

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form S-8

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

ZIOPHARM Oncology, Inc.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of
incorporation or organization)

84-1475672

(I.R.S. Employer
Identification No.)

1180 Avenue of the Americas

20th Floor

New York, NY

(Address of principal executive offices)

10036

(Zip Code)

2012 Equity Incentive Plan

(Full title of the plan)

Caesar Belbel

Chief Legal Officer

ZIOPHARM ONCOLOGY, INC.

One First Avenue, Building 34

Boston, Massachusetts 02129

(617) 259-1970

(Name, address and telephone number,
including area code, of agent for service)

With a copy to:

Marc Recht

COOLEY LLP

500 Boylston Street, 14th Floor

Boston, Massachusetts 02116

(617) 937-2300

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

(Do not check if a

smaller reporting company)

CALCULATION OF REGISTRATION FEE

Title of securities to be registered	Amount to be registered(1)	Proposed maximum offering price per share(2)	Proposed maximum aggregate offering price(2)	Amount of registration fee
Common stock, par value \$0.001 per share	4,000,000 shares	\$4.06	\$16,240,000	\$2,215.14

(1) In accordance with Rule 416 under the Securities Act of 1933, as amended, this registration statement shall be deemed to cover any additional securities that may from time to time be offered or issued to prevent dilution resulting from stock splits, stock dividends or similar transactions.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and (h) under the Securities Act of 1933, as amended, and based upon the average of the high and low prices of the registrant's common stock as reported on the NASDAQ Capital Market on December 10, 2012.

PART I

INFORMATION REQUIRED IN THE SECTION 10(a) PROSPECTUS

Item 1. Plan Information.

The information required by Item 1 is included in documents sent or given to participants in the plan covered by this registration statement pursuant to Rule 428(b)(1) of the Securities Act of 1933, as amended (the "Securities Act").

Item 2. Registrant Information and Employee Plan Annual Information.

The written statement required by Item 2 is included in documents sent or given to participants in the plan covered by this registration statement pursuant to Rule 428(b)(1) of the Securities Act.

PART II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.

The following documents filed by the registrant with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934, as amended (the "Exchange Act"), are incorporated by reference into this registration statement:

(a) the registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2011, filed on February 29, 2012;

(b) the registrant's Quarterly Reports on Form 10-Q for the quarter ended March 30, 2012, filed on May 3, 2012, for the quarter ended June 30, 2012, filed on August 2, 2012, Amendment No. 1 to the Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, filed on August 28, 2012, and for the quarter ended September 30, 2012, filed on November 8, 2012;

(c) the registrant's Current Reports on Form 8-K filed on January 20, 2012, January 25, 2012, February 14, 2012, February 29, 2012, April 2, 2012 (two), April 3, 2012 (two), May 3, 2012, May 10, 2012, June 4, 2012, June 19, 2012, June 26, 2012, July 17, 2012, August 2, 2012, September 7, 2012, October 19, 2012 and November 8, 2012 (two); and

(d) the description of the registrant's common stock contained in the registrant's Registration Statement on Form 8-A filed on September 20, 2006, and any amendment or report filed for the purpose of updating such description.

All reports and other documents subsequently filed by the registrant pursuant to sections 13(a), 13(c), 14 and 15(d) of the Exchange Act, prior to the filing of a post-effective amendment which indicates that all securities offered have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference herein and to be a part of this registration statement from the date of the filing of such reports and documents. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for the purposes of this registration statement to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this registration statement

Item 4. Description of Securities.

Not applicable.

Item 5. Interests of Named Experts and Counsel

Not applicable.

Item 6. Indemnification of Directors and Officers.

Under Article 6 of the registrant's bylaws, each director and officer of the registrant will be indemnified to the fullest extent permitted by applicable law as it presently exists or may hereafter be amended, who was or is made or is threatened to be made a party or is otherwise involved in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he or she, or a person for whom he or she is the legal representative, is or was a director or officer of the registrant or, while a director or officer of the registrant, is or was serving at the request of the registrant as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust, enterprise or nonprofit entity, including service with respect to employee benefit plans, against all liability and loss suffered and expenses (including attorneys' fees) reasonably incurred by such director or officer. However, the registrant shall be required to indemnify a director or officer in connection with a proceeding commenced by such director or officer only if the commencement of such proceeding (or part thereof) by the director or officer was authorized by the registrant's board of directors. The registrant's Amended and Restated Certificate of Incorporation also eliminates the liability of directors of the registrant for monetary damages to the fullest extent permissible under Delaware law.

Section 145 of the Delaware General Corporation Law states:

(a) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that the person's conduct was unlawful.

