July 31, 2017

ZIOPHARM Oncology Reports Second Quarter 2017 Financial Results and Provides Update on Recent Activities

Company to Host Conference Call Today at 4:30 p.m. ET

BOSTON, July 31, 2017 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIOP), a biopharmaceutical company focused on new immunotherapies, today announced its financial results for the second quarter ended June 30, 2017, and provided an update on the Company's recent activities.

"ZIOPHARM is unique in the breadth and stage of technologies delivering cell- and gene-based therapies that are impactful, controllable and, most critically, scalable," said Laurence Cooper, M.D., Ph.D., Chief Executive Officer of ZIOPHARM Oncology. "We have seen ongoing validation of RheoSwitch® gene switch technology through the now expanded Ad-RTS-hIL-12 + veledimex study in recurrent glioblastoma. We are addressing the complexities of commercializing CAR-T, T-cell receptor, and other cell-based therapies with our rapid manufacture of patient-derived T cells under point-of-care and our off-the-shelf natural killer cells. The *Sleeping Beauty* system enables us to generate CAR-T cells co-expressing important biological effectors such as membrane bound IL-15 and uniquely positions us to express TCRs to efficiently target multiple neoantigens in solid tumors. This non-viral approach to gene therapy not only allows us to customize immunotherapies, but enables controllable and cost-effective T cells with curative potential in both solid and hematologic malignancies."

"During the quarter, we presented updated data at ASCO that linked immune response to overall survival in patients with recurrent glioblastoma when treated with Ad-RTS-hIL-12 + veledimex. Additionally, we initiated a stereotactic arm in this study as a lead-in to both the pediatric and immune checkpoint combination trials. We continue to make progress toward finalizing a registration path for Ad-RTS-hIL-12 + veledimex while evaluating partnership opportunities for the program," added Francois Lebel, M.D., Executive Vice President, Research and Development, Chief Medical Officer of ZIOPHARM Oncology. "In our cell therapy programs, we continue to progress towards clinical evaluation of *Sleeping Beauty* engineered peripheral blood lymphocytes to express TCRs targeting solid tumors, we are advancing our non-viral point-of-care approach for CAR-T therapies, and we also anticipate the imminent initiation of the Phase 1 trial to evaluate CD33 as a new target for CAR^+ T cells in patients with relapsed or refractory acute myeloid leukemia (AML), a highly aggressive and underserved disease. Additionally, we look forward to the initiation of a Phase 1 trial evaluating our off-the-shelf primary NK Cells, which have demonstrated the ability to eliminate AML in preclinical models."

Recent Updates

Adoptive Cell Therapies

ZIOPHARM is developing 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) and selectively with MD Anderson Cancer Center, the National Cancer Institute (NCI) and/or Merck Serono, the biopharmaceutical business of Merck KGaA.

Announced FDA Acceptance of IND for CD33-Specific CAR-T Cell Therapy Targeting Relapsed/Refractory Acute Myeloid Leukemia. In May 2017, ZIOPHARM announced that an investigator-initiated Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) for a Phase 1 trial infusing the Company's CD33-specific CAR^+ T cells for relapsed or refractory AML is active, with the first patient expected to begin treatment in the third quarter of 2017. The genetically modified T cells incorporate a kill switch to eliminate the infused product if there are serious adverse safety events.

Announced Advancement of Next-Generation Non-Viral CAR-T Cell Platform Empowered by Membrane-Bound IL-15 Under RTS® Gene Switch Control. In April 2017, ZIOPHARM and its partners, Intrexon and Merck KGaA, Darmstadt, Germany, announced the advancement of a unique approach to develop therapeutic candidates for two CAR targets expressed on hematologic malignancies and solid tumors. The distinctive methodology centers on the proprietary RTS® platform to regulate production of membrane-bound interleukin-15 (mbIL15) co-expressed with CARs and *Sleeping Beauty*, a non-viral genetic modification system to genetically modify clinical-grade T cells. The companies expect to

advance this innovative approach towards the clinic in 2018.

The IL-15 cytokine is increasingly recognized as a key driver of therapeutic effect in CAR$^+$ T therapy, including in a recent *Journal of Clinical Oncology* publication which correlated lymphoma remissions in patients whose IL-15 levels were elevated after lymphodepleting chemotherapy.[i] Through the RTS® gene switch, the expression of mbIL15 can be regulated to help CARs target cancers in a controlled manner, thus potentiating a new paradigm in T-cell therapy.

