



**ZIOPHARM Oncology, Inc.**

**7,462,095 Shares  
Common Stock**

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The information contained in this prospectus supplement amends and updates our prospectus dated April 14, 2006 (the "Prospectus"), and should be read in conjunction therewith. Please keep this prospectus supplement with your Prospectus for future reference.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the Prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

The date of this prospectus supplement is April 26, 2006

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## Annual Stockholders Meeting

Pursuant to notice, we held our 2006 annual stockholders' meeting (the "**Annual Meeting**") on April 26, 2006. All proposals brought before the stockholders at the Annual Meeting, as discussed below, were approved by the requisite stockholder vote.

*Election of Directors.* The eight individuals who served as our directors prior to the Annual Meeting, each of whom is identified below, were re-elected to serve as members of the Board, each to hold office until the next annual stockholders' meeting, or until his successor is elected and shall have qualified.

- Jonathan Lewis, M.D., Ph.D.
- Richard E. Bagley
- Murray Brennan, M.D.
- James Cannon
- Senator Wyche Fowler, Jr., J.D.
- Gary S. Fragin
- Timothy McInerney
- Michael Weiser, M.D., Ph.D.

*Adoption of Amended and Restated Certificate of Incorporation.* Our stockholders approved the adoption of an Amended and Restated Certificate of Incorporation. See "Description of Capital Stock."

*Adoption of Amendment to 2003 Stock Option Plan.* Our stockholders approved the adoption of an amendment to our 2003 Stock Option Plan (the "**2003 Plan**") that increases the number of shares of common stock available for issuance under the 2003 Plan from 1,252,436 shares to 2,002,436 shares. See "Securities Authorized for Issuance under Equity Compensation Plans."

*Ratification of Independent Accountants.* Our stockholders ratified the appointment of Vitale, Caturano & Company, Ltd. as our independent registered public accounting firm for fiscal 2006.

## Description of Capital Stock

At the Annual Meeting, our stockholders approved the adoption of an Amended and Restated Certificate of Incorporation for the Company, which Amended and Restated Certificate of Incorporation was filed with the Delaware Secretary of State on April 26, 2006. The following is a description of our capital stock and the material provisions of our Amended and Restated Certificate of Incorporation, bylaws and other agreements to which we and our stockholders are parties, in each case upon the date of this prospectus supplement. The following is only a summary and is qualified by applicable law and by the provisions of our Amended and Restated Certificate of Incorporation, bylaws and other agreements.

### Common Stock

The Company's authorized capital stock currently consists of 280,000,000 shares, comprised of 250,000,000 shares of common stock, par value \$.001 per share, and 30,000,000 shares of preferred stock, par value \$.001 per share. We have an aggregate of 7,272,992 shares of common stock issued and outstanding and no shares of preferred stock issued and outstanding. Each such outstanding share of our common stock is validly issued, fully paid and non-assessable.

*Voting.* The holders of our common stock are entitled to one vote for each outstanding share of common stock owned by that stockholder on every matter properly submitted to the stockholders for their vote. Stockholders are not entitled to vote cumulatively for the election of directors.

*Dividend Rights.* Holders of the Company's common stock are entitled to receive ratably dividends and other distributions of cash or any other right or property as may be declared by the Board of Directors out of our assets or funds legally available for such dividends or distributions. The dividend rights of holders of common stock are subject to the dividend rights of the holders of any series of preferred stock that may be issued and outstanding from time to time.

*Liquidation Rights.* In the event of any voluntary or involuntary liquidation, dissolution or winding up of our affairs, holders of our common stock would be entitled to share ratably in our assets that are legally available for distribution to stockholders after payment of liabilities. If we have any preferred stock outstanding at such time, the holders of such preferred stock may be entitled to distribution and/or liquidation preferences that require us to pay the applicable distribution to the holders of our preferred stock before paying distributions to the holders of common stock.

*Conversion, Redemption and Preemptive Rights.* Holders of our common stock have no conversion, redemption, preemptive, subscription or similar rights.

### **Preferred Stock**

Under our Amended and Restated Certificate of Incorporation, our Board of Directors is authorized, subject to limitations prescribed by law, to issue up to 30,000,000 shares of preferred stock in one or more series without further stockholder approval. The Board of Directors has discretion to determine the rights, preferences, privileges and restrictions of, including, without limitation, voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences of, and to fix the number of shares of, each series of our preferred stock. Upon the date of this prospectus supplement, there are no shares of preferred stock outstanding.

### **Limitations on Directors' Liability**

Our Amended and Restated Certificate of Incorporation and bylaws contain provisions indemnifying our directors and officers to the fullest extent permitted by law. In addition, as permitted by Delaware law, our Amended and Restated Certificate of Incorporation provides that no director will be liable to us or our stockholders for monetary damages for breach of certain fiduciary duties as a director. The effect of this provision is to restrict our rights and the rights of our stockholders in derivative suits to recover monetary damages against a director for breach of certain fiduciary duties as a director, except that a director will be personally liable for:

- any breach of his or her duty of loyalty to us or our stockholders;
- acts or omissions not in good faith which involve intentional misconduct or a knowing violation of law;
- the payment of dividends or the redemption or purchase of stock in violation of Delaware law; or
- any transaction from which the director derived an improper personal benefit.

