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ZIOPHARM Announces Cancer Research Publication of Study Demonstrating Preferential Targeting of Solid Tumor Cells by Modified CAR T Cells

BOSTON, Sept. 1, 2015 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq: ZIOP), a biopharmaceutical company focused on the development and commercialization of new cancer immuno-therapies, today announced the publication of a preclinical study in [Cancer Research](#), a journal of the [American Association for Cancer Research](#), demonstrating the preferential targeting of solid tumor cells over healthy cells using engineered chimeric antigen receptor (CAR) T cells. The article, titled "Tuning sensitivity of CAR to EGFR density limits recognition of normal tissue while maintaining potent anti-tumor activity," is available online first at cancerres.aacrjournals.org, and was highlighted in a press release today by AACR.

Abnormally-expressed antigens on tumors, such as epidermal growth factor receptor (EGFR) on aggressive brain tumors such as glioblastoma, can be overexpressed relative to lower, basal levels on normal tissues. Taking advantage of this observation, researchers at The University of Texas MD Anderson Cancer Center tuned the binding affinity of CARs to activate T cells based on the density of EGFR expression. The approach was based on the clinical toxicity exhibited by the EGFR-specific antibodies cetuximab and nimotuzumab, which recognize overlapping epitopes and exhibit different kinetics of binding to EGFR. The lower affinity of nimotuzumab has been credited with absence of adverse events relative to cetuximab.

Researchers engineered high-affinity cetux-CAR T cells and low-affinity nimo-CAR T cells, which were tested *in vitro* on cancer cells with high levels of EGFR, and normal cells with low levels of EGFR. It was found that, while the cetux-CAR T cells killed both cancer and normal cells, the nimo-CAR T cells were selectively activated only in response to cancer cells.

The researchers then tested the two populations of genetically modified T cells in mice bearing human brain cancer cells expressing high levels of EGFR and found that both cetux- and nimo-CAR T cells were equally effective in inhibiting tumor growth. However, the cetux-CAR T cells caused significant toxicity to the mice, leading to death in some, whereas the infused nimo-CAR T cells were found to be safe. The researchers further tested both CAR T cells in mice bearing cells that had low levels of EGFR (to mimic normal human cells), and found that unlike cetux-CAR T cells, the nimo-CAR T cells did not impact the growth of these cells.

"Translating the remarkable effects of adoptive CAR T-cells from liquid to solid tumors can be challenging, as many solid tumor targets are found on healthy cells, creating the opportunity for toxicity," said Laurence Cooper, M.D., Ph.D., Chief Executive Officer of ZIOPHARM and an author of the publication. "By targeting the density of tumor antigens, we have demonstrated an approach for preferentially killing cancer cells over healthy cells. In this case, the weakness of the nimo-CAR affinity is its apparent strength."

ZIOPHARM is developing various immuno-oncology programs, including CAR-T, TCR and natural killer (NK) adoptive cell based therapies, in collaboration with the MD Anderson Cancer Center and its partner Intrexon Corporation (NYSE:XON).

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-based therapies for the treatment of cancer. The Company's synthetic 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 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: whether chimeric antigen receptor T cell (CAR T) approaches, Ad-RTS-IL-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-IL-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, 2014, and our Quarterly Report on Form 10Q for the quarter ended June 30, 2015. 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.

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