

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 8-K

**CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934**

Date of report (Date of earliest event reported): **May 20, 2011**

ZIOPHARM Oncology, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

001-33038

(Commission File Number)

84-1475672

(IRS Employer Identification No.)

1180 Avenue of the Americas

19th Floor

New York, NY

(Address of Principal Executive Offices)

10036

(Zip Code)

(646) 214-0700

(Registrant's telephone number, including area code)

Not applicable

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).
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Item 8.01 **Other Events**

On May 20, 2011, ZIOPHARM Oncology, Inc. (the “Company”) and Intrexon Corporation issued a press release announcing results from two preclinical studies examining the tightly controlled, intra-tumoral expression of a novel protein, interleukin-12 (IL-12), in melanoma, colon, lung, leukemia, breast and pancreatic cancer models in mice.

A copy of the above referenced press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 **Financial Statements and Exhibits.**

(d) Exhibits

Exhibit No.	Description
99.1	Press release dated May 20, 2011

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ZIOPHARM Oncology, Inc.

Date: May 23, 2011

By: /s/ Richard Bagley

Name: Richard Bagley

Title: President, Chief Operating Officer and Chief Financial Officer

INDEX OF EXHIBITS

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press release dated May 20, 2011



ZIOPHARM Oncology, Inc.

ZIOPHARM and Intrexon Announce Preclinical Study Results at 2011 ASGCT Meeting from Controlled *In Vivo* Expression of Genes with Broad and Potent Antitumor Activity

Human Application of Novel, Synthetic Biology Approach to be Presented at 2011 ASCO Annual Meeting

SEATTLE, WA (May 20, 2011) – ZIOPHARM Oncology, Inc. (Nasdaq: ZIOP), and Intrexon Corporation announced today that results from two preclinical studies examining the tightly controlled, intra-tumoral expression of a novel protein, interleukin-12 (IL-12), in melanoma, colon, lung, leukemia, breast and pancreatic cancer models in mice, were presented at the 2011 Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT), held May 18 – 21 in Seattle, Washington.

Interleukin-12 (IL-12) is an important regulatory protein that has a function central to the initiation and regulation of cellular immune responses. IL-12, naturally produced by dendritic cells (DCs), has demonstrated potent anti-tumor activity and has been shown to elicit anti-tumor T-cells as well as activate natural killer (NK) cells. The utility of recombinant IL-12 protein therapy, however, has been limited in clinical settings by substantial systemic toxicity.

To improve therapeutic benefit and minimize toxicity, ZIOPHARM, exclusive channel partner to Intrexon in the development and commercialization of DNA-based therapeutics in oncology, has combined Intrexon's RheoSwitch Therapeutic System™ (RTS™) with the IL-12 gene. Using RTS™ technology, IL-12 expression is regulated using a controllable gene switch, which is activated by an orally-delivered small-molecule activator ligand (AL). RTS-IL-12 is delivered to the tumor through an adenoviral vector (Ad), a tool used to deliver genetic material (and encoded protein) into cells, or through dendritic cells transduced with Ad-RTS-IL-12 (DC-RTS-IL-12), an approach validated in preclinical proof-of-concept studies.

The studies, entitled "RheoSwitch-Mediated Regulation of IL-12 Protein Delivered Using an Adenoviral Vector Results in Anti-Tumor Effects Across a Spectrum of Tumor Types" by Murugesan et al. (Poster #883, Poster Session I) and "Local and Systemic Anti-Tumor Immunity is Induced by Rheoswitch Regulated IL-12 Production after Intra-Tumoral Injection of Adenovirus Vector as well as Vector-Transduced Dendritic Cells" by Herberman et al. (poster #899, Poster Session II), are available at <http://www.asgct.org/am11/index.php>.