This provision does not affect a director's liability under the federal securities laws.

To the extent that our directors, officers and controlling persons are indemnified under the provisions contained in our Amended and Restated Certificate of Incorporation, Delaware law or contractual arrangements against liabilities arising under the Securities Act, we have 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, as amended, and is therefore unenforceable.

## Provisions that May Have an Anti-Takeover Effect

Certain provisions set forth in our Amended and Restated Certificate of Incorporation, bylaws and in Delaware law, which are summarized below, are intended to enhance the likelihood of continuity and stability in the composition of our Board of Directors and in the policies formulated by our Board of Directors and to discourage certain types of transactions that may involve an actual or threatened change of control. In that regard, these provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they also may inhibit fluctuations in the market price of our common stock that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in our management.

*Blank Check Preferred Stock.* Our Amended and Restated Certificate of Incorporation contains provisions that permit our Board of Directors to issue, without any further vote or action by the stockholders, up to 30,000,000 shares of preferred stock in one or more series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting powers (if any) of the shares of the series, and the preferences and relative, participating, optional and other special rights, if any, and any qualifications, limitations or restrictions, of the shares of such series. As a result, our Board of Directors could authorize the issuance of shares of preferred stock with terms and conditions that could have the effect of delaying, deferring or preventing a transaction or a change in control that might involve a premium price for holders of our common stock or otherwise be in their best interest.

*Special Meetings of Stockholders.* Our bylaws provide that special meetings of stockholders may be called only by the Board of Directors. Stockholders are not permitted to call a special meeting of stockholders or to require that the Board of Directors call such a special meeting.

### *Delaware Takeover Statute*

In general, Section 203 of the Delaware General Corporation Law prohibits a Delaware corporation that is a public company from engaging in any “business combination” (as defined below) with any “interested stockholder” (defined generally as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with such entity or person) for a period of three years following the date that such stockholder became an interested stockholder, unless: (1) prior to such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (2) on consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding those shares owned (x) by persons who are directors and also officers and (y) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or (3) on or subsequent to such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66<sup>2/3</sup>% of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 of the Delaware General Corporation Law defines “business combination” to include: (1) any merger or consolidation involving the corporation and the interested stockholder; (2) any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder; (3) subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; (4) any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or (5) the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

### Stock Option Grants

On the date of the Annual Meeting, the Company made stock option grants of 15,000 shares to each of its non-employee directors. Each such stock option was granted under the 2003 Plan, was vested with respect to all shares on the date of grant and has an exercise price per share equal to \$5.01 (which represents the closing price of the Company’s common stock on the trading day immediately prior to the date of grant). In addition, on the date of the Annual Meeting, the Company granted (i) 214,315 stock options to Jonathan Lewis, Chief Executive Officer, which vest with respect to all shares upon the date of grant; (ii) 94,873 stock options to Richard E. Bagley, President, Chief Operating Officer and Treasurer of the Company, which vest on the date of grant with respect to 74,873 shares and vest on December 14, 2006 with respect to the remaining 20,000 shares; and (iii) 25,000 stock options to Robert Peter Gale, Senior Vice President Research, which vest on the date of grant with respect to 12,500 shares and vest on December 14, 2006 with respect to the remaining 12,500 shares. As with the director grants, each stock option granted to such officers has an exercise price per share equal to \$5.01 (which represents the closing price of the Company’s common stock on the trading day immediately prior to the date of grant).

### Securities Authorized for Issuance under Equity Compensation Plans

The 2003 Plan, which is currently the Company’s only equity compensation plan, was initially approved by the ZIOPHARM, Inc. stockholders. On April 26, 2006, the Company’s stockholders approved the adoption of an amendment to the 2003 Plan that increased the number of shares of common stock available for issuance thereunder from 1,252,436 shares to 2,002,436 shares. The following table sets forth certain information with respect to the 2003 Plan as of April 26, 2006 (following the Annual Meeting and the increase in shares of common stock available for issuance thereunder approve thereat):

Plan category	Number of Securities to be Issued Upon Exercise of Outstanding Options (A)	Weighted-Average Exercise Price of Outstanding Options (B)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (A))
Equity compensation plans approved by security holders:			
2003 Stock Option Plan	1,440,827	\$ 3.35	561,609
<b>Total:</b>	<b>1,440,827</b>	<b>\$ 3.35</b>	<b>561,609</b>
Equity compensation plans not approved by stockholders:			
None.	—	—	—
<b>Total</b>	<b>—</b>	<b>—</b>	<b>—</b>