



ZIOPHARM Oncology, Inc.

We have filed a registration statement (including a prospectus) and a preliminary prospectus supplement with the Securities and Exchange Commission, or SEC, for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement, the preliminary prospectus supplement and other documents we have filed with the SEC for more complete information about us and this offering. You may get these documents for free by visiting EDGAR on the SEC Web site at www.sec.gov. Alternatively, we or the underwriters for this offering will arrange to send you the prospectus if you request it from Jefferies & Company, Inc., Attention: Syndicate Prospectus Department, 520 Madison Avenue, New York, NY, 10022 or toll free at (888) 449-2342. You may also access the preliminary prospectus supplement by clicking on the following link:

http://www.sec.gov/Archives/edgar/data/1107421/000114420410030506/v186611_424b5.htm

The following information supplements and updates the information contained in the prospectus in the registration statement and the preliminary prospectus supplement.

Issuer	ZIOPHARM Oncology, Inc. (NASDAQ: ZIOP)
Common stock offered by us	<p>7,000,000 shares of common stock. In addition, we have granted the underwriters an option for a period of 30 days to purchase up to an additional 1,050,000 shares of common stock to cover over allotments. Except as otherwise indicated, all information in this issuer free writing prospectus assumes no exercise by the underwriters of their over allotment option.</p> <p>Upon completion of this offering, we will have 48,836,655 shares of common stock outstanding based on the actual number of shares of common stock outstanding as of May 25, 2010, which was 41,836,655, and excludes:</p> <ul style="list-style-type: none">· 3,527,685 shares of our common stock issuable upon the exercise of stock options outstanding as of May 25, 2010, having a weighted average exercise price of \$2.94 per share;· 3,145,484 shares of our common stock available as of May 25, 2010 for future issuance pursuant to our 2003 Stock Option Plan, and 3,000,000 additional shares of our common stock that will be reserved for issuance pursuant to our 2003 Stock Option Plan if a proposed amendment to our 2003 Stock Option Plan is approved by our stockholders at our annual stockholders' meeting schedule for June 23, 2010; and· 15,931,642 shares of our common stock issuable upon the exercise of outstanding warrants as of May 25, 2010 with a weighted-average exercise price of \$4.11 per share.
Public offering price	\$5.00 per share.
Net proceeds to us	We estimate that the net proceeds from the sale of the 7,000,000 shares of common stock that we are offering will be approximately \$32.8 million, or approximately \$ 37.7 million if the underwriters exercise in full their option to purchase 1,050,000 additional shares of common stock, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.
Pricing date	May 27, 2010
Closing date	June 2, 2010

Dilution

Our net tangible book value as of March 31, 2010 was approximately \$11.4 million, or \$0.27 per share. After giving effect to the sale of 7,000,000 shares of our common stock in this offering at the public offering price of \$5.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2010 would have been approximately \$44.2 million, or \$0.91 per share. This represents an immediate increase in net tangible book value of \$0.64 per share to existing stockholders and immediate dilution in net tangible book value of \$4.09 per share to investors purchasing our common stock in this offering at the public offering price.

If the underwriters exercise in full their option to purchase 1,050,000 additional shares of common stock at the public offering price of \$5.00 per share, the as adjusted net tangible book value after this offering would be \$0.99 per share, representing an increase in net tangible book value of \$0.72 per share to existing stockholders and immediate dilution in net tangible book value of \$4.01 per share to investors purchasing our common stock in this offering at the public offering price.

The above discussion is based on 41,710,778 shares outstanding as of March 31, 2010, and excludes:

- 3,569,352 shares of our common stock issuable upon the exercise of outstanding stock options as of March 31, 2010, including those issued under our 2003 Stock Option Plan, having a weighted average exercise price of \$2.90 per share;
- 196,734 shares of our common stock reserved for future issuance as of March 31, 2010 under our 2003 Stock Option Plan, and 3,000,000 additional shares of our common stock that will be reserved for issuance under our 2003 Stock Option Plan if a proposed amendment to our 2003 Stock Option Plan is approved by our stockholders at our annual stockholders' meeting schedule for June 23, 2010; and
- 16,011,588 shares of our common stock issuable upon the exercise of outstanding warrants as of March 31, 2010 with a weighted-average exercise price of \$4.11 per share.

Sole book-running manager

Jefferies & Company

Co-managerJMP Securities
