



November 20, 2017

ZIOPHARM Presents Positive Updated Results of Ad-RTS-hIL-12 Study in Brain Cancer at Society for Neuro-Oncology Annual Meeting

- *Controlled IL-12 gene therapy turns cold tumors hot* —
- *MRI indicates decreasing size of brain tumor lesions in several patients* —
- *Median overall survival for patients with recurrent glioblastoma (rGBM) maintained at 12.5 months in 20mg cohort with longer follow-up* —
- *Company conference call today at 10:15AM ET with Drs. Chiocca, Goldman* —

BOSTON, Nov. 20, 2017 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIO), a biopharmaceutical company developing new gene and cell-based immunotherapies for cancer, today announced positive data updates supporting survival benefit and the underlying immune system mechanism for Ad-RTS-hIL-12 plus veledimex, the Company's controlled human interleukin-12 (hIL-12) gene therapy candidate for brain cancer, at the 22nd Annual Meeting and Education Day of the Society for Neuro-Oncology (SNO). This gene therapy has demonstrated a targeted, anti-tumor immune response for the treatment of recurrent glioblastoma (rGBM).

New data presented shows median overall survival (mOS) of 12.5 months has been sustained for patients treated with Ad-RTS-hIL-12 plus 20mg of veledimex (n=15) at a longer mean follow-up time of 11.1 months as of October 18, 2017. This mOS of 12.5 months continues to compare favorably to the 5 to 8 months survival established in historical controls for patients with rGBM. Furthermore, the four patients with rGBM who received low-dose steroids maintained 100 percent survival at a mean follow-up time of 11.1 months. An anti-tumor effect was also evident with centralized review of magnetic resonance imaging (MRI) showing decreasing size of brain tumor lesions in several patients.

Additionally, data linking the intra-tumor production of hIL-12 to patients' overall survival was presented by Francois Lebel, M.D., Chief Medical Officer of ZIOPHARM during an oral poster session, "A Phase 1 Study of Ad-RTS-hIL-12 plus Veledimex in Adult Recurrent Glioblastoma." Highlights of this presentation include:

- | Immunohistochemistry analyses from three of three patient biopsies after completion of veledimex demonstrated that IL-12 activates and sustains an immune response within rGBM;
- | All three biopsies of rGBM lesions demonstrated evidence of an anti-tumor response — with extensive infiltration of CD8⁺ T cells within the rGBM;
- | Biopsies all showed sustained (greater than 4 months) production of interferon-gamma, a cytokine crucial to arming an immune response in the tumor microenvironment;
- | Ratio of circulating killer CD8⁺ T cells to suppressor FOXP3⁺ T cells correlates with survival;
- | Interferon-gamma was undetectable in the blood at the time of biopsies providing further evidence of an on-target response;
- | Expression levels of both PD-1 and PD-L1 were upregulated in all the biopsies, which suggests added potential efficacy for combining Ad-RTS-hIL-12 plus veledimex with an immune checkpoint inhibitor;
- | Ad-RTS-hIL-12 plus veledimex continues to be safe and well tolerated, as adverse events (AE) were predictable and reversible, neurologic AEs were relatively mild and transient, and there were no drug-related deaths.

"These new mechanistic data, especially taken together with the promising extension of patients' median overall survival, provide additional validation that controlling IL-12 can engage the body's own immune system safely to generate a T-cell response against rGBM. We are excited to see increasing evidence of a targeted, local immune response making brain tumors hot and illustrating how this immunotherapy contributes to patients' survival," said Dr. Antonio Chiocca, M.D., Ph.D., lead author of this presentation and the 2017 President of the Society for Neuro-Oncology, Professor of Neurosurgery at Harvard Medical School, Surgical Director of the Center for Neuro-oncology at Dana-Farber Cancer Institute, and Chairman of Neurosurgery and Co-Director of the Institute for the Neurosciences at Brigham and Women's Hospital.

Additional SNO presentations included:

- | "A Phase 1 Study of Ad-RTS-hIL-12 plus Veledimex in Pediatric Brain Tumors," was presented in a poster by Stewart Goldman, M.D., Division Head Hematology-Oncology, Neuro-Oncology & Stem Cell Transplantation at Ann & Robert H. Lurie Children's Hospital in Chicago. The Company previously announced that the first patient was dosed in this

open-label study designed to assess the safety and tolerability of a single intratumoral injection of Ad-RTS-hIL-12 plus veledimex in children.