(b) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

(c) To the extent that a present or former director or officer of a corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding referred to in subsections (a) and (b) of this section, or in defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection therewith.

(d) Any indemnification under subsections (a) and (b) of this section (unless ordered by a court) shall be made by the corporation only as authorized in the specific case upon a determination that indemnification of the present or former director, officer, employee or agent is proper in the circumstances because the person has met the applicable standard of conduct set forth in subsections (a) and (b) of this section. Such determination shall be made, with respect to a person who is a director or officer of the corporation at the time of such determination:

- (1) By a majority vote of the directors who are not parties to such action, suit or proceeding, even though less than a quorum; or
- (2) By a committee of such directors designated by majority vote of such directors, even though less than a quorum; or
- (3) If there are no such directors, or if such directors so direct, by independent legal counsel in a written opinion; or
- (4) By the stockholders.

(e) Expenses (including attorneys' fees) incurred by an officer or director of the corporation in defending any civil, criminal, administrative or investigative action, suit or proceeding may be paid by the corporation in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of such director or officer to repay such amount if it shall ultimately be determined that such person is not entitled to be indemnified by the corporation as authorized in this section. Such expenses (including attorneys' fees) incurred by former directors and officers or other employees and agents of the corporation or by persons serving at the request of the corporation as directors, officers, employees or agents of another corporation, partnership, joint venture, trust or other enterprise may be so paid upon such terms and conditions, if any, as the corporation deems appropriate.

(f) The indemnification and advancement of expenses provided by, or granted pursuant to, the other subsections of this section shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in such person's official capacity and as to action in another capacity while holding such office. A right to indemnification or to advancement of expenses arising under a provision of the certificate of incorporation or a bylaw shall not be eliminated or impaired by an amendment to such provision after the occurrence of the act or omission that is the subject of the civil, criminal, administrative or investigative action, suit or proceeding for which indemnification or advancement of expenses is sought, unless the provision in effect at the time of such act or omission explicitly authorizes such elimination or impairment after such action or omission has occurred.

(g) A corporation shall have power to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the corporation would have the power to indemnify such person against such liability under this section.

(h) For purposes of this section, references to "the corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this section with respect to the resulting or surviving corporation as such person would have with respect to such constituent corporation if its separate existence had continued.

(i) For purposes of this section, references to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on a person with respect to any employee benefit plan; and references to "serving at the request of the corporation" shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner such person reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the corporation" as referred to in this section.

(j) The indemnification and advancement of expenses provided by, or granted pursuant to, this section shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

(k) The Court of Chancery is hereby vested with exclusive jurisdiction to hear and determine all actions for advancement of expenses or indemnification brought under this section or under any bylaw, agreement, vote of stockholders or disinterested directors, or otherwise. The Court of Chancery may summarily determine a corporation's obligation to advance expenses (including attorneys' fees).

The registrant maintains insurance on behalf of its officers and directors, insuring them against liabilities that they may incur in such capacities or arising out of this status.

The above discussion of the registrant's Amended and Restated Certificate of Incorporation and Bylaws and of Section 145 of the Delaware General Corporation Law is not intended to be exhaustive and is respectively qualified in its entirety by such Amended and Restated Certificate of Incorporation, Bylaws and statute.

To the extent that the registrant's directors, officers and controlling persons are indemnified under the provisions contained in the registrant's Amended and Restated Certificate of Incorporation, Delaware law or contractual arrangements against liabilities arising under the Securities Act, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act, and is therefore unenforceable.

Item 7. Exemption from Registration Claimed.

Not applicable.

Item 8. Exhibits

Exhibit No.	Description of Document
4.1	Amended and Restated Certificate of Incorporation, as filed with the Delaware Secretary of State on April 26, 2006 (incorporated by reference to Exhibit 3.1 to the registrant's Current Report on Form 8-K (SEC File No. 000-32353) filed April 26, 2006)
4.2	Bylaws, as amended to date (incorporated by reference to Exhibit 3.3 to the registrant's Current Report on Form 8-K (SEC File No. 000-32353) filed September 19, 2005)
4.3	Specimen common stock certificate (incorporated by reference to Exhibit 4.1 to the registrant's Registration Statement on Form SB-2 (SEC File No. 333-129020) filed October 14, 2005)
5.1	Legal opinion of Cooley LLP
23.1	Consent of Independent Registered Public Accounting Firm – McGladrey LLP
23.2	Consent of Independent Registered Public Accounting Firm – Caturano and Company, Inc.
23.3	Consent of Cooley LLP (included as part of Exhibit 5.1)
24.1	Power of Attorney (included on the signature page to this Registration Statement)
99.1	ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed June 26, 2012)
99.2	Form of Restricted Stock Agreement Granted Under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K filed June 26, 2012)
99.3	Form of Option Agreement Granted Under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the registrant's Current Report on Form 8-K filed June 26, 2012)

Item 9. Undertakings

1. The undersigned registrant hereby undertakes:

(a) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement.

