February 16, 2017

ZIOPHARM Reports Fourth-Quarter 2016 Financial Results and Provides Update on Recent Activities

- Company to Webcast Corporate Update Thursday, February 23, at the 2017 RBC Global Healthcare Conference -

BOSTON, Feb. 16, 2017 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIOP), a biopharmaceutical company focused on new immunotherapies, today announced financial results for the fourth quarter ended December 31, 2016, and provided an update on the Company's recent activities.

"ZIOPHARM made significant progress over the course of 2016, putting us on track to enter a pivotal study and prosecute multiple high-value studies across our oncology programs in 2017, focusing on gene therapy, CAR and TCR T-cell therapies, as well as off-the-shelf NK cells," said Laurence Cooper, M.D., Ph.D., Chief Executive Officer of ZIOPHARM. "This strategy moves us not just into a registration pathway with Ad-RTS-hIL-12 + veledimex, but clinically validates the broad potential of our technologies, including our switch systems and the *Sleeping Beauty* non-viral platform. These advances will be applied across our program areas, enabling us to increase control, reduce complexity, and manage costs, addressing some of the most significant needs in gene and cell therapy. Ultimately, the ability to deliver controlled, point-of-care therapy makes individualized treatment targeting each patient's tumor neoantigens possible, a goal with profound clinical implications."

Francois Lebel, M.D., Executive Vice President, Research and Development, Chief Medical Officer at ZIOPHARM, added: "In a recently updated presentation of results from our Phase 1, multi-center study of Ad-RTS-hIL-12 + veledimex in patients with recurrent high-grade gliomas, we observed a median overall survival of 12.7 months in the 20mg veledimex dose group. This remains a very encouraging outcome compared to historic controls. We look forward to providing an update on our registration pathway in this indication in the first quarter, and to initiating a pivotal study by the end of 2017."

Program Updates

Ad-RTS-IL-12 + veledimex

Ad-RTS-hIL-12 + veledimex is a gene therapy candidate for the controlled expression of interleukin 12 (IL-12), a critical protein for stimulating an anti-cancer immune response, using the RheoSwitch Therapeutic System® (RTS®) gene switch. ZIOPHARM is currently conducting a multi-center Phase 1 study of Ad-RTS-hIL-12 + orally-administered veledimex in patients with recurrent or progressive glioblastoma multiforme (GBM), an aggressive form of brain cancer.

- **Announced End-of-Phase 2 Meeting with the FDA.** In its presentation at the 35th Annual J.P. Morgan Healthcare Conference, the Company announced that it was granted an end-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) to determine a pivotal trial design for Ad-RTS-hIL-12 + veledimex for recurrent GBM. The Company expects to announce the outcome of this meeting in the first quarter of 2017, with the goal of initiating a pivotal clinical trial of Ad-RTS-hIL-12 + veledimex in recurrent GBM in 2017.

- **Presented Data Demonstrating Survival Benefits in Patients with Recurrent Brain Cancer Treated with Ad-RTS-hIL-12 + Veledimex.** In November 2016, ZIOPHARM presented clinical data for Ad-RTS-hIL-12 + veledimex for recurrent brain cancer at the 21st Annual Scientific Meeting of the Society for Neuro-Oncology (SNO) in Scottsdale, Arizona. In the study, recombinant IL-12, leading to the body's production of interferon-gamma (IFN-gamma), were measured in the bloodstream and found to be proportional to the three doses of veledimex (20mg, n=7; 30mg, n=4; and 40mg, n=6), demonstrating that this orally-delivered activator crossed the blood-brain barrier to engage the RTS® gene switch and express IL-12 and IFN-gamma in a dose-dependent manner. Toxicities were consistent with those previously reported and all related side effects were reversed upon cessation of veledimex. Based on tolerability and survival benefit (median OS=12.7 months, n=15, as of January 6, 2017), 20 mg was selected for an expansion cohort, with patients being followed for overall survival. Updated results from the study have been submitted for presentation at an upcoming scientific meeting.

- **Presented Results of Pre-Clinical Study Supporting Initiation of New Clinical Trial of Ad-RTS-hIL-12 + Veledimex in Pediatric Brain Tumors.** In November 2016, ZIOPHARM presented results from a preclinical 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" at the 21st Annual Scientific Meeting of the SNO in Scottsdale, Arizona. 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 increased 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.

