ZIOPHARM ONCOLOGY INC
Form 8-K
January 20, 2012

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): January 19, 2012

ZIOPHARM Oncology, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	001-33038	84-1475672
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

1180 Avenue of the Americas Suite 2020 New York, NY	10036
(Address of Principal Executive Offices)	(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:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).

Item 8.01 Other Events

Public Offering Announcement

On January 19, 2012, ZIOPHARM Oncology, Inc. (the "Company") issued a press release announcing that it intends to commence an underwritten public offering of shares of its common stock. J.P. Morgan Securities LLC will act as book-running manager for the proposed offering. The Company intends to grant the underwriters a 30-day option to purchase up to an additional 15 percent of the amount sold to cover over-allotments, if any. A copy of the press release is filed herewith as Exhibit 99.1 to this Current Report.

Updated Business Description and New Risk Factor

On January 19, 2012, the Company filed with the Securities and Exchange Commission a prospectus supplement to its Registration Statement on Form S-3 (File No. 333-177793), which included an updated business description and the new risk factor set forth below.

All references below to "ZIOPHARM Oncology," "ZIOPHARM," the "Company," "we," "us," "our," or similar references re ZIOPHARM Oncology, Inc., except where the context otherwise requires or as otherwise indicated.

Description of Business

Company overview

ZIOPHARM Oncology, Inc. is a biopharmaceutical company that is seeking to develop and commercialize a diverse portfolio of cancer drugs that can address unmet medical needs. Our principal focus has been on the licensing and development of proprietary small molecule drug candidates that are related to cancer therapeutics already on the market or in development and that can be administered by intravenous, or IV, and/or oral dosing. Our clinical programs for our small molecule candidates include palifosfamide (Zymafos® or ZIO-201), darinaparsin (Zinapar® or ZIO-101) and indibulin (ZybulinTM or ZIO-301). We are also pursuing the development of novel DNA-based biotherapeutics in the field of cancer pursuant to a partnering arrangement with Intrexon Corporation, or Intrexon. Under the arrangement, we obtained rights to Intrexon's effector platform for use in the field of oncology, which includes two existing clinical stage product candidates, ZIN-CTI-001 (or DC-RTS-IL-12 + AL) and ZIN-ATI-001 (or Ad-RTS-IL-12 + AL). We plan to leverage Intrexon's synthetic biology platform to develop products to stimulate key pathways used by the body's immune system to inhibit the growth and metastasis of cancers, adding significantly to our small molecule drug development portfolio and utilizing our capabilities to translate science to the patient setting. We believe that our strategy will result in expedited drug development programs for product candidates with a cost of manufacturing that, upon successful commercialization, would help to address changing worldwide product reimbursement requirements. We are currently in Phase 1, 2, and/or Phase 3 studies for our product candidates with a particular emphasis on completing a global palifosfamide pivotal Phase 3 trial to support registration in combination with doxorubicin in the front-line setting of metastatic soft tissue sarcoma.

Product candidates

ZIO-101, Darinaparsin, Zinapar

Darinaparsin is a novel mitochondrial- and sonic hedgehog-targeted agent (organic arsenic) in development with both IV and oral administration. Phase 1 testing of the IV form of darinaparsin in solid tumors and hematological cancers

was completed and we reported clinical activity and, importantly, a safety profile from these studies as predicted by preclinical results. We subsequently completed Phase 2 studies in advanced myeloma, primary liver cancer and in certain other hematological cancers. At the May 2009 annual meeting of the American Society of Clinical Oncology (ASCO), we reported favorable results from the IV trial in lymphoma, particularly peripheral T-cell lymphoma, or PTCL. With a subsequent focus on the relapsed setting of PTCL, a Phase 1 study of darinaparsin in combination with the treatment regimen called “CHOP” in the front-line setting of PTCL was ended. A Phase 1 trial in solid tumors with an oral form of darinaparsin is nearing completion. Data from the Phase I oral study will guide further study. We have obtained Orphan Drug Designation for darinaparsin in the United States and Europe for the treatment of PTCL and have entered into a licensing agreement with Solasia for the Asia/Pacific territory with a focus on IV-administered darinaparsin in PTCL.

