Ziopharm Oncology Presents Encouraging Clinical Data for Controlled IL-12 for the Treatment of Glioblastoma and DIPG at the 2020 Society for Neuro-Oncology Annual Meeting

November 19, 2020

– First Data from Ongoing Phase 2 Study of Controlled IL-12 in Combination with Cemiplimab Demonstrate Promising Safety Profile in rGBM, and a Confirmed Partial Response –

– Updated Interim Data from Ongoing Phase 1 Study of Controlled IL-12 in Combination with Nivolumab Show a mOS of 16.9 Months in Patients Receiving 10 mg Veledimex –

– First Data from Ongoing Phase 1/2 study of Controlled IL-12 Monotherapy Demonstrate Promising Safety Profile in Patient with DIPG –

BOSTON, Nov. 19, 2020 (GLOBE NEWSWIRE) -- Ziopharm Oncology, Inc. ("Ziopharm" or "the Company") (Nasdaq:ZIOP) today announced the presentation of new clinical data from three ongoing trials of Ad-RTS-hIL-12 plus veledimex (Controlled IL-12) for the treatment of recurrent glioblastoma (rGBM) and diffuse intrinsic pontine glioma (DIPG) at the 2020 Society for Neuro-Oncology (SNO) Annual Meeting. Data highlights include the first discussion of interim data from the phase 2 study of Controlled IL-12 in combination with cemiplimab for the treatment of rGBM that has recently completed enrollment, updated interim data from the phase 1 study of Controlled IL-12 in combination with nivolumab for the treatment of rGBM and data from the first patient enrolled in the ongoing phase 1/2 study of Controlled IL-12 monotherapy for the treatment of DIPG.

"Glioblastoma is a highly aggressive tumor and despite advances in oncology over the last few decades, median overall survival for patients with progressive GBM remains less than one year," said Rimas Lukas, M.D., Associate Professor of Neurology at Northwestern Memorial Hospital Malnati Brain Tumor Institute and investigator on the phase 2 trial of Controlled IL-12 in combination with cemiplimab. "Here we report data for the first time from the ongoing phase 2 study of Controlled IL-12 in combination with PD-1 inhibitor cemiplimab, showing activation of the immune system across patients. These data are highly encouraging and underscore the potential of Controlled IL-12 to transform the treatment landscape of recurrent glioblastoma."

"The updated data on combining Controlled IL-12 with nivolumab reveal a subset of patients with rGBM that demonstrate very encouraging survival at 16 months. This observation reveals that immune modulation with IL-12 and anti-PD-1 is well tolerated with an apparent survival benefit that will need further confirmation in upcoming more advanced clinical trials. These survival data in conjunction with previously reported MRIs showing partial responses is consistent with immune-mediated anti-tumor effects," noted E. Antonio Chiocca, M.D., Ph.D., study investigator, Chairman of Neurosurgery at Brigham and Women's Hospital, Professor of Neurosurgery at Harvard Medical School, and Surgical Director of the Center for Neuro-oncology at Dana-Farber Cancer Institute.

Laurence Cooper, M.D., Ph.D., Chief Executive Officer of Ziopharm, added, "As we reflect on the growing body of evidence across our efforts utilizing our Controlled IL-12 platform, we are encouraged by the signs of efficacy we are seeing in these very hard-to-treat cancers. Not only are we observing cytokine production, increases in intra-tumoral T cells (cold tumors turning hot), and predictable safety after treatment with Controlled IL-12 as a monotherapy and in combination with PD-1 inhibitors, but we have reported at least one partial response in each rGBM trial we have conducted to date, for a total of six. These MRI data, along with IL-12-driven immune response complement our encouraging survival data and we look forward to future data read-outs in 2021. Further, the initial look at data from the first patient in our phase 1/2 pediatric glioma study supports Controlled IL-12's safety profile and continued development."

Controlled IL-12 in combination with PD-1 inhibitor cemiplimab is currently being examined in a phase 2 study for the treatment rGBM (NCT04006119). Preliminary data highlights shared in an on-demand presentation titled ***"Phase 2 Trial of Controlled IL-12 in Combination with PD-1 Inhibitor in Adult Subjects with Recurrent Glioblastoma***" (Abstract #901183) and presented by Dr. Lukas, include:

- Serum cytokine levels, including IL-12 and downstream IFN-g, were detected following initiation of Controlled IL-12, and sustained longer than previously reported data of Controlled IL-12 as monotherapy
- Treatment resulted in activation of the immune system, with a significant increase in circulating killer (cytotoxic) T-cells by Day 28
- Serial MRIs showed evidence of an immune-mediated anti-tumor response
  - One partial response was confirmed on Week 16 and is ongoing through Week 32
- Median overall survival (mOS) has not been reached, with mean a follow-up time of 6.5 months
- Controlled IL-12 with cemiplimab was well tolerated
- Enrollment was by design biased toward unifocal cases (82.5%) and is now complete with cemiplimab dosing and follow-up ongoing
- Most patients received low dose steroids, defined as <= 20 mg cumulative dosing of dexamethasone during veledimex

administration

Controlled IL-12 in combination with the PD-1 inhibitor nivolumab is currently being examined in a phase 1 study for the treatment of rGBM (NCT03636477). Interim data highlights shared in an oral on-demand presentation titled ***"Combination of Controlled Interleukin-12 Gene Therapy with Immune Checkpoint Blockade in Recurrent Glioblastoma: Updated Results of a Multi-Institutional, Open Label Phase 1 Trial"*** (Abstract #901050) and presented by Dr. Chiocca include:

- Results are comparable to Controlled IL-12 monotherapy
  - Veledimex plasma and tumor plasma pharmacokinetics demonstrated a dose-response relationship and crossing of the blood-brain barrier
  - Serum IL-12 was detected in all subjects following Controlled IL-12 treatment, typically followed by a transient increase in downstream IFN-γ
- Pre- and post-treatment biopsies show increased levels of tumor-infiltrating T cells and decreased levels of PD-1
- mOS for the cohorts receiving 10 mg veledimex (n=6; 83% unifocal, 67% low dose steroids) was 16.9 months
- mOS among all subjects (across both 10 mg and 20 mg veledimex dosing, n=21) was 9.8 months
- Most patients (81%) in this substudy received low dose steroids
- Drug-related toxicities were comparable to Controlled IL-12 monotherapy, being predictable, dose-related, and promptly reversible upon discontinuation of veledimex
- Enrollment is complete; anti-PD-1 administration in one subject and follow-up in six patients is currently ongoing

As a follow up to our prior readout (ASCO 2020) for this combination which reported partial responses by MRI, the two patients had meaningful improvements in survival with one patient on 20 mg veledimex surviving 17.4 months (now deceased) and the other (10 mg veledimex) surviving 21.0 months (in follow up).

Controlled IL-12 monotherapy is being studied in a phase 1/2 dose escalation study (NCT03330197) for the treatment of children with gliomas, including DIPG. Data highlights from the first patient in the study shared in a poster discussion titled ***"Phase I/II Study of Controlled IL-12 as Immunotherapy for Diffuse Intrinsic Pontine Glioma (DIPG)"*** (Abstract #901123) and presented by Stewart Goldman, M.D., Division Head Hematology-Oncology, Neuro-Oncology & Stem Cell Transplantation at Lurie Children's Hospital and investigator in the study, include:

- Controlled IL-12 monotherapy was well-tolerated at the initial dose level (10 mg/day veledimex, BSA adjusted)
  - High veledimex compliance was reported, with no dose limiting toxicity (DLTs), Serious Adverse Events (SAEs) or suspected unexpected serious adverse reactions (SUSARs) occurring during the active study period
  - Adverse Events (AEs) were similar to adult and older pediatric supratentorial brain tumor subjects in being mild to moderate and predominantly reversible upon withholding of veledimex doses
- Preliminary evidence of immune system activation
  - Although an increase in serum recombinant IL-12 was not detected after initial dosing of veledimex (patient received 5 mg per day), endogenous IFN-γ was detected which peaked at Day 3 consistent with downstream IL-12-driven immune response
  - Circulating cytotoxic T-lymphocyte levels increased between Days 7 and 28
  - Partial eyebrow loss was observed, suggestive of immune-mediated alopecia areata
- Survival of the first subject dosed was within the historical reference range
- Enrollment is ongoing with the plan to investigate two dose levels of veledimex (10 to 20 mg, BSA adjusted) as planned per protocol

"It is important to note that these trials, including our previously disclosed monotherapy study now consist of over 125 patients with rGBM. These provide deep learning that is ongoing and is part of the efforts to develop Controlled IL-12 as a potential therapy for brain cancers. We will continue to monitor the data across both the monotherapy and checkpoint inhibitor combination studies in the coming months. We believe there are multiple potential paths to registration for our Controlled IL-12 program, either as a monotherapy therapy or in combination with other agents," concluded Dr. Cooper.

More information about Controlled IL-12 is available on the Company's website at https://ziopharm.com/controlled-il-12/. Additionally, the presentations presented at the SNO 2020 Virtual Meeting will be available on the Company's website in the "Scientific and Medical Publications" section.

About Ziopharm Oncology, Inc.
Ziopharm is developing non-viral and cytokine-driven cell and gene therapies that weaponize the body's immune system to treat the millions of people globally diagnosed with a solid tumor each year. With its multiplatform approach, Ziopharm is at the forefront of immuno-oncology with a goal to treat any type of solid tumor. Ziopharm's pipeline is built for commercially scalable, cost effective T-cell receptor T-cell therapies based on its non-viral *Sleeping Beauty* gene transfer platform, a precisely controlled IL-12 gene therapy, and rapidly manufactured *Sleeping Beauty*-enabled CD19-specific CAR-T program. The Company has clinical and strategic partnerships with the National Cancer Institute, The University of Texas MD Anderson Cancer Center and others. For more information, please visit www.ziopharm.com.

Forward-Looking Statements Disclaimer
This press 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 Company's business and strategic plans and the progress and timing of the Company's research and development programs, including the anticipated dates for the readouts of its clinical trials and the Company's expectations regarding future enrollment in its clinical trials. Although Ziopharm's management team believes that the

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