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**Registered
Proposed
Maximum
Offering Price
Per Share (1)
Aggregate
Offering Price (1)
Amount of
Registration Fee**

Common Stock, par value \$.001 per share

750,000

\$5.565

\$4,173,750

\$446.59

(1) Estimated solely for the purpose of determining the registration fee pursuant to Rule 457(c) and (h) and based upon the average low and high sales prices of the Registrant's Common Stock on May 16, 2006, as reported on the OTC bulletin board.

PART I

As permitted by the rules of the Securities and Exchange Commission, this registration statement omits the information specified in Part I of Form S-8. The documents containing the information specified in Part I of this registration statement will be sent or given to eligible employees as specified in Rule 428(b) promulgated under the Securities Act of 1933, as amended (the "Securities Act"). Such documents are not being filed with the Commission either as part of this registration statement or as prospectuses or prospectus supplements pursuant to Rule 424 promulgated under the Securities Act.

PART II

Item 3. Incorporation of Documents by Reference.

The following documents filed by the Registrant with the Securities and Exchange Commission are hereby incorporated by reference herein:

- (a) Annual Report on Form 10-KSB for the fiscal year ended December 31, 2005 filed on March 20, 2006, as amended by Form 10-KSB/A filed on April 12, 2006;
- (a) Quarterly Report on Form 10-QSB for the fiscal quarter ended March 31, 2006 filed on May 15, 2006;
- (b) Current Reports on Form 8-K filed on April 26, 2006 and May 3, 2006; and
- (c) Registration Statement on Form SB-2 filed November 14, 2005 (SEC File No. 333-129680), as amended by Post-effective Amendment No. 1 to Form SB-2 filed April 3, 2006, containing the description of capital stock as set forth in the section entitled "Description of Capital Stock," as such description is amended in the section entitled "Description of Capital Stock" in Prospectus Supplement No. 1 filed April 26, 2006 pursuant to Rule 424(b) promulgated under the Securities Act of 1933, as amended.

All documents subsequently filed by the Registrant pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, 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 in this Registration Statement and to be a part hereof from the date of filing of such documents.

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 Board. 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 the 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 arising by or in the right of the corporation) by reason of the fact that he 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 him in connection with such action, suit or proceeding if he acted in good faith and in a manner he 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 his 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 he 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 his 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 he 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 him in connection with the defense or settlement of such action or suit if he acted in good faith and in a manner he 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 to 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 expense which the Court of Chancery or such other court shall deem proper.

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.

Item 7. Exemption from Registration Claimed.

Not applicable.

Item 8. Exhibits.

<u>Exhibit</u>	<u>Description</u>
4.1	ZIOPHARM Oncology, Inc. 2003 Stock Option Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form SB-2, SEC File No. 333-129020, filed on October 14, 2005)
4.2	Amendment No. 1 to ZIOPHARM Oncology, Inc. 2003 Stock Option Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on April 26, 2006)
5.1	Opinion of Maslon Edelman Borman & Brand, LLP as to the legality of the securities being registered
23.1	Consent of Independent Registered Public Accounting Firm - Vitale, Caturano & Company, Ltd.
23.3	Consent of Maslon Edelman Borman & Brand, LLP (included in Exhibit 5.1)
24.1	Power of Attorney (included on signature page hereof)

Item 9. Undertakings.

(a) The Registrant hereby undertakes:

(1) 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 of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of this 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 this registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and prices represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective 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)(1)(i) and (a)(1)(ii) do not apply if the Registration Statement is on Form S-3, Form S-8 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the Registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the Registration Statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof; and

(3) 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.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference into this Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 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 of 1933 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 connected 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 of 1933 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 New York and the State of New York, on the 19th day of May, 2006.

ZIOPHARM Oncology, Inc.

By: /s/ Jonathan Lewis

Jonathan Lewis
Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature to this Registration Statement appears below hereby constitutes and appoints Jonathan Lewis as his true and lawful attorney-in-fact and agent, with full power of substitution, to sign on his or her behalf individually and in the capacity stated below and to perform any acts necessary to be done in order to file all amendments to this Registration Statement and any and all instruments or documents filed as part of or in connection with this Registration Statement or the amendments thereto and each of the undersigned does hereby ratify and confirm all that said attorney-in-fact and agent, or his substitutes, shall do or cause to be done by virtue hereof. The undersigned also grants to said attorney-in-fact, full power and authority to do and perform any and all acts necessary or incidental to the performance and execution of the powers herein expressly granted. This Power of Attorney shall remain in effect until revoked in writing by the undersigned.

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:

<u>Name</u>	<u>Title</u>	<u>Date</u>
/s/ Jonathan Lewis Jonathan Lewis	Director and Chief Executive Officer (Principal Executive Officer)	May 19, 2006
/s/ Richard Bagley Richard Bagley	Director, President, Treasurer and Chief Operating Officer (Principal Accounting and Financial Officer)	May 19, 2006
Murray Brennan	Director	May 19, 2006
/s/ James Cannon James Cannon	Director	May 19, 2006
/s/ Timothy McInerney	Director	May 19, 2006

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Timothy McInerney

/s/ Wyche Fowler, Jr.
Wyche Fowler, Jr.

Director

May 19, 2006

/s/ Gary S. Fragin
Gary S. Fragin

Director

May 19, 2006

/s/ Michael Weiser
Michael Weiser

Director

May 19, 2006

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INDEX TO EXHIBITS

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