



Ziopharm Oncology Completes Enrollment of Controlled IL-12 plus Opdivo® (nivolumab) Phase 1 Combination Trial in Brain Cancer

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– Enrollment completed in third cohort of dose-escalation study at leading brain cancer hospitals in US; Investigators indicate interest in expanding study –

BOSTON, June 26, 2019 (GLOBE NEWSWIRE) -- [Ziopharm Oncology](#), Inc. ("Ziopharm" or "the Company") (Nasdaq:ZIOP) today announced completion of enrollment of the third cohort of a phase 1 clinical trial evaluating Controlled IL-12 (Ad-RTS-hIL-12 plus veledimex, Ad+V), in combination with the PD-1 inhibitor OPDIVO® (nivolumab) for the treatment of recurrent or progressive glioblastoma multiforme (rGBM) in adults.

Investigators from this multi-center trial, conducted at Northwestern University in Chicago, Brigham and Women's Hospital in Boston, and The University of Texas MD Anderson Cancer Center in Houston, have indicated interest in expanding the study and the Company now expects to enroll additional patients at the highest dosing level, subject to final agreement by the Data and Safety Monitoring Board.

"We are pleased to complete enrollment of the dose escalation of Ad-RTS-hIL-12 + veledimex and nivolumab and explore the potential to expand this combination trial to further enrich our clinical experience," said Laurence Cooper, M.D., Ph.D., Chief Executive Officer of Ziopharm. "The enthusiasm for combining PD-1 inhibitors with IL-12 in the current study is evident, and we also look forward to initiating a phase 2 trial with Ad-RTS-hIL-12 plus veledimex and cemiplimab in the coming days."

Ziopharm's Controlled IL-12 platform is an investigational gene therapy designed to induce and control the production of human interleukin 12 (hIL-12) a master-regulator of the immune system. In the setting of rGBM, the Company is leveraging the anti-tumor effects for Controlled IL-12 as monotherapy by combining with PD-1 inhibitors. Previously reported data from serial biopsies in patients with rGBM revealed that Controlled IL-12 results in sustained influx of T cells and upregulation of PD-1 expression, providing a compelling rationale for this combination. Initial phase 1 data from this trial were presented at the American Society for Clinical Oncology (ASCO) Annual Meeting on June 2, 2019, showing Controlled IL-12 can be combined with PD-1 inhibitor OPDIVO and the initial data were consistent with immune mediated anti-tumor effects with a favorable safety profile.

Ziopharm anticipates reporting on further data from this combination trial ([Clinicaltrials.gov NCT03636477](#)) at medical meetings later this year and into 2020.

About Ad-RTS-hIL-12 plus veledimex

The Company has treated more than 100 patients, including more than 75 patients with rGBM, with Ad-RTS-hIL-12 plus veledimex and administered more than 1,300 doses of veledimex across three types of solid tumors, building a significant safety profile, mechanistic dataset and evidence of anti-tumor effects.

At the 2018 annual meeting of the Society for Neuro-Oncology, Ziopharm presented data from its phase 1 dose-escalation trial showing that Controlled IL-12 (Ad-RTS-hIL-12 plus veledimex) had a positive survival benefit, with 15 patients who received 20mg veledimex reaching 12.7 months median overall survival (mOS) at a mean follow up of 13.1 months. A subset of these patients (n=6) who received low-dose steroids (20mg or less of dexamethasone cumulatively over 15 days while receiving veledimex) had mOS of 17.8 months compared to 6.4 months mOS for patients (n=9) who received more than 20mg of dexamethasone during the same period. The survival data from patients who received the preferred dosing regimen of Controlled IL-12 with 20mg veledimex and low-dose steroids compare favorably to a benchmark mOS of 6 to 9 months for patients with rGBM that serves as historical control.

In February 2019, the Company announced that it rapidly completed enrollment and treated 36 additional patients at 20mg veledimex dosing in less than six months in a substudy ([Clinicaltrials.gov NCT03679754](#)) to expand a phase 1 trial evaluating its Controlled IL-12 platform as a monotherapy for the treatment of rGBM. A majority (75%) of patients enrolled in the substudy were treated with low-dose steroids. At ASCO 2019, the Company presented data which confirmed that local, regulated IL-12 production using Ad+V in subjects with rGBM rapidly and safely activates the immune system, with adverse reactions consistent and predictable to those seen in prior studies, and promptly reversible upon discontinuation of veledimex. Mean follow-up was 3.7 months.

