived CAR T cells. The patients had advanced disease at the time of HSCT and CAR T cells were administered without additional lymphodepletion. Eleven of 19 patients remain in remission with 1-year PFS and OS rates of 53% and 63%, respectively.
- ┆ *HLA partially-matched allogeneic CAR-T*: When the subset of allogeneic recipients of HSCT receiving haplo-identical CAR T cells were examined, eight patients had 1-year PFS and OS rates of 75% and 100%, respectively.

SB-mediated gene transfer and stimulation resulted in large *ex vivo* expansion of T cells while retaining CAR expression and without integration hotspots. Autologous and allogeneic T cells survived after infusion an average of 201 and 51 days, respectively. No unexpected acute infusion or delayed toxicities were noted in the autologous or allogeneic recipients. Mild elevations in cytokines were observed without cytokine storm.

Francois Lebel, M.D., Executive Vice President, Research and Development, Chief Medical Officer at ZIOPHARM, states: "By following these patients over an extended duration, as we do in these studies, we can better understand the added benefit of CAR-T over HSCT alone. Although the primary objective of these trials was not to establish efficacy, the recipients' outcomes are encouraging with apparent doubling of survivals compared to historical controls. We are encouraged by these clinical data and look forward to results from our Phase 1 study infusing our next generation CD19-specific CAR T cells in patients with advanced lymphoid malignancies."

Supported by results from two Phase I clinical studies conducted by investigators at MD Anderson Cancer Center, the publication describes how the use of the SB transposon/transposase platform could reduce the costs and complexity associated with recombinant viral vector-based immunotherapy. Additionally, by infusing a CD19-specific CAR T cells to target minimal residual disease after autologous and allogeneic HSCT, the SB system may improve tolerability by avoiding cytokine storm.

"The use of the non-viral *Sleeping Beauty* platform provides us with leverage to both decrease the cost of modifying T cells and reduce the T-cell manufacturing steps requiring GMP," said Laurence Cooper, M.D., Ph.D., Chief Executive Officer of ZIOPHARM. "As we continue to advance *Sleeping Beauty* engineered designs, ZIOPHARM benefits from both viral and non-viral approaches within CAR-T, while focusing efforts on non-viral gene delivery for TCR given its unique ability to enable personalized therapies for patients with solid tumors."

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. 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 March 31, 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.

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