Ziopharm Oncology Presents Encouraging Clinical Data for Controlled IL-12 for the Treatment of Recurrent Glioblastoma at the 2019 Society for Neuro-Oncology Annual Meeting

November 23, 2019

– Controlled IL-12 evaluated as monotherapy in an expanded number of patients reinforced favorable safety profile and initial data consistent with immune-mediated anti-tumor effects –

– Controlled IL-12 can be combined with full dose of a PD-1 inhibitor; favorable safety profile and initial data consistent with immune-mediated anti-tumor effects –

– Immune-mediated pseudoprogression followed by reduction in tumor burden observed in both monotherapy and combination studies with Controlled IL-12 –

Phoenix, November 23, 2019 -- Ziopharm Oncology, Inc. ("Ziopharm" or the "Company") (Nasdaq:ZIOP), 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 2019 Society for Neuro-Oncology (SNO) Annual Meeting in Phoenix.

"Recurrent GBM is a complex disease which grows by walling itself off from the immune system, making it so devastating. It appears that placing IL-12 within the tumor and then controlling the production of this cytokine, drives T cells into the tumor, enabling the immune system to adapt, which leads to anti-tumor activity," said Laurence Cooper, M.D., Ph.D., CEO of Ziopharm. "We are encouraged by the findings presented at SNO, as we advance the clinical development of Controlled IL-12 as a monotherapy and in combination with immune checkpoint inhibitors, including a phase 2 study which is currently enrolling."

The Company announced in February 2019 the completion of the enrollment in an "Expansion" substudy (Clinicaltrials.gov NCT03679754) that enlarged the phase 1 "Main" trial (Clinicaltrials.gov NCT02026271) by an additional 36 patients with rGBM receiving Ad-RTS-hIL-12 plus 20mg/day veledimex for up to 14 days. Results from this substudy were presented yesterday (7:30 pm MST) in a poster presentation titled *"Survival of Subjects with Recurrent Glioblastoma Receiving Intra-tumoral Administration of IL-12 Managed with Low-dose Dexamethasone"*:

Interim Update Reported

- Decrease in tumor from baseline (time of Ad+V administration) resulting in a patient's lesion being too small to measure, assessed as a partial response (per iRANO), with follow up ongoing
- Subjects were comparable to the Main study except a higher percentage in the Expansion substudy had multifocal disease vs. unifocal disease and fewer recurrences

- Based on study design there was, as expected, a higher percentage of subjects in the Expansion substudy as compared with Main study (75% vs 40%) who received low-dose concurrent steroids
- Local, regulated IL-12 production using Ad+V in subjects with rGBM rapidly and safely activates the immune system
- Peak serum IL-12 at Day 3 with downstream production of endogenous IFN-g peaking at Day 7 in Expansion substudy (and Main study)
- MRI findings of pseudoprogression, consistent with immune-mediated anti-tumor effects
- 20mg V subjects (Main + Expansion, n=20) with unifocal disease at entry, receiving low-dose steroids (defined as <20 mg cumulative dosing of dexamethasone) continued to show a trend towards longer median overall survival (mOS, 16.2 months)
- Adverse reactions (ARs) were consistent with prior studies of Ad+V, predictable, dose-related, and promptly reversible upon discontinuation of veledimex
- No drug-related deaths were reported

In the Main study, six subjects with unifocal disease at entry, receiving low-dose steroids (defined as <20 mg cumulative dosing of dexamethasone) were previously reported to have mOS of 17.8 months. The mOS for these patients in the Expansion substudy (n=14) has not been reached at a mean follow up of 9.7 months.

Literature shows that multifocal GBM is associated with worse prognosis compared to unifocal disease.[1],2 The data from the Main study and the Expansion substudy are consistent with this prognosis, with mOS of 10.1 months for patients (n=13) with multifocal disease at entry that received 20mg veledimex and low-dose steroids.

The Company previously reported on serial biopsies in patients with rGBM which demonstrated Controlled IL-12 resulted in sustained influx of T cells with upregulation of PD-1 expression. This supports combining Ad-RTS-hIL-12 plus veledimex for up to 14 days with the PD-1 inhibitor nivolumab (Clinicaltrials.gov NCT03636477). The Company announced completion of dose escalation in June 2019 and recently reported enrollment of an additional 12 patients at the highest dosing level. Data and observations presented today (5 pm MST) in a poster presentation titled *"PD-1 Inhibition can be Combined with IL-12 in Subjects with Recurrent Glioblastoma"* :

Interim Update Reported

- Decrease by 64% in a patient's tumor from baseline (time of Ad+V administration) resulting in a partial response (per iRANO) with follow up ongoing
- Enrollment is complete per 3+3 (Ad+V and nivolumab) dose-escalation, as well as an additional 12 patients enrolled to the third cohort (highest dose)
- Mean follow up is 4.8 months (with a minimum of 0.9 months and a maximum of 16.9 months); active dosing is ongoing, and mOS has not been reached
- Serum IL-12 was detected in all subjects following initiation of Ad+V, which is consistent with previously reported data on Ad+V as monotherapy
- MRI findings of pseudoprogression, consistent with immune-mediated impact on tumor
- No dose limiting toxicities, no serious adverse events that were considered related to the combination with nivolumab and no clinically significant overlapping toxicities were observed
- Drug-related toxicities in the combination substudy were comparable to the Main study, being

predictable, dose-related, and promptly reversible upon discontinuation of veledimex and with no drug related deaths

“The two phase 1 trials evaluating Controlled IL-12 yield encouraging clinical data. We now have the experience to dose Ad-RTS-hIL-12 + veledimex as monotherapy and in combination with immune checkpoint inhibitors in patients with recurrent glioblastoma. While it is early days, the approach appears to be working as we can regulate IL-12 using a switch, we see evidence of pseudoprogression followed by anti-tumor effects, and there is encouraging survival in some patients with rGBM which is typically rapidly fatal,” 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.

“Recurrent 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, supports combining Controlled IL-12 with a PD-1 inhibitor. This combination builds on a solid scientific rationale and has yielded data of relevant immune activity that supports continued development,” Rimas Lukas, M.D., poster author and Associate Professor of Neurology (Neuro-Oncology), Northwestern University Feinberg School of Medicine and Department of Neurology, University of Chicago.

These data support Ziopharm’s continued development of its Ad-RTS-hIL-12 plus veledimex as a drug to control the production of IL-12 as monotherapy and in combination with PD-1 inhibition. The Company commenced a phase 2 trial to evaluate Controlled IL-12 in combination with Regeneron Pharmaceuticals’ PD-1 antibody Libtayo ® (cemiplimab-rwlc) in June 2019.

Learn more about Controlled IL-12 online at https://ziopharm.com/controlled-il-12/. The posters presented at the SNO 2019 Annual Meeting will be available on the Company’s website in the “Scientific and Medical Publications” section.

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 T-cell receptor (TCR) and chimeric antigen receptor (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 TCRs to target neoantigens inside and outside hotspots for solid tumors and CAR to target CD19 for blood cancers using the Company’s RPM to produce and release CAR-T as soon as the day after gene transfer. 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 is also 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.

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. 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.

Contact for Ziopharm Oncology:
Chris Taylor
VP, Investor Relations and Corporate Communications
617-502-1881
ctaylor@ziopharm.com

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[1] Cancer Manag Res. 2018;10:4229–4235

2 Int. J. Mol. Sci. 2017, 18, 2469