“The use of recombinant proteins is one of the most important advances in therapeutic drug development over the past 30 years, but the limits of systemic delivery of proteins such as IL-12 are evident since they cannot readily be given safely at therapeutic levels,” said Ronald B. Herberman, M.D., Chief Medical Officer of Intrexon and lead author of the ‘899’ study. “As we demonstrated in these studies, however, the tightly controlled production of IL-12 directly within the tumor allows us to modulate its broad antitumor response. Specifically, these data highlight the potential therapeutic benefit of direct adenoviral-based immune-therapy with Ad-RTS-IL-12, which is a simpler approach than using autologous, transduced dendritic cells. Clearly, the data warrant further evaluation in the clinic. The RTS™ technology used to achieve this preclinical result is at the cutting edge of medical and scientific research, and it represents a novel approach where the body itself is used to manufacture the effector protein, in the right place and at the right time.”

On May 13, 2011, ZIOPHARM announced its submission of an Investigational New Drug (IND) application with the U.S. Food and Drug Administration to commence a Phase I study of Ad-RTS-IL-12 + AL in the first half of 2011. A Phase Ib study of DC-RTS-IL-12 + AL is ongoing with initial results to be presented at the 2011 Annual Meeting of ASCO in Chicago to be held June 3 - 7, 2011.

Results in Detail

- In Murugesan et al., the induction of IL-12 expression in the presence of the AL was first established *in vitro*. No induction of IL-12 was detected when the activator was omitted whereas an up to >6000-fold induction of human IL-12 expression above background levels was established depending on the exposure concentration of the AL. Dose response for both the AL and virus vector dose were then investigated *in vivo* using murine IL-12 (mIL-12) in a B16FO melanoma model. Significant tumor inhibition (91-98%) compared to controls was observed when Ad-RTS-mIL-12 + AL was delivered at doses ranging from 100-1000mg/kg of rodent feed, without observable reduction in animal body weight. At a constant AL dose and varying virus vector doses (1×10^7 - 5×10^{10} viral particles), Ad-RTS-mIL-12 + AL produced 73% tumor growth inhibition at low dose and a 95-99% tumor reduction at high doses ($p < 0.005$), with no major body weight loss.
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Ad-RTS-mIL-12 + AL demonstrated similar tolerability and statistically significant tumor-growth inhibition relative to controls in several additional murine tumor models including colon, lung, leukemia breast and pancreatic cancer models. These data suggest the RTS-controlled IL-12 expression delivered through direct intra-tumoral adenoviral delivery is effective and tolerable, with a broad therapeutic window for both the activator and vector dose.

- Herberman et al. sought to determine whether the immunologic mechanism of action of direct intratumoral injection of Ad-RTS-IL-12 + AL was similar to that of DC-RTS-IL-12 (dendritic cells transduced with Ad-RTS-IL-12) + AL, the subject of Komita et al. (Cancer Gene Therapy, 2009) as well as a Phase Ib clinical study to be presented at the 2011 Annual Meeting of the American Society of Clinical Oncology (ASCO). Komita et al. reported that the mechanism of action of DC-RTS-mIL-12 with the AL appeared to be induction of systemic anti-tumor immunity, with CD8+ T cells (killer T cells) secreting increased levels of IFN γ , a protein with anti-tumor properties, in response to specific tumor cells, as well as the persistence and accumulation of dendritic cells in treated tumors. Recent studies have indicated that mice treated with DC-RTS-mIL-12 + AL had, in both the tumor-draining lymph nodes and spleen, increased numbers of tumor-specific T-cells capable of secreting granzyme B (GzB) and IFN γ in response to both CD8+ and CD4+ tumor peptides.

To evaluate cell types transduced by direct adenovirus injection, adenovirus expressing green fluorescent protein (GFP) under a strong constitutive promoter was injected into established B16F0 melanoma tumors, and within 12 hours the virus was detectable in dendritic cells and T-cells as well as in melanoma cells. At day seven (7) after intra-tumoral injection of Ad-RTS-mIL-12 + AL, increased percentages of T cell subsets, natural killer cells and dendritic cells were observed in the tumor microenvironment, and cells isolated from the tumor-draining lymph nodes and spleens of the treated animals showed increased numbers of GzB and IFN γ -secreting T-cells in response to CD8+ and CD4+ melanoma peptides. Taken together, these data indicate that intra-tumoral injection of either Ad-RTS-mIL-12 or DC-RTS-mIL-12, in combination with daily oral AL, induced changes in the tumor micro-environment that favor anti-tumor immune responses and systemic anti-tumor immunity.