About Ad-RTS-hIL-12 plus veledimex in combination with PD-1 inhibitors

In this ongoing phase 1 trial to evaluate Controlled IL-12 in combination with the PD-1 inhibitor OPDIVO® (nivolumab) ([Clinicaltrials.gov NCT03636477](#)), the Company reported initial data and observations at the 2019 ASCO Annual Meeting earlier this month. With a mean follow-up of 4.5 months, the Cytoindex (an emerging biomarker) improved compared with Ad+V as monotherapy lending support that the combination may lead to improved overall survival. Data from the first two cohorts evaluated increasing doses of PD-1 inhibitor revealed a similar safety profile as Ad+V monotherapy. Adverse reactions from the first two cohorts were manageable and reversible without synergistic toxicities, while adverse reactions during follow-on nivolumab dosing were consistent with reports for PD-1 inhibition. More than two-thirds of the patients in the study received low-dose steroids.

The Company expects to begin a phase 2 trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with Regeneron Pharmaceuticals' PD-1 antibody Libtayo® (cemiplimab-rwlc) in the coming days.

FDA Fast Track Designation

In April 2019, Ziopharm announced that the U.S. Food and Drug Administration (FDA) had granted Fast Track designation for the Company's Controlled IL-12 program for the treatment of rGBM in adults. The Fast Track program is designed to facilitate the expedited development and review of drugs that are intended to treat serious or life-threatening conditions and demonstrate the potential to address unmet medical needs.

Learn more about Controlled IL-12 online at <https://ziopharm.com/controlled-il-12/>.

About Ziopharm Oncology, Inc.

Ziopharm Oncology is an immuno-oncology company focused on developing end-to-end cost-effective solutions using its non-viral *Sleeping Beauty* platform for TCR and CAR T-cell therapies and immune-stimulating gene therapy with Controlled Interleukin 12 (IL-12). The *Sleeping Beauty* platform genetically modifies T cells with DNA plasmids to express T-cell receptors (TCRs) to target specific antigens in solid tumors and chimeric antigen receptors (CARs) to target CD19 in blood cancers with the Company's very rapid T-cell manufacturing process. The *Sleeping Beauty* platform is being advanced in collaboration with the National Cancer Institute, The University of Texas MD Anderson Cancer Center and Eden BioCell. The Company also is developing its Controlled IL-12 platform, or Ad-RTS-hIL-12 plus veledimex, as monotherapy and in combination with immune checkpoint inhibitors to treat brain cancer, including in collaboration with Regeneron Pharmaceuticals.

Note Regarding Forward-Looking Statements

This news release contains forward-looking statements as defined in 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 potential clinical benefits of its Controlled IL-12 program in treating patients with rGBM and the progress and timing of the development of Ziopharm's research and development programs, including the timing for the initiation and completion of its clinical trials. Although Ziopharm's management team believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Ziopharm, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, changes in our operating plans that may impact our cash expenditures, the uncertainties inherent in research and development, future clinical data and analysis, including whether any of Ziopharm's product candidates will advance further in the preclinical research or clinical trial process, including receiving clearance from the U.S. Food and Drug Administration (FDA) or equivalent foreign regulatory agencies to conduct clinical trials and whether and when, if at all, they will receive final approval from the FDA or equivalent foreign regulatory agencies and for which indication; the strength and enforceability of Ziopharm's intellectual property rights; competition from other pharmaceutical and biotechnology companies as well as risk factors discussed or identified in the public filings with the Securities and Exchange Commission made by Ziopharm, including those risks and uncertainties listed in Ziopharm's most recent Quarterly Report on Form 10-Q filed by Ziopharm with the Securities and Exchange Commission. We are providing this information as of the date of this press release, and Ziopharm does not undertake any obligation to update or revise the information contained in this press release whether as a result of new information, future events or any other reason.

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