Additionally, the non-viral *Sleeping Beauty* transposon-transposase system is an exceptional therapeutic tool that holds multiple advantages over viral-based delivery systems for stably introducing genes encoding CARs and TCRs into T cells. It simplifies genetic modification, and when coupled with reduced *ex vivo* processing, offers a pathway to shortened manufacturing and personalized T-cell therapies.

Continued to Advance Research under the Cooperative Research and Development Agreement with the National Cancer Institute Utilizing the *Sleeping Beauty* System to Generate TCR-modified T cells Targeting Neoantigens. ZIOPHARM continued to advance research being carried out under the Cooperative Research and Development Agreement (CRADA) that the Company maintains with the NCI. Announced in January 2017 by ZIOPHARM and partner Intrexon, research conducted under the CRADA will be carried out under the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI's Center for Cancer Research. Dr. Rosenberg and his team are advancing the *Sleeping Beauty* system into clinical trials to target neoantigens in solid tumors on a patient-by-patient basis. These efforts are based on published works in which the *Sleeping Beauty* system is described as the most clinically advanced non-viral gene transfer tool to reprogram T cells for personalized immunotherapy.[ii,iii]

Ad-RTS-hIL-12 + veledimex

Ad-RTS-hIL-12 + veledimex is ZIOPHARM's gene therapy candidate for the controlled expression of interleukin-12 (IL-12), a critical protein for stimulating an anti-cancer immune response, using an RTS® inducible gene switch that enables controlled *in vivo* expression of therapeutic proteins.

Announced Initiation of Stereotactic Treatment Cohort in Phase 1 Study of Ad-RTS-hIL-12 + Veledimex in Recurrent Glioblastoma. In June 2017, ZIOPHARM announced the initiation of enrollment in the stereotactic arm of its Phase 1 multicenter study of Ad-RTS-hIL-12 + veledimex, a gene therapy for controlled expression of IL-12, in patients with recurrent glioblastoma multiforme (rGBM). The stereotactic cohort will include rGBM patients, that are not scheduled to undergo surgical resection, to assess the safety and tolerability of a single dose of Ad-RTS-hIL-12 administered via injection and activated with orally-administered veledimex (20 mg QD, days 1-14). Stereotactic treatment will serve as a lead-in to the Company's next phase of development for Ad-RTS-hIL-12 + veledimex in brain tumors, including planned anti-PD-1 combination therapy and pediatric studies.

Announced Positive Updated Results of Ad-RTS-hIL-12 + Veledimex in Recurrent Glioblastoma at the 2017 ASCO Annual Meeting. In June 2017, ZIOPHARM announced updated results from its Phase 1 multicenter study of Ad-RTS-hIL-12 + veledimex, including the 20 mg expansion cohort in patients with recurrent or progressive GBM at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting June 2-6 in Chicago. As of May 24, 2017, the median overall survival of all patients receiving intratumoral Ad-RTS-hIL-12 with 20 mg of orally-administered veledimex was 12.5 months, with a mean follow-up time of 9.2 months. The majority of the 15 patients in the 20 mg cohort had two or more recurrences prior to entry in the study, indicating very advanced disease.

Based on the increased ratio of CD8$^+$/FOXP3$^+$ (effector/suppressor) T cells measured in peripheral blood 14 to 28 days after viral injection, overall survival appears correlated with IL-12-mediated cellular immune activation. Furthermore, patients who received low dose or no steroids showed a much better survival rate than those who received elevated systemic steroids, as the latter presumably interferes with immune activation.

As previously reported, a strong, dose-dependent correlation between veledimex dose, veledimex blood-brain-barrier penetration, and IL-12 and IFN-gamma production was observed. Drug-related toxicities, which were primarily non-neurologic, showed a dose response to veledimex, were consistent with those previously reported, and importantly, continue to be reversed upon cessation of the activator ligand, with no drug-related deaths.

