Ziopharm Oncology Enrolls First Patient in Phase 1 Trial Evaluating Combination Therapy of Controlled IL-12 and OPDIVO®

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Phase 1 trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with nivolumab for treatment of recurrent glioblastoma

BOSTON, June 28, 2018 (GLOBE NEWSWIRE) -- Ziopharm Oncology, Inc. (Nasdaq:ZIOP), a biotechnology company focused on development of next generation immunotherapies utilizing gene- and cell-based therapies to treat patients with cancer, today announced that it has enrolled the first patient in its Phase 1 clinical trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab), an immune checkpoint, or PD-1, inhibitor, in adult patients with recurrent glioblastoma (rGBM).

"We are excited about the first-ever dosing of this combination and its potential to bring a potent and controlled anti-tumor immune response to glioblastoma," said Francois Lebel, M.D., Executive Vice President, Research and Development, Chief Medical Officer at Ziopharm. "By controlling interleukin 12, Ad-RTS-hIL-12 plus veledimex already has shown it can recruit killer T cells into the tumor and increase expression of checkpoints in this microenvironment. The combination with an anti-PD-1 has the potential to further improve anti-cancer effects of IL-12 and provide a much-needed new therapeutic option for patients with brain cancer."

The Company expects to enroll up to 18 patients with recurrent glioblastoma in this single-arm study to evaluate the safety and tolerability of this combination regimen, establish optimal dosing of veledimex and nivolumab, and measure overall patient survival. Patients with rGBM scheduled for resection who have not been treated previously with inhibitors of immune-checkpoint pathways will receive Ad-RTS-hIL-12 intratumorally at the time of surgical resection plus an escalating dose of veledimex (10 and 20mg), an oral activator ligand, daily for 14 days. Patients will receive nivolumab intravenously (either 1 mg/kg or 3 mg/kg) one week before resection, 15 days post-resection and approximately every two weeks until documented progression or withdrawal from the study. This study is enrolling patients at multiple leading brain cancer centers in the United States.

About Controlled IL-12

Ad-RTS-hIL-12 plus veledimex, or Controlled IL-12, is a novel gene therapy candidate designed to express human interleukin 12 (hIL-12) under the control of an orally administered activator ligand, veledimex through a proprietary RheoSwitch Therapeutic System® (RTS®) gene switch. IL-12 is a powerful cytokine that has demonstrated a targeted, anti-tumor immune response with the ability to activate and recruit killer T cells to the tumor site. Biopsy data from a Phase 1 study evaluating Ad-RTS-hIL-12 plus veledimex as a single agent to treat patients with rGBM showed consistent, dose-dependent production of IL-12 and interferon gamma, an influx of $CD3^+$ $CD8^+$ cytotoxic T cells and evidence of overexpression of PD-1/PD-L1 markers. Data from this same trial show median overall survival (mOS) of 12.7 months has been sustained for patients treated with Ad-RTS-hIL-12 plus 20mg of veledimex (n=15) at a mean follow-up time of 12.9 months as of May 4, 2018. This mOS of 12.7 months compares favorably to the 5 to 8 months survival established in historical controls for patients with rGBM in a similar patient population. Preclinical data from a study evaluating Ad-RTS-IL-12 plus veledimex in combination with an anti-PD-1 are promising, including 100 percent survival in one dosing cohort. An ongoing Phase 1 trial is evaluating Ad-RTS-hIL-12 plus veledimex as a monotherapy to treat patients with rGBM, and the Company also is enrolling pediatric patients in its Phase 1 trial of Ad-RTS-hIL-12 with veledimex for the treatment of brain tumors at multiple U.S. sites. In addition to these trials, Ziopharm is exploring combination therapies with Controlled IL-12 and checkpoint inhibitors in additional tumor types.

About Ziopharm Oncology, Inc.

Ziopharm Oncology is a Boston-based biotechnology company focused on the development of next-generation immunotherapies utilizing gene- and cell-based therapies to treat patients with cancer. In partnership with Precigen Inc., a wholly-owned subsidiary of Intrexon Corporation (NYSE:XON), Ziopharm is focused on the development of two platform technologies designed to deliver safe, effective and scalable cell- and viral-based therapies for the treatment of multiple cancer types: Controlled IL-12 and *Sleeping Beauty* for genetically modifying T cells. The Company's lead asset, Ad-RTS-hIL-12 plus veledimex, has demonstrated in clinical trials the potential to control interleukin-12, leading to an infiltration of T cells that fight brain cancer. The Company also is advancing therapies using *Sleeping Beauty*, a non-viral approach to genetically modify chimeric antigen receptor (CAR^+) and T-cell receptor (TCR^+) T cells, which target specific antigens in blood cancers and neoantigens in solid tumors. *Sleeping Beauty* is designed using the Company's point-of-care technology, a shortened manufacturing process which potentially can be developed as a decentralized manufacturing process based in hospitals. These programs are being advanced in collaboration with Precigen and with MD Anderson Cancer Center, the National Cancer Institute and Merck KGaA, Darmstadt, Germany.

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 Company's business and strategic plans, the availability of cash resources, the Company's ability to establish a commercially-viable manufacturing approach as well as the progress and timing of the development of the Company's research and development programs. 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 chimeric antigen receptor T cell (CAR-T) approaches, Ad-RTS-hIL-12, TCR and NK cell-based therapies, or any of other product candidates will advance further in the preclinical research or clinical trial process and whether and when, if at all, they will receive final approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies and for which indications; whether chimeric antigen receptor T cell (CAR-T) approaches, Ad-RTS-hIL-12, TCR and NK cell-based therapies, and the Company's other therapeutic products it develops will be successfully marketed if approved; 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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