- | "Controlled Expression of IL-12 Improves Survival in Glioma by Activating the Immune Response in Mice and Humans," was presented during an oral session by John A. Barrett, Ph.D., Vice President of R&D/Translational Medicine at ZIOPHARM.
- | Dr. Barrett delivered a second oral presentation, "Controlled Expression of IL-12 Improves Survival in Glioma by Activating the Immune Response in Mice and Humans."

A copy of all four SNO presentations is available in the [Presentations and Publications](#) section of the Company's website, www.ziopharm.com.

"The established safety profile and tolerability of intra-tumor administration of Ad-RTS-hIL-12 plus oral veledimex, the durability of the overall survival results, and now the powerful evidence of sustained immune activation all support our goal of delivering a new treatment option to patients with recurrent glioblastoma," said Dr. Lebel. "We continue to work with regulators and thought leaders to initiate a pivotal study of Ad-RTS-hIL-12 plus veledimex in this setting before year end. In addition, the immunohistochemistry analyses revealing extensive and persistent immune cell infiltration within brain tumors and upregulation of immune checkpoint biomarkers support our initiation of a study of Ad-RTS-hIL-12 plus veledimex combined with an anti-PD-1 drug this year."

Conference Call and Webcast

In connection with this announcement, ZIOPHARM will host a conference call and webcast slide presentation featuring Drs. Chiocca and Goldman today, Nov. 20, at 10:15 a.m. ET. The call can be accessed by dialing 1-844-309-0618 (U.S. and Canada) or 1-661-378-9465 (international). The conference ID number is 8089664. To access the accompanying slides and live webcast, or the subsequent archived recording, visit the "Investors & Media" section of the ZIOPHARM website at www.ziopharm.com. The webcast will be recorded and available for replay on the Company's website for two weeks.

About Ad-RTS-hIL-12 plus Veledimex:

ZIOPHARM is advancing Ad-RTS-hIL-12 plus veledimex as a gene therapy for glioblastoma. Ad-RTS-hIL-12 is an adenoviral vector administered via a single injection into the tumor and engineered to express hIL-12, a powerful cytokine that has demonstrated the potential to stimulate a targeted, anti-tumor immune response. The expression of hIL-12 is controlled and modulated with the RheoSwitch Therapeutic System[®] (RTS[®]) by the small molecule veledimex, an activator ligand which has been shown to cross the blood-brain barrier. The Company completed enrollment in a multi-center, Phase 1 dose escalation trial designed to evaluate Ad-RTS-hIL-12 in patients with recurrent or progressive Grade III or IV glioma. The trial evaluated three veledimex dosing cohorts (20mg, n = 15; 30mg, n = 4; and 40mg, n = 6). Patients undergoing resection were injected intratumorally with Ad 2×10^{11} viral particles and received daily oral activator veledimex for 15 doses. The majority of patients in the 20mg cohort had 2 or more recurrences prior to entry in the study, indicating very advanced disease. ZIOPHARM anticipates initiation of a pivotal registration trial for Ad-RTS-hIL-12 plus veledimex for the treatment of rGBM by the end of 2017. The Company has also initiated a Phase 1 study to evaluate the stereotactic administration of Ad-RTS-hIL-12 plus veledimex in adult patients with rGBM, as well as a trial to evaluate the gene therapy as a treatment for pediatric brain tumors. In addition, ZIOPHARM plans to initiate enrollment of adult patients with rGBM who will receive a single dose of Ad-RTS-hIL-12 plus veledimex in combination with a checkpoint inhibitor targeting programmed cell death protein 1 (PD-1) by the end of 2017.

About ZIOPHARM Oncology, Inc.:

ZIOPHARM Oncology is a Boston, Massachusetts-based biotechnology company employing innovative 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[®] (RTS[®]) 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 and timing of the development 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: the Company's ability to finance its 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 other product candidates will advance further in the preclinical research or clinical trial 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 the Company's other therapeutic products it develops will be successfully marketed if approved; the strength and enforceability of the Company's intellectual property rights; competition from other pharmaceutical and biotechnology companies; as well as other risk factors contained in the Company's periodic and interim reports filed from time to time with the Securities and Exchange Commission, including but not limited to, the risks and uncertainties set forth in the "Risk Factors" section of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 and subsequent reports that the Company may file with the Securities and Exchange Commission. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and the Company does 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[®] and RTS[®] are registered trademarks of Intrexon Corporation.

Contact:

David Connolly

ZIOPHARM Oncology

617-502-1881

dconnolly@ziopharm.com

David Pitts

Argot Partners

212-600-1902

david@argotpartners.com