Ziopharm Oncology Provides Positive Clinical Data for Controlled IL-12 for the Treatment of Recurrent Glioblastoma at the 2019 ASCO Annual Meeting

June 2, 2019

– Controlled IL-12 evaluated as monotherapy in an expanded number of patients confirmed rapid and safe activation of immune system –

–Controlled IL-12 can be combined with increasing doses of a PD-1 inhibitor and immune profiling data is encouraging –

BOSTON, June 02, 2019 (GLOBE NEWSWIRE) -- Ziopharm Oncology, Inc. ("Ziopharm" or the "Company") (Nasdaq:ZIOP), a clinical stage immuno-oncology company developing next-generation cell and gene therapies, today announced the presentation of new interim analyses of clinical data from two ongoing substudies in its Controlled IL-12 platform, or Ad-RTS-hIL-12 plus veledimex (Ad+V), both as monotherapy and in combination with a PD-1 inhibitor, for the treatment of recurrent or progressive glioblastoma multiforme (rGBM) in adults, at the American Society for Clinical Oncology (ASCO) Annual Meeting taking place in Chicago from May 31 to June 4, 2019.

"Profiling an expanded number of patients with rGBM shows that Controlled IL-12 engages patients' immune systems which we previously showed was an indicator of improved overall survival," said Laurence Cooper, M.D., Ph.D., CEO of Ziopharm. "Furthermore, we demonstrate that Controlled IL-12 can be combined with a PD-1 inhibitor and the initial data from this phase 1 trial are consistent with immune-mediated anti-tumor effects with a favorable safety profile. As the follow up from these substudies continues, we remain encouraged by the application of Controlled IL-12 as monotherapy and the combination data support our plans to initiate a phase 2 trial combining Controlled IL-12 with a second PD-1 inhibitor in the next few weeks."

In the setting of rGBM, the Company previously reported phase 1 data from the "Main Study" which demonstrated an increased median overall survival (mOS) of 12.7 months with 13.1 months follow up for 15 patients that received 20mg/day veledimex, which further improved to 17.8 months in the 40% of patients receiving low-dose steroids.[1] In this study, improvements in mOS correlated with IL-12-mediated activation of peripheral blood immune cells as assessed by serially measuring the ratio of $CD8^+/FoxP3^+$ ("killer/suppressor") T cells described as "cytoindex."

The Company announced earlier this year the completion of the enrollment in an "Expansion Substudy" (Clinicaltrials.gov NCT03679754) that enlarged the phase 1 trial by an additional 36 patients with Ad-RTS-hIL-12 plus 20mg/day veledimex for up to 14 days. Interim results from this substudy were presented today in the poster presentation *"Evaluation of Controlled IL-12 as Monotherapy in Subjects with Recurrent GBM"* and demonstrated:

- Local, regulated IL-12 production using Ad+V in subjects with rGBM rapidly and safely activates the immune system;
- 75% of patients received low-dose steroids (≤ 20 mg cumulative dexamethasone dosed over 15 days);
- Adverse reactions (ARs) were consistent with prior studies of Ad+V, predictable, dose-related, and promptly reversible upon discontinuation of veledimex;
- Cytoindex, an emerging biomarker, showed immune activation; Consistent with results seen in Main Study (Clinicaltrials.gov NCT02026271) which correlated with mOS;
- No drug-related deaths were reported;
- Mean follow-up is 3.7 months (with min. of 1 month and max of 7.5 months).

The Company previously reported on serial biopsies in patients with rGBM that Controlled IL-12 resulted in sustained influx of T cells and upregulation of PD-1 expression.[2] This supports combining Ad-RTS-hIL-12 plus 10 to 20mg/day veledimex for up to 14 days with the PD-1 inhibitor nivolumab (Clinicaltrials.gov NCT03636477). Initial data and observations were presented today in the poster presentation *"Evaluation of Controlled IL-12 in Combination with a PD-1 Inhibitor in Subjects with Recurrent GBM",* and part of the oral discussion "Selected Abstracts of Excellence" at 4:30 pm (CT) on Sunday, June 2. The following were shown:

- 66% of patients in the first two cohorts received low-dose steroids (< 20 mg cumulative dexamethasone dosed over 14 days);
- Cytoindex improved compared with Ad+V as monotherapy lending support that combination may lead to improved mOS;
- First two cohorts evaluating increasing doses of PD-1 inhibitor revealed a similar safety profile as Ad+V monotherapy and ARs were manageable and reversible without synergistic toxicities;
- ARs during follow-on nivolumab dosing were consistent with reports for PD-1 inhibition;
- Enrollment is ongoing per 3+3 dose-escalation;
- Mean follow-up is 4.5 months (with min. of 0.4 months and max of 10.1 months).

“Glioblastoma is a devastating brain cancer with few treatment options demonstrating success and a significant need for new treatment options. The Controlled IL-12 platform that appears to have activity as monotherapy is now being studied in an expanded group of patients and the new data confirms that combining Controlled IL-12 with PD-1 inhibitor is a rational combination. The encouraging safety and efficacy data previously observed in monotherapy may be enhanced with immune checkpoint inhibitors to engage the body's own immune system to generate an anti-tumor response against recurrent glioblastoma,” said Dr. Antonio Chiocca, M.D., Ph.D., poster author and 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.

These data support Ziopharm’s continued development of its Ad-RTS-hIL-12 plus veledimex as a drug to control the production of interleukin 12 (IL-12).

About Ad-RTS-hIL-12 plus veledimex
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.

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. Biopsy data demonstrated that Controlled IL-12 turns immunologically-cold tumors hot based on sustained infiltration of $CD8^+$ T cells which is likely responsible for the anti-tumor effects apparently observed with use of Ad-RTS-hIL-12 plus veledimex as monotherapy in patients with rGBM. Biopsy data also revealed upregulation of immune checkpoints providing a compelling rationale for combining Controlled IL-12 with PD-1 inhibitors.

About Ad-RTS-hIL-12 plus veledimex in combination with PD-1 inhibitors
In addition to developing Ad-RTS-hIL-12 plus veledimex as monotherapy, the Company also is advancing Controlled IL-12 as a combination therapy with PD-1 inhibitors. Enrollment in a substudy of the ongoing Phase 1 trial to evaluate Controlled IL-12 in combination with the PD-1 inhibitor OPDIVO® (nivolumab) is expected to be completed in the second quarter of this year. The Company is expected 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 second quarter of 2019.

FDA Fast Track Designation
Ziopharm announced in April 2019 that 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/. The posters will be presented today at 8:00 am Central Time and will be available on the Company’s website in the “Scientific and Medical Publications” section after the presentation.

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 or equivalent foreign regulatory agencies to conduct clinical trials and whether and when, if at all, they will receive final approval from the U.S. 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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[1]Ziopharm Oncology presentation at the Society for Neuro-Oncology Annual Meeting and news release on Nov. 16, 2018

[2]Ziopharm Oncology presentation at the ASCO Annual Meeting and news release on June 4, 2018

Source: ZIOPHARM Oncology Inc