



**ZIOPHARM Oncology, Inc.**

April 9, 2013

## **ZIOPHARM Presents Preclinical Data Supporting DNA-Based IL-12 Therapy for Breast Cancer**

### **Immunotherapeutic Strategy Results Presented at AACR 2013 Annual Meeting**

NEW YORK, April 9, 2013 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIOP), a biopharmaceutical company focused on the development and commercialization of new cancer therapies, announced today the presentation of results from a study in a breast cancer murine model demonstrating the anti-tumor effects and tolerability of Ad-RTS-mIL-12, a viral vector DNA-based therapeutic for the controlled, local expression of IL-12, an important protein for enhancing antitumor immunity. The data were presented at the American Association for Cancer Research 2013 Annual Meeting (AACR 2013) taking place April 6-10, 2013 in Washington, D.C. The study was conducted jointly by ZIOPHARM and Intrexon Corporation, a synthetic biology company that utilizes its proprietary technologies to provide control over cellular function. ZIOPHARM is Intrexon's exclusive channel partner for the development of *in vivo* therapeutics in oncology.

For the study, intratumoral administration of Ad-RTS-mIL-12 (Ad) was examined in a 4T1 BALB/c mouse breast carcinoma model. Production of murine IL-12 was controlled using Intrexon's RheoSwitch Therapeutic System<sup>®</sup> (RTS<sup>®</sup>) platform and oral administration of the activator ligand INXN-1001 (AL). Oral administration of AL was found to elicit a dose-related increase in plasma AL levels, which correlated with increasing tumor levels of AL. The increase in tumor AL levels in combination with Ad in turn resulted in a dose-related increase in expression of mIL-12 in the tumor, with minimal increase in serum mIL-12. This increase in AL-regulated tumor IL-12 levels correlated with an increase in tumor-infiltrating CD4<sup>+</sup> and CD8<sup>+</sup> T cells in and adjacent to the tumor, concomitant with a decrease in tumor regulatory T cells. This resulted in a dose-related decrease in tumor growth rate. Moreover, the therapeutic strategy appears to be well tolerated, as no change in clinical signs or body weight was observed in the treated animals when compared with vehicle alone.

Samuel Broder, M.D., Chairman of Intrexon's Therapeutic Opportunities Committee and former Director of the NCI (National Cancer Institute), stated, "Two major obstacles for the development of immunotherapeutics in the treatment of cancer are the ability of tumors to evade the anti-cancer capabilities of the immune system and the toxicity often associated with the systemic administration of immunomodulating agents. To overcome these challenges, we have developed Ad-RTS-IL-12, a DNA-based system for the regulated expression of IL-12, that allows for localized, controlled expression of immunomodulating cytokines and activation of their corresponding anti-tumor effects. This strategy is now being tested in the clinic, with the recent launch of a Phase 2 Study of Ad-RTS-IL-12 combined with palifosfamide in the treatment of advanced breast cancer."

Jonathan Lewis, M.D., Ph.D., Chief Executive Officer of ZIOPHARM, commented, "These results support the hypothesis that localized delivery of IL-12 results in an increase in tumor infiltrating lymphocytes concomitant with a reduction in tumor growth. These findings suggest the applicability of this strategy in the treatment of breast cancer, especially in the context of recent literature addressing the positive correlation of survival with immune response measured in breast cancer tumors treated with non-immune therapies. This novel synthetic biology approach, which is being explored in several ongoing clinical studies, holds transformative potential for the treatment of cancer."

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

ZIOPHARM Oncology is a biopharmaceutical company focused on the development and commercialization of new cancer therapies. The Company's clinical programs include:

Ad-RTS-IL-12 is currently being tested in two Phase 2 studies, the first for the treatment of advanced melanoma, and the second in combination with palifosfamide for the treatment of non-resectable recurrent or metastatic breast cancer. Ad-RTS-IL-12 uses synthetic biology to enable controlled delivery of therapeutic interleukin-12 (IL-12), a protein important for enhancing the development of an immune response to cancer. Being developed in partnership with Intrexon Corporation, ZIOPHARM's DNA synthetic biology platform employs an inducible gene-delivery system that enables controlled delivery of genes that produce therapeutic proteins to treat cancer. This is achieved by placing IL-12 under the control of Intrexon's proprietary biological "switch" (the RheoSwitch Therapeutic System<sup>®</sup> or RTS<sup>®</sup> platform) to turn on/off the therapeutic protein expression at the tumor site.

Palifosfamide (ZIO-201) is a potent, bi-functional DNA alkylating agent that has activity in multiple tumors by evading typical resistance pathways. Palifosfamide is in the same class as bendamustine, cyclophosphamide, and ifosfamide.

Indibulin (ZIO-301) is a novel, tubulin binding agent that is expected to have several potential benefits, including oral dosing, application in multi-drug resistant tumors, no neuropathy and a tolerable toxicity profile. It is currently being studied in a Phase 1/2 trial in metastatic breast cancer.

Darinaparsin (ZIO-101) is a novel mitochondrial-and hedgehog-targeted agent (organic arsenic) currently in ongoing studies with Solasia Pharma K.K.

ZIOPHARM's operations are located in Boston, MA, and New York City. Further information about ZIOPHARM may be found at [www.ziopharm.com](http://www.ziopharm.com).

**Forward-Looking Safe Harbor Statement:**

This press release contains certain forward-looking information about ZIOPHARM Oncology 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. Words such as "expect(s)," "feel(s)," "believe(s)," "will," "may," "anticipate(s)" and similar expressions are intended to identify forward-looking statements. These statements include, but are not limited to, statements regarding our ability to successfully develop and commercialize our therapeutic products; our ability to expand our long-term business opportunities; financial projections and estimates and their underlying assumptions; and future performance. 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 or projected by, the forward-looking information and statements. These risks and uncertainties include, but are not limited to: whether Palifosfamide, Ad-RTS IL-12, Darinaparsin, Indibulin, or any of our other therapeutic products will advance further in the 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 Palifosfamide, Ad-RTS IL-12, Darinaparsin, Indibulin, and our other therapeutic products will be successfully marketed if approved; whether any of our other therapeutic product discovery and development efforts will be successful; our ability to achieve the results contemplated by our collaboration agreements; the strength and enforceability of our intellectual property rights; competition from pharmaceutical and biotechnology companies; the development of and our ability to take advantage of the market for our therapeutic products; our ability to raise additional capital to fund our operations on terms acceptable to us; general economic conditions; 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, 2012. 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.

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