



**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, as supplemented by Prospectus Supplement No. 1 dated April 26, 2006 (collectively, 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 May 3, 2006

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## Completion of Private Placement - Sale of Common Stock and Warrants

Pursuant to subscription agreements with certain institutional and other accredited investors, on May 3, 2006 we completed the sale of an aggregate of 7,991,256 shares (the "Shares") of our common stock at a price of \$4.63 per share in a private placement. Each investor also received a five-year warrant to purchase, at an exercise price of \$5.56 per share, an additional number of shares of common stock equal to 30 percent of the shares purchased by such investor in the private placement. In the aggregate, these warrants entitle investors to purchase an additional 2,397,392 shares of our common stock. The total gross proceeds resulting from the private placement was approximately \$37 million, before deducting selling commissions and expenses. Following the completion of the private placement, we have 15,264,248 shares of common stock outstanding.

We engaged Paramount BioCapital, Inc. and Griffin Securities, Inc. as co-placement agents in connection with the private placement. In consideration for their services, we paid the co-placement agents, and certain selected dealers engaged by them, aggregate cash commissions of \$2,589,966 and issued 7-year placement agent warrants to purchase an aggregate of 799,126 shares (10 percent of the shares sold in the private placement) at an exercise price of \$5.09 per share. We also agreed to reimburse the co-placement agents for their accountable expenses incurred in connection with the private placement.

Pursuant to the private placement, we agreed to use our best efforts to (i) file a registration statement covering the resale of the shares of common stock sold in the private placement, and the shares of common stock issuable upon exercise of the investor warrants and the placement agent warrants, within 30 days following the closing date of the private placement, and (ii) use our reasonable commercial efforts to cause the registration statement to be effective within 120 days after the closing date.

None of the securities sold and issued in the private placement (including the shares of common stock issuable upon exercise of the investor warrants and placement agent warrants), were registered under the Securities Act of 1933, as amended, and therefore may not be offered or sold in the United States absent registration or an applicable exemption from registration requirements. For these issuances, we relied on the exemption from federal registration under Section 4(2) of the Securities Act and/or Rule 506 promulgated thereunder, based on our belief that the offer and sale of the securities did not involve a public offering as each investor was "accredited" and no general solicitation was involved in the private placement.