ZIO-201, Palifosfamide, Zymafos

Palifosfamide is a novel DNA cross-linker (stabilized active metabolite of ifosfamide) in class with bendemustine, ifosfamide, and cyclophosphamide and currently in development with IV administration (oral in late preclinical). Following Phase 1 study, we completed Phase 2 testing of the IV form of palifosfamide as a single agent to treat advanced sarcoma. In both Phase 1 and Phase 2 testing, palifosfamide has been administered without the "uroprotectant" mesna, as is required with ifosfamide, and the toxicities associated with other ifosfamide metabolites, acrolein and chloroacetaldehyde, have not been observed. We reported clinical activity of palifosfamide when used alone in the Phase 2 study addressing advanced sarcoma. Following review of preclinical combination studies, we initiated a Phase 1 dose escalation study of palifosfamide in combination with doxorubicin, primarily in patients with soft tissue sarcoma. We reported favorable results and safety profile from this study at ASCO's 2009 annual meeting. In light of reported favorable Phase 2 single agent clinical activity data and with the combination being well tolerated in the Phase 1 trial, we initiated a Phase 2 randomized controlled trial, which we refer to as PICASSO, in the second half of 2008 to compare doxorubicin plus palifosfamide to doxorubicin alone in patients with front- and second-line metastatic or unresectable soft tissue sarcoma. The study generated positive top line interim data in 2009. Upon successfully reaching a pre-specified efficacy milestone and following safety and efficacy data review by the Data Committee, sarcoma experts, and our Medical Advisory Board, we elected to suspend enrollment in the trial in October 2009. We subsequently presented further positive interim data from the trial at the 15th Annual Connective Tissue Oncology Society meeting held in November 2009 and again at the 2010 ASCO annual meeting in June 2010, where the presentation was selected for "Best of ASCO." In July 2010, we announced the initiation of a worldwide registration trial on a protocol design developed through a U.S. Food and Drug Administration, or FDA, End-of-Phase 2 meeting and the Special Protocol Assessment, or SPA, process. Although we did engage in the SPA process, we, with guidance from the FDA, elected to initiate the trial without having obtained SPA agreement from the FDA. The Phase 3 trial is in front-line metastatic soft tissue sarcoma, entitled PICASSO 3, and is an international, randomized, double-blinded, placebo-controlled trial with a targeted enrollment of 424 patients. The study is designed to evaluate the safety and efficacy of palifosfamide administered with doxorubicin compared with doxorubicin administered with placebo, with no cross-over between the arms. Progression-free survival is the primary endpoint for accelerated approval, with overall survival as the primary endpoint for full approval. PICASSO 3 has no interim efficacy analysis, while the trial is monitored by a Data Monitoring Committee, or DMC, of outside, independent experts for safety and futility. The DMC has met twice to review trial data for safety and futility and on both occasions has recommended trial continuation. Orphan Drug Designation for palifosfamide has been obtained in both the United States and the European Union for the treatment of soft tissue sarcomas.

A Phase 1 trial is 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 small-cell lung cancer, or SCLC, expected to initiate in the second half of 2012. An oral form of palifosfamide has been the subject of preclinical studies necessary for an Investigational New Drug, or IND, application to support commencing Phase 1 study. Based on an initial review, the FDA requested that we repeat an animal study, now completed and submitted to the FDA.

According to the American Cancer Society, it was estimated that 569,490 Americans would die from cancer in 2010 — more than 1,500 each day. The cost of treating cancer is significant. The National Institute of Health estimated that the overall cost of cancer in 2010 was $263.8 billion. This cost included an estimate of $102.8 billion in direct medical expenses and $140.1 billion in indirect mortality costs.

Both front-line metastatic soft tissue sarcoma, or STS, and extensive SCLC represent significant unmet medical needs with standard of care considerably dated. We believe approximately 100,000 patients worldwide have been initially diagnosed with STS. For patients diagnosed with STS, primary care is surgery, sometimes with radiation therapy. Many patients enter a period of remission that is unpredictable and can even represent a "cure." Metastatic STS arises when the disease has re-occurred and surgery is no longer an option. Chemotherapy is the standard of care for front-line metastatic STS and doxorubicin is the only front-line therapy approved in the United States for its treatment. The annual projection in the United States for front-line metastatic STS treatment is approximately 9,000 patients. While data sources for Europe are unavailable, we believe the annual projection in Europe for front-line metastatic STS treatment is approximately 14,000 patients, for a combined U.S. and European estimate of 23,000 patients annually. For SCLC, the estimated U.S. annual incidence is 30 – 35,000 patients, and 200,000 patients worldwide. Approximately 80 – 90% of patients have extensive disease, the population for the planned pivotal trial. Cis/carboplatin and etoposide are standard of care in the front-line setting. A formal retrospective mortality study also suggests that the SCLC population in China is substantial and projected from the study to be greater than 150,000 patients and growing. We believe there is more than $1.0 billion in total market potential for worldwide sales of cancer drugs relating to the treatment of STS and SCLC.

