



Ziopharm Oncology Presents Encouraging Clinical Data for Controlled IL-12 for the Treatment of Recurrent Glioblastoma at the 2020 American Society of Clinical Oncology

May 29, 2020

- Longer term follow-up from Controlled IL-12 monotherapy studies reinforces encouraging median overall survival and favorable safety profile –
- Controlled IL-12 in combination with PD-1 inhibitor has favorable safety profile and initial survival data are encouraging –
- Data again consistent with immune-mediated anti-tumor effects –

BOSTON, May 29, 2020 (GLOBE NEWSWIRE) -- [Ziopharm Oncology](#), Inc. (Nasdaq: ZIOP), today announced the presentation of final clinical data from its phase 1 monotherapy (“Main”) study of Controlled IL-12, Ad-RTS-hIL-12 plus veledimex (Ad+V), as well as updated clinical data from two phase 1 substudies of Ad+V, a monotherapy expansion study (“Expansion”) and a combination study with a PD-1 inhibitor, for the treatment of adult recurrent or progressive glioblastoma multiforme (rGBM) at the 2020 American Society of Clinical Oncology (ASCO) Annual (Virtual) Meeting.

“The results we have seen from the two Controlled IL-12 monotherapy studies are particularly promising, with median overall survival in unifocal patients after monotherapy Ad+V treatment remaining at 16.2 months after longer term follow-up, as well as encouraging preliminary data from the PD-1 combination study where median overall survival has not yet been reached,” said Dr. Antonio Chiocca, M.D., Ph.D., Trial Investigator 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. “We also reported three additional partial responses, one in the monotherapy Main study, one in the Expansion study and one in the combination study, bringing the total number of partial responses (PRs) to five. Observing responses in brain tumors in the setting of recurrence is unusual and highly encouraging, and, along with the survival data, highlight the potential of Ad+V for the treatment of rGBM.”

Laurence Cooper, M.D., Ph.D., Chief Executive Officer of Ziopharm, added, “According to most recent data, even with the best available therapies, median overall survival for unifocal rGBM patients appears to be 6-12 months. We are therefore heartened by the collection of data presented at ASCO across our three studies, which demonstrate survival benefits beyond a year supported by imaging studies showing tumor regression and biopsies revealing that Ad+V administration turns ‘cold’ tumors ‘hot’ by recruiting T cells into the tumor. We look forward to continuing to report follow-up monotherapy and combination phase 1 data, as well as initial data from the ongoing phase 2 study of Ad+V in combination with Libtayo[®], which is nearing completion of enrollment.”

Ad-RTS-hIL-12 plus 20 mg/day veledimex is currently being examined in a phase 1 monotherapy “Expansion” substudy for the treatment of rGBM ([NCT03679754](#)) that enlarged the phase 1 “Main” veledimex dose escalation trial ([NCT02026271](#)) by an additional 36 patients. New clinical results in monotherapy were shared in poster presentations.

Final data highlights from the “Main” dose escalation monotherapy study, titled **“Final results of Controlled IL-12 Monotherapy in Adults with Grade III or IV Gliomas,”** (Abstract #3040) include:

- Subjects (n=6, unifocal, craniotomy) who received low-dose (≤ 20 mg cumulative) corticosteroids during veledimex dosing (Days 0 to 14, coinciding with administration of veledimex) had a median overall survival (mOS) of 17.8 months (mean follow-up of 18.4 months)
- 15 subjects (n=14, unifocal, craniotomy) treated with Ad (Day 0) and 20 mg veledimex with any dosing of corticosteroids had a mOS of 12.7 months (mean follow-up of 13.1 months)
- Serial MRIs show patient with confirmed PR at 72 weeks, with durability at 96 weeks and monitoring ongoing
- Veledimex-dependent and proportional increases in IL-12 and IFN- γ , resulting in immune activation
- Favorable safety profile:
 - Ad+V was safely administered and tolerable in both craniotomy (Group 1, n=31) and stereotactic subjects (Group 2, n=7)
 - 52 serious adverse event (SAEs) were reported in 21 subjects (55%) and 14 related SAEs were reported in 12 subjects (32%). There have been no study treatment related deaths
- The 20 mg veledimex dose is the recommended phase 2 dose as confirmed in the “Expansion” substudy focusing on veledimex 20 mg (n=36; ASCO 2020 #2564)
- The 10 mg veledimex dose level was studied to move forward as the starting dose in the monotherapy study for pediatric subjects ([NCT03330197](#)) and in combination therapy with PD-1 inhibitor in adults with rGBM (ASCO 2020 #2510)

