



November 17, 2016

## ZIOPHARM Announces Clinical Data on Ad-RTS-hIL-12 Demonstrates Survival Benefits in Patients with Recurrent Brain Cancer

— Data to Be Presented at the 21<sup>st</sup> Society for Neuro-Oncology Annual Meeting —

— Non-clinical Study Supports Initiation of New Clinical Trial of Ad-RTS-hIL-12 in Pediatric Brain Tumors —

— Company to Host Conference Call Today at 8:00a.m. ET —

BOSTON, Nov. 17, 2016 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIO), a biopharmaceutical company focused on new immunotherapies, today announced the presentation of both clinical and nonclinical data for Ad-RTS-hIL-12 + orally-administered veledimex for recurrent brain cancer at the 21<sup>st</sup> Annual Scientific Meeting of the Society for Neuro-Oncology (SNO) held November 17-20, 2016 in Scottsdale, Arizona. Ad-RTS-hIL-12 + veledimex is a novel viral gene therapy candidate utilizing the proprietary RheoSwitch Therapeutic System<sup>®</sup> (RTS<sup>®</sup>) technology for the controlled expression of interleukin 12 (IL-12), a critical protein for stimulating a vigorous immune response against cancers.

In a poster presentation titled "Phase 1 study of intra-tumoral viral delivery of Ad-RTS-hIL-12 + oral veledimex is well tolerated and suggests survival benefit in recurrent high-grade glioma," the Company will report interim results from patients with recurrent high-grade gliomas enrolled in three veledimex dosing cohorts (20mg, n=7; 30mg, n=4; and 40mg, n=6). Subjects with relapsed high-grade gliomas, either glioblastoma (GBM) or anaplastic astrocytoma (AA), undergoing re-resection were intra-tumorally injected once with Ad-RTS-hIL-12 along with oral doses of veledimex to activate and control production of IL-12.

As of October 14, 2016, the date of data collection for the SNO presentation, median overall survival (mOS) was 12.8 months, with 11 of 17 subjects alive. Survival rates at 6, 9, and 12 months for patients with multiple recurrences prior to administration of Ad-RTS-hIL-12 are described in the table:

Treatment	N	Relapsed Brain Tumor	Medium # Recurrences	mOS (months)	Survival Rate (%)		
					6 months	9 months	12 months
Ad + V (Overall)	17	16 GBM, 1 AA	3	12.8	87	65	54
Ad + V (20 mg)	7	6 GBM, 1 AA	3	12.8	100	86	71

GBM is an aggressive brain tumor affecting approximately 74,000 people worldwide each year.<sup>i,ii</sup> For patients who have experienced recurrences the prognosis is particularly poor, with a mOS of 6-7 months, while mOS in patients that have failed temozolomide and bevacizumab, or equivalent salvage chemotherapy, is approximately 3-5 months.<sup>iii, iv</sup>

In the study, IL-12 leading to the production of interferon-gamma in the bloodstream was measured and found to be proportional to the three doses of veledimex, demonstrating that this orally-delivered activator crossed the blood brain barrier to engage the RTS<sup>®</sup> gene switch and express IL-12 in a dose-dependent manner. Toxicities in all three dose cohorts were consistent with those previously reported, with a higher incidence of grade 3 or greater adverse events in the 40 mg dose group. Importantly, all related side effects were reversed upon cessation of veledimex. Based on the tolerability and survival benefit seen, the 20 mg dose of veledimex has been selected for an ongoing expansion cohort.

"These translational data confirm the activity of Ad-RTS-hIL-12 + veledimex in the clinic, demonstrating that veledimex crosses the blood brain barrier to activate the RheoSwitch<sup>®</sup> gene switch and produce IL-12, resulting in an immune response to the tumor and now, impressively, overall survival outcomes," said Francois Lebel, M.D., Executive Vice President, Research and Development, Chief Medical Officer at ZIOPHARM. "With median overall survival beyond 12 months in these patients who have experienced multiple recurrences, the therapeutic potential of Ad-RTS-hIL-12 + veledimex is very promising. We look forward to enrolling additional patients in the expanded 20 mg dose cohort and to discussing the results of the Phase I multi-center study with the FDA, with the goal of determining a registration pathway for

this therapeutic in a disease with far too few treatment options."

