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ZIOPHARM Oncology Announces Initiation of Stereotactic Treatment Cohort in Phase 1 Study of Ad-RTS-hIL-12 + Veledimex in Recurrent Glioblastoma

Stereotactic Study Arm Serves as Runway to Clinical Studies of Controlled IL-12 Gene Therapy in Pediatric Patients and in Combination with Checkpoint Inhibitors

BOSTON, June 28, 2017 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIOP), a biopharmaceutical company focused on new immunotherapies, today announced the initiation of enrollment in the stereotactic arm of its Phase 1 multicenter study of Ad-RTS-hIL-12 + veledimex, a gene therapy for controlled expression of IL-12, in patients with recurrent glioblastoma multiforme (rGBM). The stereotactic cohort will include rGBM patients that are not scheduled to undergo surgical resection to assess the safety and tolerability of a single dose of Ad-RTS-hIL-12 administered via injection and activated with orally-administered veledimex (20 mg QD, days 1-14).

"Supported by strong clinical data highlighting the potential for controlled immune activation to affect survival outcomes in recurrent GBM, we are expanding our innovative Ad-RTS-hIL-12 + veledimex gene therapy into new treatment settings and combinations," said Francois Lebel, M.D., Executive Vice President, Research and Development, Chief Medical Officer at ZIOPHARM. "By introducing stereotactic administration, we broaden the population of patients who may be eligible for treatment, including pediatric patients with diffuse intrinsic pontine glioma, a rapidly fatal and inoperable form of brain cancer. Additionally, preclinical studies of this tunable IL-12 gene therapy in combination with an immune checkpoint inhibitor have yielded promising results, notably a 100 percent survival rate of treated mice, and we look forward to bringing this approach into the clinic."

Following an observation period, the Company expects to immediately:

- Initiate enrollment in a study of adult patients with rGBM who will receive a single dose of Ad-RTS-hIL-12 + veledimex in combination with a checkpoint inhibitor targeting programmed cell death protein 1 (PD-1);
- Initiate enrollment in a study of pediatric patients with recurrent/progressive glioma who will receive a single dose of Ad-RTS-hIL-12 + veledimex. The Company anticipates children with diffuse intrinsic pontine glioma (DIPG) will be eligible for enrollment.

At the 2017 American Society of Clinical Oncology Annual Meeting held in June, the Company reported encouraging results from patients receiving intratumoral Ad-RTS-hIL-12 with 20 mg of orally-administered veledimex (n = 15) following craniotomy, with a median overall survival (mOS) of 12.5 months comparing favorably to historical controls. Based on the observed ratio of $CD8^+/FOXP3^+$ (effector/suppressor) T cells, overall survival appears directly correlated with IL-12-mediated cellular immune activation. Furthermore, patients who received low dose steroids have a much better survival rate than those who received elevated systemic steroids, as the latter presumably interferes with immune activation. The Company continues to progress towards a registration study for Ad-RTS-hIL-12 + veledimex for rGBM to start in 2017 and is also evaluating partnership opportunities for this promising treatment candidate.

"Stereotactic treatment serves as a runway into our next phase of development for Ad-RTS-hIL-12 + veledimex including combination therapy and pediatric studies," said Laurence Cooper, M.D., Ph.D., Chief Executive Officer of ZIOPHARM Oncology. "We anticipate translating the combination approach to patients imminently and further leveraging initial observations on the survival benefit of IL-12-driven immune activation. As a pediatric oncologist, I know full well the devastating impact of DIPG and am also looking forward to seeing the effect of controlling IL-12 in this difficult-to-treat disease."

Brain tumors

Recurrent GBM represents approximately 15% of all primary adult 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] DIPG is a rapidly progressive brain tumor of children with tragically near universal fatal outcomes and a median survival less than 12

months.[v]

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 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 or relapse and prognosis after bevacizumab failure in recurrent glioblastoma. Neurology 2009; 73 (15):1200-1206

[v] Hargrave D, Bartels U, Bouffet E. Diffuse brainstem glioma in children: critical review of clinical trials. Lancet Oncol. 2006 Mar;7(3):241-8.

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