Ziopharm Oncology Announces Immuno-oncology Clinical Supply Agreement with Regeneron to Evaluate Combination Therapy for Patients with Brain Cancer

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BOSTON, Nov. 12, 2018 (GLOBE NEWSWIRE) -- Ziopharm Oncology, Inc., (Nasdaq:ZIOP) today announced a clinical supply agreement with Regeneron Pharmaceuticals, Inc. to evaluate Ziopharm's Ad-RTS-hIL-12 plus veledimex in combination with Regeneron's PD-1 antibody Libtayo ® (cemiplimab-rwlc) to treat patients with recurrent glioblastoma (rGBM). Ad-RTS-hIL-12 plus veledimex is an investigational gene therapy designed to induce and control the production of human interleukin 12 (hIL-12) that activates the immune system and recruits cancer-fighting T cells into tumors. Libtayo has been approved in the United States for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation.

"Our PD-1 inhibitor Libtayo has been developed as the backbone of Regeneron's immuno-oncology pipeline and to facilitate innovative combination immunotherapies," said Israel Lowy, M.D., Ph.D., Head of Clinical and Translational Sciences, Oncology at Regeneron. "With Ziopharm, we are excited to learn more about the benefit of combining Libtayo with local production of the IL-12 cytokine to potentially augment the cancer-fighting capability of the immune system."

Under the terms of the agreement, Ziopharm and Regeneron will initiate a Phase 2 study in the first half of 2019 in patients with rGBM to measure preliminary safety and efficacy of Ad-RTS-hIL-12 plus veledimex in combination with Libtayo. Ziopharm will be responsible for the conduct and costs of the clinical trial, and Regeneron will supply Libtayo for the study. The companies potentially may explore the Ad-RTS-hIL-12 plus veledimex in combination with Libtayo in additional indications. Regeneron, in collaboration with Sanofi, is developing Libtayo both alone and in combination with other therapies for the treatment of various cancers.

"We are excited to collaborate with the oncology team at Regeneron, a world-class, science-driven company with robust oncology expertise," said Laurence Cooper, M.D., Ph.D., Chief Executive Officer of Ziopharm. "With IL-12 expression under the control of the RheoSwitch Therapeutic System®, we have seen anti-tumor activity as a monotherapy and there is potential to improve upon that response in combination with Libtayo to provide much-needed therapeutic options for patients with rGBM."

GBM is the most aggressive malignant primary brain tumor with an estimated incidence rate of 3.3 per 100,000 persons in the United States and an estimated 3.5 new cases per 100,000 people per year worldwide.[1] With GBM's potential for rapid tumor growth and aggressive local spread, the survival rate for adults after five years is approximately 3 percent to 5 percent.[2] Prognosis for adult patients is poor as nearly all cases of GBM recur despite treatment combining multiple approaches such as surgery, radiation and chemotherapy.[3] Globally, about 189,000 people each year die because of brain cancer with GBM being the most common form of the disease[4].

About Controlled IL-12 Platform

Ad-RTS-hIL-12 plus veledimex, within Ziopharm's Controlled IL-12 platform, is a novel gene therapy candidate that conditionally expresses recombinant hIL-12 under the control of orally-administered veledimex. This activator ligand acts via the proprietary RheoSwitch Therapeutic System® (RTS®) gene switch to control transcription and thus expression of hIL-12. This cytokine is considered a master regulator of the immune system and has demonstrated an ability to activate and recruit killer T cells to sites of cancer resulting in anti-tumor responses. A Phase 1 study evaluating Ad-RTS-hIL-12 plus escalating amounts of veledimex administered to patients with rGBM revealed dose-dependent production of both hIL-12 as well as endogenous interferon gamma and biopsy data demonstrated an influx of $CD3^+CD8^+$ cytotoxic T cells and overexpression of PD-1/PD-L1 markers. Data from this same trial showed a median overall survival (mOS) of 12.7 months for patients treated with 20mg of veledimex (n=15) at a mean follow-up time of 12.9 months (as of May 4, 2018). This compares favorably to the 5 to 8 months OS established in a similar patient population of historical controls with rGBM. Preclinical data from a mouse study evaluating Ad-RTS-mIL-12 plus veledimex to produce mouse IL-12 (mIL-12) in combination with an anti-PD-1 are promising, including 100 percent survival in one dosing cohort.

About Ziopharm Oncology, Inc.

Ziopharm Oncology is a biotechnology company focused on the development of next-generation immunotherapies utilizing gene- and cell-based therapies to treat patients with cancer. Ziopharm is focused on the development of two platform technologies designed to deliver safe, effective, and scalable immunotherapies for the treatment of multiple cancer types: Controlled IL-12 platform for Ad-RTS-hIL-12 plus veledimex and *Sleeping Beauty* platform for genetically modifying T cells. Ad-RTS-hIL-12 plus veledimex, has demonstrated controlled production of IL-12 in clinical trials, leading to an infiltration of T cells to target solid tumors, including rGBM. Ad-RTS-hIL-12 plus veledimex is being evaluated as monotherapy and in combination with immune checkpoint inhibitors to treat brain cancer. The Company is also advancing immunotherapies using the *Sleeping Beauty* platform, a non-viral approach to genetically modifying T cells with DNA plasmids to express chimeric antigen receptors (CAR) and T-cell receptors (TCR) to target specific antigens in blood cancers and neoantigens in solid tumors. *Sleeping Beauty* is currently in a clinical trial to generate CD19-specific T cells and supports the Company's very short T-cell manufacturing process encompassed within the technology referred to as "point-of-care". The platform is being advanced in collaboration with MD Anderson Cancer Center to generate CAR-expressing T cells and the National Cancer Institute to generate TCR-expressing T cells.

1. GlobalData, estimated for 2018, Glioblastoma Multiforme (GBM) Diagnosed, Incidence (Cases Per 100,000 Population), June 2016.
2. *World Cancer Report* 2014, World Health Organization.
3. Loeffler JS, *et al*. Clinical patterns of failure following stereotactic interstitial irradiation for malignant gliomas. Int J Radiat Oncol Biol Phys. 1990;19:1455–62.
4. *Cancer Incidence and Mortality Worldwide,* International Agency for Research on Cancer 2013.

Forward-Looking Disclaimer

This press release contains certain forward-looking statements within the meaning of 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 timing for the enrollment in Regeneron's and the Company's Phase 2 study in rGBM patients. All such statements are subject to certain risks and uncertainties, many of which are difficult to predict and generally beyond the control of the Company, that could cause actual results to differ materially from those expressed in, or implied by, the forward-looking statements. These risks and uncertainties include, but are not limited to: changes in the Company's financial condition and cash needs; funding or other strategic opportunities that become available to the Company; the Company's ability to finance its operations and business initiatives and obtain funding for such activities; whether any of the Company'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 FDA, to conduct its clinical trials; the strength and enforceability of the Company's intellectual property rights; competition from other pharmaceutical and biotechnology companies; as well as other risk factors contained in the Company's periodic and interim reports filed from time to time with the Securities and Exchange Commission, including but not limited to, the risks and uncertainties set forth in the "Risk Factors" section of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2017 and subsequent reports that the Company may file with the Securities and Exchange Commission. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and the Company does not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events.

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