ZIO-301, Indibulin, Zybulin

Indibulin is a novel orally administered tubulin binding agent. Phase 1 study as a single agent in patients with advanced solid tumors has been completed. We have reported clinical activity at well-tolerated doses using a continuous dosing scheme without the development of clinically relevant peripheral neuropathy. Following encouraging preclinical results obtained with indibulin in combination with other chemotherapies, two Phase 1 combination studies were initiated with TarcevaTM and XelodaTM, respectively. The favorable activity and safety profile of oral indibulin with oral XelodaTM was reported at ASCO's annual meeting in May 2009. In all studies, a maximum tolerated dose, or MTD, was not established. Preclinical work with our consultant established a dosing schedule to enhance activity and reduce toxicity, which is presently five days on drug and nine days off in a Phase 1 study in late stage metastatic breast cancer. In light of the lack of establishing an MTD and the need to administer many capsules several times a day, we have recently modified the dosage form to administer once a day dosing in the Phase 1 trial.

ZIN-CTI-001 (or DC-RTS-IL-12 + AL) and ZIN-ATI-001 (or Ad-RTS-IL-12 + AL)

We are also pursuing the development of novel DNA-based therapeutics in the field of cancer pursuant to an exclusive channel partnership with Intrexon. The partnership includes two existing clinical-stage product candidates. ZIN-CTI-001 is in a Phase 1b trial in the United States and employs intratumoral injection of modified dendritic cells from each patient and oral dosing of an activator ligand to turn on in vivo expression of interleukin-12, or IL-12. ZIN-CTI-001 uses a RheoSwitch Therapeutic System®, or RTS, to control the timing and level of transgene expression for gene and cell therapy. The RTS technology functions as a "gene switch" for the regulated expression of human IL-12 in the patients' dendritic cells which are transduced with a replication deficient adenoviral vector carrying the IL-12 gene under the control of the RTS, and in this study, injected intratumorally for the treatment of patients with stage III or IV melanoma. The binding of the small molecule activator to the fusion proteins of RTS is intended to regulate the timing and level of IL-12 expression. In the absence of the activator ligand, the level of IL-12 is below detectable levels.

The activator ligand has been the subject of a number of preclinical, safety and pharmacology studies under FDA and International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use guidelines. Preclinical studies in the B16 mouse melanoma model consistently induced regression of established melanoma lesions, both in those directly injected and those elsewhere in the body. Preclinical studies have shown DC-RTS-IL-12, in combination with an activator ligand, to have strong activity against a broad array of

cancers, including brain, colon, renal and pancreatic cancers and melanoma.

A Phase 1a clinical study of the activator ligand was conducted in 65 healthy volunteers, with the two most common side effects being dysgeusia (impairment of taste) and throat irritation. A subsequent Phase 1b trial, which is ongoing in patients with advanced melanoma, has been amended to study efficacy and immunological and biological effects in addition to safety with cohort-based dose escalation of the activator ligand during repeated treatment cycles. Initial positive clinical results from the Phase 1b trial were presented at the June 2011 ASCO annual meeting. The trial enrolled ten patients (median age 61) with unresectable Stage III or IV melanoma. Among eight evaluable patients, partial or complete regression of injected and some uninjected lesions was observed by computed axial tomography, or CT, scans in three patients, with one patient having a RECIST PR of >11 months and three patients demonstrating stable disease by RECIST, for an overall disease control rate of 50%. Treatment was generally well tolerated, and maximum tolerated dose has not yet been reached. Adverse events were mild to moderate, with one to two patients each experiencing nausea, vomiting, anorexia, arthralgia, fever or chills. One severe adverse event was reported 18 hours after treatment onset with 60 mg AL + ZIN-CTI-001, and included diarrhea, followed by hypotension and reversible acute renal failure, which completely resolved.

