



**ZIOPHARM Oncology, Inc.**

## **ZIOPHARM Oncology Presents Preclinical Data at AACR Meeting Demonstrating Significant Anti-Tumor Activity With Two Immunotherapies Expressed *In Vivo* by a Regulated Gene System**

### **Program Committee Recognizes Presentation as Among the Best Science at AACR**

CHICAGO, April 2, 2012 (GLOBE NEWSWIRE) -- ZIOPHARM Oncology, Inc. (Nasdaq:ZIOP), a biopharmaceutical company with small molecule and synthetic biology approaches to new cancer therapies, announced today the presentation of preclinical data demonstrating the significant anti-tumor activity of Interleukin-12 (IL-12) and interferon alpha (IFN $\alpha$ ), two proteins involved in immune response to cancers, expressed *in vivo* utilizing a regulated gene system. The presentation was made at the 2012 American Association for Cancer Research (AACR) Annual Meeting, being held March 31 — April 4 in Chicago, IL, and was recognized as among the best science by the AACR Program Committee, a designation awarded to the top 2.5 percent of abstracts. The Committee designates meritorious presentations as "highly-rated" to assist attendees in identifying the best science at the meeting. ZIOPHARM is the exclusive channel partner to Intrexon Corporation, a privately held synthetic biology engineering company, in the discovery and development of DNA therapies in oncology.

The study assessed anti-tumor activity in lung and breast cancer mouse models utilizing intratumoral administration of adenovirus (Ad) with the novel RheoSwitch Therapeutic System<sup>®</sup> (RTS<sup>®</sup>) technology, a DNA-based inducible promoter system, for regulated expression of murine IL-12 (mIL-12) or murine IFN $\alpha$  (mIFN $\alpha$ ). Oral administration of a small molecule activator ligand (AL), INXN-1001, was used to regulate the expression of mIL-12 in Ad-RTS-mIL-12 and mIFN $\alpha$  in Ad-RTS-mIFN $\alpha$ .

In the lung cancer model, each therapy, combined with AL, was found to induce significant tumor growth inhibition by day 25 (72%, mIL-12, and 71%, mIFN $\alpha$ ;  $p < 0.05$ ). Notably, combined treatment with Ad-RTS-mIL-12 and Ad-RTS-mIFN $\alpha$  with oral AL resulted in significantly enhanced anti-tumor effect compared to either treatment alone (96% growth inhibition;  $p < 0.05$ ) without overt toxicity as assessed by no change in body weight. In the breast cancer model, treatment led to 58% (mIL-12) and 53% (mIFN $\alpha$ ) inhibition of tumor growth compared to control untreated tumors by day 34 ( $p < 0.05$ ). Again, concomitant treatment resulted in significantly enhanced anti-tumor activity with 80% growth inhibition.

"Current cancer immunotherapies have provided limited success in the clinic and innovative strategies are required to further enhance the effectiveness of an anti-tumor immune response," said Ronald B. Herberman, M.D., Chief Medical Officer — Oncology of Intrexon Corporation. "Synthetic biology, specifically, the use of regulated gene systems, offers us the ability to tightly control the delivery of immune therapies *in vivo* in a way which optimizes benefit relative to risk. We have seen the benefit of this approach in a Phase 1 clinical trial using a regulated IL-12 gene expression, and now, in the promise of a combined therapy approach using a regulated combination of IL-12 and IFN $\alpha$  in preclinical models."

"These data indicate that a combined treatment strategy using RheoSwitch<sup>®</sup>-regulated IL-12 and IFN $\alpha$  induces effective therapeutic activity and minimal toxicity against aggressive murine tumors," said Hagop Youssoufian, M.Sc., M.D., President of Research and Development and Chief Medical Officer. "Using DNA to express these proteins *in vivo* and to control their expression with an oral activator is a novel approach with significant potential. Future preclinical studies will investigate the mechanism by which both IL-12 and IFN $\alpha$  exert their anti-tumor effect, an approach we hope to move into the clinic once validated."

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

ZIOPHARM Oncology is a biopharmaceutical company engaged in the development and commercialization of small molecule and synthetic biology approaches to new cancer therapies. The Company's clinical programs include:

Palifosfamide (Zymafos<sup>®</sup> or ZIO-201) is a novel DNA cross-linker that in preclinical study has been shown to bypass resistance mediated by aldehyde dehydrogenase (ALDH), in addition to conferring a favorable toxicity profile compared to other in-class agents. Palifosfamide, administered intravenously, is currently in a randomized, double-blinded, placebo-controlled Phase 3 trial for the treatment of metastatic soft tissue sarcoma in the front-line setting. A Phase 1 trial is also nearing completion with palifosfamide in combination with etoposide and carboplatin to determine appropriate safety for initiating a potentially pivotal, adaptive Phase 3 trial in front-line, extensive SCLC expected to initiate in the second half of 2012. Additionally, an investigational new drug application has been accepted for the oral form of palifosfamide.

DNA-based therapeutics (synthetic biology), in partnership with Intrexon Corporation, include two clinical-stage product candidates, both of which are DNA IL-12 using the RheoSwitch Therapeutic System<sup>®</sup> to be turned *on/off* by an oral activator ligand and are currently in Phase 1. Additionally, multiple INDs are expected in the next 12-24 months resulting from preclinical and discovery work underway to advance multiple antibody, immunotoxin, and protein decoy candidates, systemic delivery and a next generation RheoSwitch Therapeutic System<sup>®</sup>.

Indibulin (Zybulin<sup>™</sup> or ZI001) is a novel, oral tubulin binding agent that is expected to have several potential benefits including oral dosing, application in multi-drug resistant tumors, no neuropathy and a quite tolerable toxicity profile. It is currently being studied in Phase 1/2 in metastatic breast cancer.

Darinaparsin (Zinapar<sup>®</sup> or ZIO-101) is a novel mitochondrial- and hedgehog-targeted agent (organic arsenic) currently in a solid tumor Phase 1 study with oral administration and has been developed intravenously for the treatment of relapsed peripheral T-cell lymphoma.

ZIOPHARM's operations are located in Boston, MA, Germantown, MD 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, 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, Darinaparsin, Indibulin, and our other therapeutic products will be successfully marketed if approved; whether our DNA-based biotherapeutics 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 DNA-based biotherapeutics; 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, 2011. 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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