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(i) and (a)(ii) do not apply if the registration statement is on Form S-8, and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to section 13 or section 15(d) of the Exchange Act that are incorporated by reference in the registration statement.

(b) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered herein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

2. The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered herein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

3. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Boston, Commonwealth of Massachusetts, as of December 12, 2012.

ZIOPHARM Oncology, Inc.

/s/ Jason A. Amello

Jason A. Amello

Executive Vice President and Chief Financial Officer

POWER OF ATTORNEY AND SIGNATURES

Each person whose signature appears below hereby constitutes and appoints Jonathan Lewis, Jason A. Amello and Caesar Belbel, and each of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ Jonathan Lewis</u> Jonathan Lewis	Director and Chief Executive Officer (Principal Executive Officer)	December 12, 2012
<u>/s/ Jason A. Amello</u> Jason A. Amello	Executive Vice President and Chief Financial Officer (Principal Accounting and Financial Officer)	December 12, 2012
<u>/s/ Murray Brennan</u> Murray Brennan	Director	December 12, 2012
<u>/s/ James Cannon</u> James Cannon	Director	December 12, 2012
<u>/s/ Wyche Fowler, Jr.</u> Wyche Fowler, Jr.	Director	December 12, 2012
<u>/s/ Randal J. Kirk</u> Randal J. Kirk	Director	December 12, 2012
<u>/s/ Timothy McInerney</u> Timothy McInerney	Director	December 12, 2012
<u>/s/ Michael Weiser</u> Michael Weiser	Director	December 12, 2012

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Marc A. Recht
T: +1 617 937 2316
mrecht@cooley.com

December 12, 2012

ZIOPHARM Oncology, Inc.
1180 Avenue of the Americas, 20th Floor
New York, NY 10036

Ladies and Gentlemen:

You have requested our opinion with respect to certain matters in connection with the filing by ZIOPHARM Oncology, Inc., a Delaware corporation (the "**Company**"), of a Registration Statement on Form S-8 (the "**Registration Statement**") with the Securities and Exchange Commission under the Securities Act of 1933, as amended, covering the offering of up to 4,000,000 shares of the Company's common stock, \$0.001 par value per share (the "**Shares**"), pursuant to the Company's 2012 Equity Incentive Plan (the "**Plan**").

In connection with this opinion, we have examined and relied upon the Registration Statement, the Company's Restated Certificate of Incorporation and Amended and Restated By-Laws, each as currently in effect, the Plan, and originals, or copies certified to our satisfaction, of such other documents, records, certificates, memoranda and other instruments as we deemed necessary or appropriate to enable us to render the opinion expressed below. We have assumed the genuineness and authenticity of all documents submitted to us as originals, the conformity to originals of all documents submitted to us as copies thereof, and the due execution and delivery of all documents where due execution and delivery are a prerequisite to the effectiveness thereof. Our opinion is expressed only with respect to the General Corporation Law of the State of Delaware.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares, when issued and sold in accordance with the Plan and the Registration Statement, will be validly issued, fully paid and nonassessable (except as to Shares issued pursuant to certain deferred payment arrangements, which will be fully paid and nonassessable when such deferred payments are made in full).

We consent to the filing of this opinion as an exhibit to the Registration Statement.

Very truly yours,

COOLEY LLP

By: /s/ Marc A. Recht
Marc A. Recht

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in this Registration Statement on Form S-8 filed on December 12, 2012 of ZIOPHARM Oncology, Inc. of our report dated February 29, 2012, relating to our audits of the financial statements and internal control over financial reporting, which appear in the Annual Report on Form 10-K of ZIOPHARM Oncology, Inc. for the year ended December 31, 2011.

/s/ McGladrey LLP

Boston, Massachusetts
December 12, 2012

Consent of Independent Registered Public Accounting Firm

As independent registered public accountants, we hereby consent to the incorporation by reference of the report of Caturano and Company, P.C. (whose name has since been changed to Caturano and Company, Inc.) dated March 17, 2010 relating to the financial statements of ZIOPHARM Oncology, Inc. for the year ended December 31, 2009 and for the period from September 9, 2003 (date of inception) to December 31, 2009, and to all references to our Firm made part of this Registration Statement on Form S-8 filed on December 12, 2012.

/s/ Caturano and Company, Inc.

Boston, Massachusetts
December 12, 2012