Data highlights from the "Expansion" study, titled ***"Survival of Subjects with Recurrent Glioblastoma Receiving Intratumoral Administration of Controlled IL-12 with Limited Exposure to Dexamethasone,"*** (Abstract #2564) include:

- Subjects receiving Ad (Day 0, craniotomy) and 20 mg (Days 0 to 14) veledimex with unifocal disease ("Main" and "Expansion" n=20) administered low-dose corticosteroids showed mOS of 16.2 months (mean follow-up of 14.1 months)
- Serial MRIs show patient with previously reported pseudoprogression now has confirmed PR at 30 weeks and response durability out to 48 weeks (follow-up ongoing), in addition to the PR previously reported¹
- Adverse reactions remained consistent with previously reported results, being predictable and promptly reversible upon discontinuation of veledimex, and there were no drug-related deaths
- Veledimex dosing compliance was comparable to and slightly higher than the "Main" study

Combination of Ad+V with the PD-1 inhibitor nivolumab (nivo) is being examined in a phase 1 substudy for the treatment of rGBM ([NCT03636477](https://clinicaltrials.gov/ct2/show/study/NCT03636477)). Data highlights shared in a poster discussion titled ***"Controlled IL-12 in Combination with a PD-1 Inhibitor: Subjects with Recurrent Glioblastoma"*** (Abstract #2510) include:

- mOS has not been reached, with mean follow-up at 8.3 months
- Drug-related toxicities were comparable to monotherapy, being predictable, dose-related, and promptly reversible upon discontinuation of veledimex
- As previously reported from Ad+V monotherapy, plasma pharmacokinetics (PK) demonstrates an exposure-response relationship for veledimex
- Serum IL-12 was detected in all subjects following initiation of Ad+V, typically followed by a transient increase in downstream serum IFN- γ , which is consistent with previously reported data of Ad+V monotherapy
- There is evidence of immune-mediated anti-tumor effects, with serial MRIs showing pseudoprogression and one new PR, in addition to the PR previously reported²

To further investigate Ad+V in combination with an immune checkpoint inhibitor in rGBM subjects, a phase 2 trial of Ad+V in combination with cemiplimab-rwlc (Libtayo[®]) is currently ongoing ([NCT04006119](https://clinicaltrials.gov/ct2/show/study/NCT04006119)).

More information about Controlled IL-12 is available on the Company's website at <https://ziopharm.com/controlled-il-12/>. Additionally, the posters presented at the ASCO 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, the availability of cash resources, the Company's hiring expectations and expected additions to its Board of Directors, the progress, design and timing of the Company's research and development programs, including the anticipated dates for the initiation, completion and readouts of its clinical trials, the Company's expectations regarding the number of patients in its clinical trials, and the Company's expectations regarding the impact of the ongoing COVID-19 pandemic, including the expected duration of disruption and immediate and long-term impact and effect on its business and operations. 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 Quarterly Report on Form 10-Q filed by Ziopharm with the Securities and Exchange Commission. In addition, the extent to which the COVID-19 pandemic impacts the Company's business, clinical development and regulatory efforts and the value of its common stock, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements, and the effectiveness of actions taken globally to contain and treat the disease. The global economic slowdown, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic could have a material adverse effect on the Company's business, financial condition, results of operations and growth prospects. 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 Lukas *et al.* (2019). [Survival of Subjects with Recurrent Glioblastoma Receiving Intra-tumoral Administration of IL-12 Managed with Low-dose Dexamethasone](#); Society of Neuro-Oncology Annual Meeting

² Chiocca *et al.* (2019). [PD-1 Inhibition can be Combined with IL-12 in Subjects with Recurrent Glioblastoma](#); Society of Neuro-Oncology Annual Meeting



Source: ZIOPHARM Oncology Inc