



June 5, 2017

ZiOPHARM Oncology Announces Positive Updated Results of Ad-RTS-hIL-12 + Veledimex in Recurrent Glioblastoma at the 2017 ASCO Annual Meeting

Median Overall Survival in Expanded 20 mg Cohort Maintained at 12.5 Months and Continues to Compare Favorably to Historical Controls

Impact of Steroids and Circulating Immune Cells Correlate with Immune Activation by IL-12

BOSTON, June 05, 2017 (GLOBE NEWSWIRE) -- [ZiOPHARM Oncology, Inc.](http://www.ziopharm.com) (Nasdaq:ZIOP), a biopharmaceutical company focused on new immunotherapies, today announced updated results from its Phase 1 multicenter study of Ad-RTS-hIL-12 + veledimex including the 20 mg expansion cohort in patients with recurrent or progressive glioblastoma (GBM) at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting June 2-6 in Chicago.

In a poster presentation titled "*Expanded phase I study of intratumoral Ad-RTS-hIL-12 + oral veledimex: tolerability and survival in recurrent glioblastoma*," the Company reported results from 25 patients with recurrent or progressive Grade III or IV glioma enrolled in three veledimex dosing cohorts (20 mg, n = 15; 30 mg, n = 4; and 40 mg, n = 6). Subjects with recurrent or progressive Grade III or IV glioma undergoing resection were injected intratumorally with Ad 2×10^{11} viral particles and received daily oral activator veledimex for 15 doses.

As of May 24, 2017, the cutoff date for the ASCO presentation, median overall survival (mOS) of all patients receiving intratumoral Ad-RTS-hIL-12 with 20 mg of orally-administered veledimex was maintained at 12.5 months, with a mean follow-up time of 9.2 months. The majority of patients in the 20 mg cohort had 2 or more recurrences prior to entry in the study, indicating very advanced disease.

"With the ability to control and turn IL-12 expression on and off from within the brain tumor, Ad-RTS-hIL-12 + veledimex offers the potential to safely direct one of the most potent anti-cancer immune cytokines against one of the most aggressive and lethal cancers," said E. Antonio Chiocca, MD, PhD, Harvey W. Cushing Professor of Neurosurgery, Department of Surgery, Harvard Medical School, Surgical Director, Center for Neuro-oncology, Dana-Farber Cancer Institute, Chairman, Neurosurgery, Brigham and Women's Hospital and Co-Director, Institute for the Neurosciences, Brigham and Women's Hospital.

Dr. Chiocca added, "These data suggest that intra-tumor expression of IL-12 is well tolerated by patients with recurrent glioblastoma. There are also highly encouraging observations that activation of the immune system in the patients may result in anti-tumor effects. I look forward to understanding Ad-RTS-IL-12 + veledimex's full potential in this challenging disease in a larger study."

Based on the ratio of CD8⁺/FOXP3⁺ (effector/suppressor) T cells measured in peripheral blood 14 to 28 days after viral injection, survival appears correlated with IL-12-mediated cellular immune activation. Consistent with this observation, steroid use in the first 15 days after injection of the virus appears to have a deleterious effect on patient survival, presumably due to interference with immune activation. Drug-related toxicities, which were primarily non-neurologic, showed a dose response to veledimex, were consistent with those previously reported, and importantly, continue to be reversed upon cessation of the activator ligand, with no drug-related deaths. As previously reported, a strong, dose-dependent correlation between veledimex dose, veledimex blood brain barrier penetration, IL-12 and IFN-gamma production was also observed.

"We are now seeing a correlation between survival and cellular immune modulation, in addition to maintenance of the survival benefit in the expanded 20 mg veledimex dose cohort," said Francois Lebel, M.D., Executive Vice President, Research and Development, Chief Medical Officer at ZiOPHARM. "We have uncovered that the effects of an IL-12-driven immune activation is dampened by the concurrent use of high-dose steroids. This is reflected in the survival of the patients, where patients who received less than 10 mg of dexamethasone have a much better survival than those on elevated systemic steroids. We are excited about Ad-RTS-hIL-12 + veledimex moving into a pivotal study this year, following completion of our discussions with regulators."

A copy of the poster presentation is available at www.ziopharm.com.

Details for the poster presentation at ASCO 2017:

Title: Expanded phase I study of intratumoral Ad-RTS-hIL-12 + oral veledimex: tolerability and survival in recurrent glioblastoma

Abstract Number: [2044](#)

Session: Central Nervous System Tumors

Date and Time: Monday, June 5, 2017, 1:15 — 4:45 p.m. CT

Ad-RTS-hIL-12 + veledimex

Ad-RTS-hIL-12 + veledimex is a novel, viral gene therapy candidate for the controlled expression of interleukin-12 (IL-12), a pro-inflammatory cytokine critical for stimulating anti-cancer immune responses.

Recurrent Glioblastoma (GBM)

Glioblastoma represents approximately 15% of all primary brain tumors and remains a high unmet clinical need that affects roughly 74,000 people worldwide annually.^{i,ii} GBM is an aggressive form of brain cancer with recurrence rates near 90%, and prognosis for patients is poor with treatment often combining multiple approaches including surgery, radiation, and chemotherapy. Patients with recurrent GBM typically have a mOS of 6-7 months, and overall survival in patients who have failed temozolomide, bevacizumab or equivalent salvage chemotherapy, is approximately 3-5 months.^{iii,iv}

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 preclinical 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 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, 2016 and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2017. 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.

ⁱ Mrugala MM. Advances and challenges in the treatment of glioblastoma: a clinician's perspective. *Discov Med.* 2013;15:221-230. <http://www.discoverymedicine.com/Maciej-M-Mrugala/2013/04/25/advances-and-challenges-in-the-treatment-of-glioblastoma-a-clinicians-perspective/>. Accessed March 24, 2015.

- ii McCubrey JA, LaHair MM, Franklin RA. OSU—0312 in the treatment of glioblastoma. *Mol Pharmacol*. 2006;70:437-439.
- iii Omuro, A. Glioblastoma and Other Malignant Gliomas. A Clinical Review *JAMA*. 2013 Nov 6;310(17):1842-50.
- iv Iwamoto et al. Patterns of relapse and prognosis after bevacizumab failure in recurrent glioblastoma. *Neurology* 2009; 73 (15):1200-1206

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