The Company will also present results from a pre-clinical study of Ad-RTS-mIL-12 + veledimex as an investigational therapy for pediatric glioma in a poster titled "Local regulated IL-12 expression as an immunotherapy for the treatment of pontine glioma". Glioma in the pontine region of the brain accounts for approximately 15% of all cases of pediatric brain tumors, with a median survival time of less than one year. In an orthotopic pons model, veledimex was shown to cross the blood brain barrier to control mouse IL-12 production from the tumor, which stimulated the immune system and resulted in a profound increase in overall survival. Based on these results, the Company plans to initiate a Phase 1 clinical trial in pediatric brain tumors, including diffuse intrinsic pontine glioma (DIPG) in 2017.

"DIPG is an aggressive disease, and because of its location in the brain, it is virtually untreatable," added Laurence Cooper, M.D., Ph.D., Chief Executive Officer of ZIOPHARM. "Ad-RTS-hIL-12 + veledimex has unique potential in this indication especially given our ability to not only turn IL-12 on and off, but also to titrate IL-12 levels thanks to the RTS<sup>®</sup> technology. Our Ad-RTS-IL-12 + veledimex program continues to gain momentum, with the potential for a registration pathway in recurrent high-grade glioma in adults and expected study initiations as monotherapy in pediatric patients, as well as, in combination with checkpoint inhibitors in adult patients with brain cancer."

All poster presentations will be available online at [www.ziopharm.com](http://www.ziopharm.com).

### **Conference Call and Slide Webcast**

ZIOPHARM will host a conference call and webcast slide presentation today, Thursday, November 17, 2016, at 8:00 am ET to discuss updated data from the Company's Phase 1 study of Ad-RTS-hIL-12 + veledimex in high-grade glioma. The call can be accessed by dialing (844) 309-0618 (U.S. and Canada) or (661) 378-9465 (international). The passcode for the conference call is 11110235. To access the slides and live audio webcast, or the subsequent archived recording, visit the "Investors & Media" section of the ZIOPHARM website at [www.ziopharm.com](http://www.ziopharm.com). The webcast will be recorded and available for replay on the Company's website for two (2) weeks.

### **About ZIOPHARM Oncology, Inc.:**

ZIOPHARM Oncology is a Boston, Massachusetts-based biotechnology company employing novel gene expression, control and cell technologies to deliver safe, effective and scalable cell- and viral-based therapies for the treatment of cancer and graft-versus-host-disease. The Company's immuno-oncology programs, in collaboration with Intrexon Corporation (NYSE:XON) and the MD Anderson Cancer Center, include chimeric antigen receptor T cell (CAR-T) and other adoptive cell-based approaches that use non-viral gene transfer methods for broad scalability. The Company is advancing programs in multiple stages of development together with Intrexon Corporation's RheoSwitch Therapeutic System<sup>®</sup> technology, a switch to turn on and off, and precisely modulate, gene expression in order to improve therapeutic index. The Company's pipeline includes a number of cell-based therapeutics in both clinical and preclinical testing which are focused on hematologic and solid tumor malignancies.

### **Forward-Looking Safe-Harbor Statement:**

This press release contains certain forward-looking information about ZIOPHARM Oncology, Inc. that is intended to be covered by the safe harbor for "forward-looking statements" provided by 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 plans and expectations regarding its securities offerings, fundraising activities and financial strategy, the progress, timing and results of preclinical and clinical trials involving the Company's drug candidates, and the progress of the Company's research and development programs. All of 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: our ability to finance our 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 our other therapeutic candidates will advance further in the pre-clinical or clinical trials 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 our other therapeutic products will be successfully marketed if approved; the strength and enforceability of our intellectual property rights; competition from other pharmaceutical and biotechnology companies; and the other risk factors contained in our periodic and interim SEC reports filed from time to time with the Securities and Exchange Commission, including but not limited to, our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, and our Quarterly Report for the quarter ended September 30, 2016. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do 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.

## Trademarks

RheoSwitch Therapeutic System<sup>®</sup> and RTS<sup>®</sup> are registered trademarks of Intrexon Corporation.

- i. Mrugala MM. Advances and challenges in the treatment of glioblastoma: a clinician's perspective. *Discov Med*. 2013;15:221-230. <http://www.discoverymedicine.com/Maciej-M-Mrugala/2013/04/25/advances-and-challenges-in-the-treatment-of-glioblastoma-a-clinicians-perspective/>. Accessed March 24, 2015.
- ii. McCubrey JA, LaHair MM, Franklin RA. OSU—0312 in the treatment of glioblastoma. *Mol Pharmacol*. 2006;70:437-439.
- iii. Omuro, A. Glioblastoma and Other Malignant Gliomas. A Clinical Review *JAMA*. 2013 Nov 6;310(17):1842-50.
- iv. Iwamoto et al. Patterns of relapse and prognosis after bevacizumab failure in recurrent glioblastoma. *Neurology* 2009; 73 (15):1200-1206

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