- **Presented Data Demonstrating Activation of Anti-Tumor Immune Response Using Ad-RTS-hIL-12 + Veledimex in Patients with Advanced Breast Cancer.** In October 2016, ZIOPHARM announced the presentation of preliminary data from the Company's Phase 1b/2 study of Ad-RTS-hIL-12 + veledimex following standard chemotherapy for the treatment of patients with locally advanced or metastatic breast cancer at the European Society for Medical Oncology (ESMO) 2016 Congress in Copenhagen, Denmark. Results showed that Ad-RTS-hIL-12 + seven days of veledimex consistently elicited production of IL-12 which in turn produced IFN-gamma. It was notable that the influx of $CD8^+$ T cells making IFN-gamma within the tumor were present five weeks after completion of veledimex, consistent with the ability of Ad-RTS-hIL-12 to favorably impact the tumor environment over the long term. In two patients, Ad-RTS-hIL-12 + veledimex provided a meaningful chemotherapy holiday, with durable responses for 18 and 35 weeks.

Adoptive Cell Therapies

ZIOPHARM is developing various immuno-oncology programs, including chimeric antigen receptor (CAR) T cell (CAR-T), T-cell receptor (TCR) T cell (TCR-T), and natural killer (NK) adoptive cell-based therapies. These programs are being advanced in collaboration with Intrexon Corporation (NYSE:XON), MD Anderson Cancer Center, and Merck Serono, the biopharmaceutical business of Merck KGaA (CAR-T only).

- **Announced Advances in Point-of-Care Approach for Rapidly Producing CAR-Expressing T Cells Utilizing the *Sleeping Beauty* System.** In January 2017, ZIOPHARM announced improved production times utilizing its non-viral platform to engineer T cells in an ongoing Phase 1 study of second-generation *Sleeping Beauty* (SB) CD19-specific CAR^+ T cells. Plans to progress the Company's point-of-care (POC) approach with administration of CAR-T cell therapy in less than 2 days are also underway, helping expand access to innovative T-cell therapies.

- **Cooperative Research and Development Agreement with the National Cancer Institute Utilizing *Sleeping Beauty* System to Generate T cells Targeting Neoantigens**. In January 2017, ZIOPHARM and partner Intrexon announced the signing of a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI) for the development of adoptive cell transfer-based immunotherapies genetically modified using the SB system to express TCRs for the treatment of solid tumors. Research conducted under the CRADA will be at the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI's Center for Cancer Research.

- **Results from Four Studies of Adoptive Cell-based Therapeutic Programs Presented at the 2016 American Society of Hematology Annual Meeting.** In December 2016, ZIOPHARM presented data from the Company's adoptive cell-based therapeutic programs at the 58th American Society of Hematology Annual Meeting and Exposition held December 3-6, 2016 in San Diego. The research, conducted at the MD Anderson Cancer Center and Intrexon, demonstrates, among other results, that T cells can be very rapidly produced with the SB system and that a non-viral approach to gene therapy can be harnessed to generate CAR- and TCR-expressing effector cells.

- **Announced Publication Demonstrating Membrane-bound IL-15 (mbIL15) Enhanced Persistence of CD19-Specific T Cells.** In November 2016, ZIOPHARM announced the publication of data demonstrating enhanced persistence of genetically modified T cells targeting leukemia through utilization of its non-viral SB system to co-express mbIL15 and a CD19-specific CAR. The article, titled "Tethered IL-15 augments antitumor activity and promotes a stem-cell memory subset in tumor-specific T cells," was published in the *Proceedings of the National Academy of Sciences* and is available online here.

  Using the SB system, researchers generated genetically modified T cells that preserved stem-cell memory (T_{SCM}) cells by co-expressing the CAR with mbIL15. Engineered T cells were effective in treating established $CD19^+$ leukemia in mice by facilitating the long-term persistence of T_{SCM} cells sustained by signaling through recombinant IL-15. These findings provide for a translational pipeline of immunotherapies with improved potential by combining mbIL15 and T cells with diverse specificities.

  The Company previously announced the publication of data highlighting the benefits of using the non-viral SB system to genetically modify T cells to express a CAR for use against CD19-expressing leukemias and lymphomas. The article, titled "Phase I trials using Sleeping Beauty to generate CD19-specific CAR T cells," was published in the Journal of Clinical Investigation (doi:10.1172/JCI86721), and is available online here.