Clinical study of ZIN-ATI-001, essentially ZIN-CTI-001 without dendritic cells, has also initiated in Phase 1 study in advanced melanoma. The Phase 1 study will evaluate safety in addition to immunological and biological effects and efficacy of the therapeutic candidate in patients with melanoma.

We intend to evaluate both ZIN-CTI-001 and ZIN-ATI-001 with the intent to advance ZIN-ATI-001 into at least two Phase 2 trials, one a potentially pivotal trial for accelerated approval in an indication with significant unmet medical need.

We are also in late preclinical evaluation with respect to several additional potential product candidates under our channel partnership with Intrexon, and we anticipate continuing evaluation to select product candidates for clinical study, which could commence as early as this year. We also anticipate continuing discovery efforts aimed at identifying additional potential product candidates under the Intrexon channel partnership for study thereafter.

Development plans

We are currently pursuing several clinical programs, which include:

- palifosfamide (Zymafos or ZIO-201) — completing our Phase 3 pivotal trial in front-line metastatic soft tissue sarcoma, entitled PICASSO 3, and completing our Phase 1 trial with palifosfamide in combination with etoposide and carboplatin to determine appropriate safety for initiating the subsequent randomized trial in front-line, extensive small-cell lung cancer.
    - darinaparsin (Zinapar or ZIO-101) — completing an ongoing Phase 1 study with an oral form.
- indibulin (Zybulin or ZIO-301) — entering the Phase 2 portion of the Phase 1/2 trial having established the MTD in Phase 1 with once daily dosing.
- ZIN-CTI-001 — completing a Phase 1b trial in patients with advanced melanoma that is on-going in the United States.
- ZIN-ATI-001 — completing the Phase 1 trial treatment of patients with late-stage malignant melanoma andadvancing to Phase 2 study.

Our current plans involve using considerably internal financial resources to develop palifosfamide and to broaden extensively the synthetic biology program, with the intention of ultimately partnering or otherwise raising additional resources to support further development activities for all of our product candidates. The successful development of our product candidates is highly uncertain. Product development costs and timelines can vary significantly for each product candidate, are difficult to accurately predict, and will require us to obtain additional funding, either alone or in connection with partnering arrangements. Various statutes and regulations also govern or influence the manufacturing,

safety, labeling, storage, record keeping and marketing of each product. The lengthy process of seeking approval and the subsequent compliance with applicable statutes and regulations require the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals could materially, adversely affect our business. To date, we have not received approval for the sale of any product candidates in any market and, therefore, have not generated any revenues from our product candidates.

Risk Factor

Our ability to use net operating loss carryforwards to reduce future tax payments may be limited or restricted.

We have generated significant net operating loss carryforwards, or NOLs, as a result of our incurrence of losses since inception. We generally are able to carry NOLs forward to reduce taxable income in future years. However, our ability to utilize the NOLs is subject to the rules of Section 382 of the Internal Revenue Code. Section 382 generally restricts the use of NOLs after an "ownership change." An ownership change occurs if, among other things, the stockholders (or specified groups of stockholders) who own or have owned, directly or indirectly, 5% or more of a corporation's common stock or are otherwise treated as 5% stockholders under Section 382 and the U.S. Treasury Department regulations promulgated thereunder increase their aggregate percentage ownership of that corporation's stock by more than 50 percentage points over the lowest percentage of the stock owned by these stockholders over a three-year rolling period. In the event of an ownership change, Section 382 imposes an annual limitation on the amount of taxable income a corporation may offset with NOL carry forwards. This annual limitation is generally equal to the product of the value of the corporation's stock on the date of the ownership change, multiplied by the long-term tax-exempt rate published monthly by the Internal Revenue Service. Any unused annual limitation may be carried over to later years until the applicable expiration date for the respective NOL carry forwards. This offering may cause an "ownership change" within the meaning of Section 382, and we may have experienced such ownership changes in the past. As a result, our NOLs may be subject to limitations and we may be required to pay taxes earlier and in larger amounts than would be the case if our NOLs were freely usable.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated January 19, 2012

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: January 19, 2012	By:	/s/ Caesar Belbel Name: Caesar Belbel Title: Executive Vice President, Chief Legal Officer and Secretary

INDEX OF EXHIBITS

Exhibit No.	Description
99.1	Press Release, dated January 19, 2012