Anticipated and Achieved 2017 Milestones

- Intra-tumoral IL-12 RheoSwitch® programs:
  - Updated clinical data from Phase 1 of Ad-RTS-hIL-12 + veledimex for rGBM presented at ASCO
  - Initiate pivotal clinical trial for rGBM
  - Initiate stereotactic administration of Ad-RTS-hIL-12 + veledimex for rGBM:

- Initiate combination study of Ad-RTS-hIL-12 + veledimex with anti-PD-1 for rGBM
- Initiate Phase 1 study in the treatment of brain tumors in children

- Update program at the Society of Neuro-Oncology Annual Meeting

- CAR+ T programs:
  - Continue CD19-specific CAR^+ T 2^{nd}-generation clinical study, enrolling patients under shortened manufacturing protocol
  - Advance mbIL15 CD19-specific CAR^+ T 3^{rd} generation toward a Phase 1 clinical study evaluating point-of-care
  - Initiate a CD33-specific CAR^+ T clinical study in adults and children for relapsed or refractory AML
  - Advance CAR^+ T preclinical studies for at least one hematological malignancy under a shortened manufacturing process towards point-of-care
- TCR programs
  - Execute CRADA with NCI utilizing *Sleeping Beauty* to generate T cells targeting neoantigens for treatment of patients with solid tumor malignancies
  - Advance development of process for delivering personalized gene-modified T-cell products against neoantigens
- NK cell programs
  - Initiate a Phase 1 study of off-the-shelf NK cells for elderly patients with AML not eligible for standard intensive chemotherapy
- GvHD programs
  - Advance preclinical studies

Second-Quarter 2017 Financial Results

- Net loss applicable to the common shareholders for the second quarter of 2017 was $17.7 million, or $(0.13) per share, compared to a net loss of $131.2 million, or $(1.01) per share, for the second quarter of 2016. The decrease is primarily due to the commitment to issue Series 1 preferred stock at fair value under the 2016 ECP Amendment and 2016 GvHD Amendment with Intrexon resulting in a $119.1 million non-cash charge during the three months ended June 30, 2016 that was not incurred during the three months ended June 30, 2017.
- Research and development expenses were $10.8 million for the second quarter of 2017, compared to $129.2 million for the second quarter of 2016. The decrease in research and development expenses for the three months ended June 30, 2017 is primarily due to the Series 1 preferred stock issuance previously noted.
- General and administrative expenses were $3.8 million for the second quarter of 2017, compared to $3.7 million for the second quarter of 2016.
- The Company ended the quarter with unrestricted cash resources of approximately $97.2 million, plus approximately $27.3M in cash on hand at MD Anderson Cancer Center for programs to be conducted at MD Anderson Cancer Center under the current Research and Development Agreement. The Company believes its current resources will be sufficient to fund its currently planned operations into the fourth quarter of 2018.

Conference Call and Slide Webcast

ZIOPHARM will host a conference call and webcast slide presentation today, Monday, July 31, 2017, at 4:30 p.m. ET. 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 53023904. 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. The webcast will be recorded and available for replay on the Company's website for two weeks.

About ZIOPHARM Oncology, Inc.

ZIOPHARM Oncology is a Boston, Massachusetts-based biotechnology company employing innovative 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® (RTS®) 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 preclinical 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 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 and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2017. 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.

[i] Kochenderfer et. al. (2017). Lymphoma Remissions Caused by Anti-CD19 Chimeric Antigen Receptor T Cells Are Associated With High Serum Interleukin-15 Levels. *Journal of Clinical Oncology*, 35(16), 1803-1813.

[ii] Deniger et. al. (2016). Stable, Nonviral Expression of Mutated Tumor Neoantigen-specific T-cell Receptors Using the Sleeping Beauty Transposon/Transposase System. *Molecular Therapy, 24*(6), 1078-1089.

[iii] Klebanoff, Rosenberg, & Restifo (2016). Prospects for gene-engineered T cell immunotherapy for solid cancers. *Nature Medicine*, 22(1), 26-36.

(Tables follow)

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

	Three Months Ended June 30,	
	2017	**2016**
Collaboration revenue	$ 1,597	$ 1,697
Operating expenses:		
Research and development, including cost of contracts	10,831	129,228
General and administrative	3,780	3,711
Total operating expenses	14,611	132,939
Loss from operations	(13,014)	(131,242)
Other income (expense), net	86	42
Change in derivative liabilities	66	-
Net loss	(12,862)	(131,200)
Preferred stock dividends	(4,865)	-
Net loss applicable to common stockholders	$ (17,727)	$ (131,200)

Basic and diluted net loss per share	$ (0.13)	$ (1.01)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	135,630,210	130,385,077

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

	June 30, 2017	December 31, 2016
Cash and cash equivalents	97,194	81,053
Working capital	109,142	89,075
Total assets	126,813	106,348
Total stockholders' (deficit)	(64,274)	(77,298)

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