

Prospectus Supplement No. 2  
(To Prospectus dated October 6, 2009)



**ZIOPHARM Oncology**

# **ZIOPHARM Oncology, Inc.**

**5,683,291 Shares**

**Common Stock**

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This prospectus supplement (this “Supplement”) supplements and amends the prospectus dated October 6, 2009 (the “Prospectus”), relating to the sale of up to 5,683,291 shares of our common stock by the selling stockholders named in the Prospectus or their donees, pledgees, transferees or other successors in interest, including 2,772,337 shares issued to investors in a private placement transaction that we completed on September 15, 2009 (the “September 2009 Private Placement”) and 2,910,954 additional shares issuable upon the exercise of warrants that were issued to investors and placement agents in the September 2009 Private Placement. This Supplement does not relate to our issuance of additional shares of common stock beyond the 5,683,291 originally covered by the Prospectus.

This Supplement should be read in conjunction with, and may not be delivered or utilized without, the Prospectus, which is to be delivered with this Supplement. This Supplement is qualified by reference to the Prospectus, except to the extent that the information in this Supplement updates and supersedes the information contained in the Prospectus.

Our common stock trades on the NASDAQ Capital Market under the symbol “ZIOP.” The last reported sale price of our common stock on November 25, 2014 was \$4.09 per share. You are urged to obtain current market quotations for the common stock.

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**Investing in our common stock involves risks.  
See “Risk Factors” beginning on page 5 of the Prospectus.**

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

**The date of this prospectus supplement is November 26, 2014.**

## SELLING STOCKHOLDERS

The information in the table appearing under the caption “Selling Stockholders” commencing on page 18 of the Prospectus is hereby supplemented and amended by adding the information below with respect to selling stockholders not previously listed in the Prospectus, and by superseding the information with respect to the selling stockholders identified below that were previously listed in the Prospectus with the information below.

**This information has been updated only to reflect the assignment by Kingsbrook Opportunities Master Fund LP to Iroquois Master Fund, Ltd. of a warrant to purchase 54,795 shares of our common stock.**

We have prepared the table below based on information provided to us by or on behalf of the selling stockholders on or prior to November 21, 2014. Since the date on which we were provided with the information regarding their security ownership in ZIOPHARM Oncology, Inc., selling stockholders may have acquired, sold, transferred or otherwise disposed of all or a portion of their securities. Accordingly, the information provided herein for any particular selling stockholder may understate or overstate, as the case may be, such stockholder’s current ownership.

Selling Stockholder	Shares Beneficially Owned Before Offering(1)	Total Shares Offered by Selling Stockholder(2)	Shares Beneficially Owned After Offering(3)	Percentage of Beneficial Ownership After Offering(3)
Kingsbrook Opportunities Master Fund LP(a)	54,795(4)	54,795	—	—
Iroquois Master Fund, Ltd.(b)	54,795(4)	54,795	—	—

- (1) Beneficial ownership is determined in accordance with Securities and Exchange Commission rules. Beneficial ownership includes any shares as to which the security or stockholder has sole or shared voting power or investment power, and also any shares which the security or stockholder has the right to acquire within 60 days of the date hereof, whether through the exercise or conversion of any stock option, convertible security, warrant or other right. The indication herein that shares are beneficially owned is not an admission on the part of the security or stockholder that he, she or it is a direct or indirect beneficial owner of those shares.
  - (2) Includes outstanding shares of common stock, including shares of common stock issued upon the exercise of warrants previously held by the selling stockholder.
  - (3) Assumes that the selling stockholder sells all of the shares offered by this prospectus that are beneficially owned by such selling stockholder and that prior to the sale of such shares the selling stockholder does not acquire additional shares or dispose of shares beneficially owned by the stockholder that are not being offered pursuant to this prospectus.
  - (4) Represents shares issued upon the exercise of warrants previously held by the selling stockholder.
- (a) Kingsbrook Partners LP (“Kingsbrook Partners”) is the investment manager of Kingsbrook Opportunities Master Fund LP (“Kingsbrook Opportunities”) and consequently has voting control and investment discretion over securities held by Kingsbrook Opportunities. Kingsbrook Opportunities GP LLC (“Opportunities GP”) is the general partner of Kingsbrook Opportunities and may be considered the beneficial owner of any securities deemed to be beneficially owned by Kingsbrook Opportunities. KB GP LLC (“GP LLC”) is the general partner of Kingsbrook Partners and may be considered the beneficial owner of any securities deemed to be beneficially owned by Kingsbrook Partners. Ari J. Storch, Adam J. Chill and Scott M. Wallace are the sole managing members of Opportunities GP and GP LLC and as a result may be considered beneficial owners of any securities deemed beneficially owned by Opportunities GP and GP LLC. Each of Kingsbrook Partners, Opportunities GP, GP LLC and Messrs. Storch, Chill and Wallace disclaim beneficial ownership of these securities.
  - (b) Iroquois Capital Management, LLC (“Iroquois”), as the investment adviser of Iroquois Master Fund Ltd. (“Iroquois Master Fund”), may be deemed to beneficially own the shares beneficially owned by Iroquois Master Fund. Joshua Silverman, as a managing member of Iroquois, the investment adviser of Iroquois Master Fund, may be deemed to beneficially own the shares beneficially owned by Iroquois Master Fund.