Anticipated 2017 Milestones

- Intra-tumoral IL-12 RheoSwitch® programs:
  - Clinical data from Phase 1 of Ad-RTS-hIL-12 + veledimex for GBM to be presented at a scientific meeting in 2017
  - Initiate pivotal clinical trial for GBM in 2017
  - Initiate combination study of Ad-RTS-hIL-12 + veledimex with immune checkpoint inhibitor (PD-1) during the first half of 2017
  - Initiate Phase 1 study in the treatment of brain tumors in children during the first half of 2017
- CAR-T programs:
  - Continue CD19-specific CAR$^+$ T clinical study in 2017 enrolling patients under shortened manufacturing process towards point of care
  - Initiate a CD33-specific CAR$^+$ T clinical study for relapsed or refractory AML in 2017
  - Advance CAR$^+$ T-cell preclinical studies for at least one hematological malignancy under a shortened manufacturing process towards point of care
- TCR-T programs:
  - Execute CRADA with NCI utilizing SB to generate T cells targeting neoantigens
- NK cell programs:
  - Initiate a Phase 1 study of off the shelf NK cells for AML in 2017
- GvHD programs:
  - Advance preclinical studies in 2017

2017 RBC Global Healthcare Conference

The Company also announced that Dr. Cooper will present at the 2017 RBC Global Healthcare Conference on Thursday, February 23rd, 2017 at 1:35 p.m. ET. The conference will be held at the Lotte New York Palace in New York City.

To access a live audio webcast of the presentation, please visit the Investor Relations section at www.ziopharm.com.

Fourth-Quarter 2016 Financial Results

- Net loss applicable to common shareholders for the fourth quarter of 2016 was $14.8 million, or $(0.11) per share, compared to a net loss of $9.5 million, or $(0.07) per share, for the fourth quarter of 2015. The increase in net loss for the three months ended December 31, 2016 is primarily due to a $1.2 million increase in expenses related to the gene therapy and cell therapy programs, decreased collaboration revenue of $0.3 million, an increase in the charge for the change in derivative liabilities of $0.1 million and income attributable to preferred stockholders of $3.5 million.

- Research and development expenses were $9.4 million for the fourth quarter of 2016 compared to $8.1 million for the fourth quarter of 2015. The increase in research and development expenses for the three months ended December 31, 2016 is primarily due to a $1.2 million increase in expenses related to the gene therapy and cell therapy programs.

- General and administrative expenses were $3.3 million for the fourth quarter of 2016 and 2015.

The Company ended the quarter with cash and cash equivalents of approximately $81.1 million, which the Company believes will be sufficient to fund its currently planned activities into the fourth quarter of 2017. The cash burn is expected to increase substantially during 2017 due to the anticipated initiation of a pivotal trial in GBM.

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® 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, 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® and RTS® are registered trademarks of Intrexon Corporation.

ZIOPHARM Oncology, Inc.
Statements of Operations
(in thousands except share and per share data)
(unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2016	2015	2016	2015
Collaboration revenue	$ 1,597	$ 1,919	$ 6,861	$ 4,332
Operating expenses:				
Research and development, including cost of contracts	9,389	8,142	157,791	106,785
General and administrative	3,319	3,259	14,377	17,647
Total operating expenses	12,708	11,401	172,168	124,432
Loss from operations	(11,111)	(9,482)	(165,307)	(120,100)
Other income (expense), net	32	6	134	12
Change in derivative liabilities	(145)	-	(124)	-
Net loss	(11,224)	(9,476)	$ (165,297)	$ (120,088)
Preferred stock dividends	(3,532)	-	(7,123)	-
Net loss applicable to common stockholders	$ (14,756)	$ (9,476)	$ (172,420)	$ (120,088)
Basic and diluted net loss per share	$ (0.11)	$ (0.07)	$ (1.32)	$ (0.96)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	130,524,204	129,879,897	130,391,463	125,416,084

ZIOPHARM Oncology, Inc.
Balance Sheet Data
(in thousands)
(unaudited)

	December 31, 2016	December 31, 2015
Cash and cash equivalents	81,053	140,717
Working capital	89,075	134,398
Total assets	106,348	153,724
Total stockholders' equity (deficit)	(77,298)	87,371

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