

Prospectus Supplement No. 1
(To Prospectus dated October 6, 2009)



ZIOPHARM Oncology

ZIOPHARM Oncology, Inc.

5,683,291 Shares

Common Stock

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."

**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 February 2, 2012.

SELLING STOCKHOLDERS

The information in the table appearing under the caption “Selling Stockholders” commencing on page S-1 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 Brookline Ziopharm Investment Fund, LLC to various assignees of a warrant to purchase 931,506 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 February 1, 2012. 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⁾
Brookline Ziopharm Investment Fund, LLC ^(a)	931,506	931,506	0	0%
Lyle Beasley Living Trust U/A DTD 07/01/08 ^(b)	49,315 ⁽⁴⁾	49,315	—	—
Suzanne Brandt	12,329 ⁽⁴⁾	12,329	—	—
Brookline Investments, Inc. ^(c)	12,329 ⁽⁴⁾	12,329	—	—
James E. Cantrell, Jr.	61,644 ⁽⁴⁾	61,644	—	—
Percy V. Crocker, Jr.	12,329 ⁽⁴⁾	12,329	—	—
Martha C. Davis	12,329 ⁽⁴⁾	12,329	—	—
Marjorie E. Davis	12,329 ⁽⁴⁾	12,329	—	—
Hartwell Davis, Jr.	147,945 ⁽⁴⁾	147,945	—	—
Robert P. Dickinson	12,329 ⁽⁴⁾	12,329	—	—
Lewis Jeffers Fowlkes	24,658 ⁽⁴⁾	24,658	—	—
Hollis N. Geiger, Jr.	12,329 ⁽⁴⁾	12,329	—	—
Brenda M. Hackney	24,658 ⁽⁴⁾	24,658	—	—
Hackney One Investments LLC ^(d)	24,658 ⁽⁴⁾	24,658	—	—
Jimmie H. Harvey, Jr.	24,658 ⁽⁴⁾	24,658	—	—
Birmingham Hematology & Oncology Assoc 401K FBO Dr. Jimmie H. Harvey, Jr.	24,658 ⁽⁴⁾	24,658	—	—
Charles Hartman King	12,329 ⁽⁴⁾	12,329	—	—
Matthew A. King	12,329 ⁽⁴⁾	12,329	—	—
Etrade C/F Madding King IRA	24,658 ⁽⁴⁾	24,658	—	—
Thomas A. Lambert III	12,329 ⁽⁴⁾	12,329	—	—
William A. Legg, Jr.	24,658 ⁽⁴⁾	24,658	—	—
Sam J. Lewis, Jr.	12,329 ⁽⁴⁾	12,329	—	—
W. Charles Mayer, III	12,329 ⁽⁴⁾	12,329	—	—
Sterne, Agree & Leach C/F J. Findley McRae IRA	24,658 ⁽⁴⁾	24,658	—	—
Daryoush Mortazavi	12,329 ⁽⁴⁾	12,329	—	—
Alastair Muir-Taylor	12,329 ⁽⁴⁾	12,329	—	—
Robert O. Rolfe	49,315	49,315	—	—
Knight Sauls	12,329 ⁽⁴⁾	12,329	—	—
R. Mark Saviers	12,329 ⁽⁴⁾	12,329	—	—
Scott Sink	12,329 ⁽⁴⁾	12,329	—	—

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⁾
SPECTRE, LLC ^(e)	24,658 ⁽⁴⁾	24,658	—	—
MCT Investments LLC ^(f)	49,315 ⁽⁴⁾	49,315	—	—
John Williams	24,658 ⁽⁴⁾	24,658	—	—
Paul Woodall	12,329 ⁽⁴⁾	12,329	—	—
Erich W. Wouters	12,329 ⁽⁴⁾	12,329	—	—
Brookline Financial Partners, Inc. ^(g)	46,566 ⁽⁴⁾	46,566	—	—
Jimmie H. Harvey, Jr.	18,630 ⁽⁴⁾	18,630	—	—
James E. Cantrell, Jr.	18,630 ⁽⁴⁾	18,630	—	—
Madding King III	9,315 ⁽⁴⁾	9,315	—	—

- (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 and, if applicable, shares of common stock issuable upon the exercise of warrants 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 issuable upon the exercise of warrants.
- (a) Madding King has voting and investment control over the shares held by the selling stockholder.
- (b) Lyle Beasley and Lisa G. Beasley, as trustees, share voting and investment control over the shares held by the selling stockholder.
- (c) J. Rainer Twiford and Hollis N. Geiger, Jr. share voting and investment control over the shares held by the selling stockholder.
- (d) Brenda M. Hackney and T. Morris Hackney, as managing members, share voting and investment control over the shares held by the selling stockholder.
- (e) Madding King and Hartman King, as managing members, share voting and investment control over the shares held by the selling stockholder.
- (f) Marsha C. Twiford has voting and investment control over the shares held by the selling stockholder.
- (g) J. Rainer Twiford and Hollis N. Geiger, Jr. share voting and investment control over the shares held by the selling stockholder.