About ZIOPHARM Oncology, Inc.:

ZIOPHARM Oncology is a biopharmaceutical company engaged in the development and commercialization of a diverse portfolio of cancer therapeutics. The Company is currently focused on several clinical programs.

Palifosfamide (Zymafos™ or ZIO-201) is a novel DNA cross-linker in class with bendamustine, ifosfamide, and cyclophosphamide. ZIOPHARM is currently enrolling patients in a randomized, double-blinded, placebo-controlled Phase III trial with palifosfamide administered intravenously for the treatment of metastatic soft tissue sarcoma in the front-line setting. The company is also currently conducting a Phase I intravenous study of palifosfamide in combination with standard of care addressing small cell lung cancer and an oral form of the drug for treatment of solid tumors is currently in the advanced preclinical stage of development.

Darinaparsin (Zinapar™ or ZIO-101) is a novel mitochondrial-targeted agent (organic arsenic) being developed intravenously for the treatment of relapsed peripheral T-cell lymphoma likely with a two-stage potentially pivotal study expected to begin in late 2011. An oral form is in a Phase I trial in solid tumors.

Indibulin (Zybulin™ or ZIO-301) 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 I/II in metastatic breast cancer.

ZIOPHARM is also pursuing the development of novel DNA-based therapeutics in the field of cancer pursuant to an exclusive channel partnership with Intrexon Corporation. The partnership includes two existing clinical-stage product candidates, the first of which is in a Phase Ib study and the second is currently the subject of an Investigational New Drug (IND) application filed with the U.S. Food and Drug Administration.

ZIOPHARM's operations are located in Boston, MA and Germantown, MD with an executive office in New York City. Further information about ZIOPHARM may be found at www.ziopharm.com.

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About Intrexon Corporation:

Intrexon Corporation is a privately held synthetic biology company that employs modular DNA control systems to enhance capabilities, improve safety and lower cost in human therapeutics, protein production, industrial products, animal science and agricultural biotechnology. The company's advanced transgene engineering platform enables Better DNA™ by combining breakthroughs in DNA control systems with corresponding advancements in modular transgene design, assembly and optimization. The company is currently using these advanced capabilities to undertake foremost challenges across the spectrum for biological applications. More information about the company is available at www.DNA.com.

Forward-Looking Safe Harbor Statement:

This press release contains forward-looking statements for ZIOPHARM Oncology, Inc. that involve risks and uncertainties that could cause ZIOPHARM Oncology's actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These statements are based on current expectations, forecasts and assumptions that are subject to risks and uncertainties, which could cause actual outcomes and results to differ materially from these statements. Among other things, there can be no assurance that any of ZIOPHARM Oncology's development efforts relating to its product candidates will be successful, or such product candidates will be successfully commercialized. Other risks that affect forward-looking information contained in this press release include the possibility of being unable to obtain regulatory approval of ZIOPHARM Oncology's product candidates, the risk that the results of clinical trials may not support ZIOPHARM Oncology's claims, the risk that pre-clinical or clinical trials will proceed on schedules that are consistent with ZIOPHARM Oncology's current expectations or at all, risks related to ZIOPHARM Oncology's ability to protect its intellectual property and its reliance on third parties to develop its product candidates, risks related to the sufficiency of existing capital reserves to fund continued operations for a particular amount of time and uncertainties regarding ZIOPHARM Oncology's ability to obtain additional financing to support its operations thereafter, as well as other risks regarding ZIOPHARM Oncology's that are discussed under the heading "Risk Factors" in ZIOPHARM Oncology's filings with the United States Securities and Exchange Commission. Forward-looking statements can be identified by the use of words such as "may," "will," "intend," "should," "could," "can," "would," "expect," "believe," "estimate," "predict," "potential," "plan," "is designed to," "target" and similar expressions. ZIOPHARM Oncology assumes no obligation to update these forward-looking statements, except as required by law.

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