

---

---

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

---

**Form S-8**  
**REGISTRATION STATEMENT**  
*UNDER*  
**THE SECURITIES ACT OF 1933**

---

**ZIOPHARM Oncology, Inc.**  
(Exact name of registrant as specified in its charter)

---

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**84-1475642**  
(I.R.S. Employer  
Identification No.)

**One First Avenue  
Parris Building 34  
Navy Yard Plaza  
Boston, Massachusetts**  
(Address of principal executive offices)

**02129**  
(Zip Code)

**ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan**  
(Full title of the plan)

---

**Robert Hadfield**  
**General Counsel and Secretary**  
**ZIOPHARM Oncology, Inc.**  
**One First Avenue, Parris Building 34, Navy Yard Plaza**  
**Boston, Massachusetts 02129**  
**(617) 259-1970**  
(Name, address and telephone number,  
including area code, of agent for service)

*With a copy to:*

**Marc A. Recht**  
**Josh Rottner**  
**Courtney T. Thorne**  
**Cooley LLP**  
**500 Boylston Street, 14th Floor**  
**Boston, Massachusetts 02116**  
**(617) 937-2300**

---

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large Accelerated filer   
Non-accelerated filer

Accelerated filer   
Smaller reporting company   
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

---

**CALCULATION OF REGISTRATION FEE**

<b>Title of securities to be registered</b>	<b>Amount to be registered<sup>(1)(2)</sup></b>	<b>Proposed maximum offering price per share</b>	<b>Proposed maximum aggregate offering price</b>	<b>Amount of registration fee</b>
Common stock, par value \$0.001 per share	5,000,000 shares	\$2.34 <sup>(3)</sup>	\$11,675,000 <sup>(3)</sup>	\$1,415.01

- (1) In accordance with Rule 416 under the Securities Act of 1933, as amended, this registration statement shall be deemed to cover any additional securities that may from time to time be offered or issued to prevent dilution resulting from stock splits, stock dividends or similar transactions.
- (2) This registration statement registers an additional 5,000,000 shares issuable under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (the "2012 Plan"). These 5,000,000 shares represent an increase in the number of shares of common stock reserved for issuance under the 2012 Plan, which increase was approved by the registrant's stockholders on September 18, 2018 at the registrant's 2018 Annual Meeting of Stockholders. We have previously registered 9,000,000 shares issuable on under the 2012 Plan on our Registration Statements on Form S-8 (File Nos. 333-185433 and 333-199304) as filed with the Securities and Exchange Commission on December 12, 2012 and October 14, 2014.
- (3) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and (h) under the Securities Act of 1933, as amended, and based upon the average of the high and low prices of the registrant's common stock as reported on the Nasdaq Capital Market on November 5, 2018.
- 
-

---

**EXPLANATORY NOTE; INCORPORATION BY REFERENCE OF CONTENTS OF  
REGISTRATION STATEMENTS ON FORM S-8 (File NOs. 333-185433, 333-199304)**

This Registration Statement is being filed by ZIOPHARM Oncology, Inc. (the “registrant”) for the purpose of registering additional securities of the same class as other securities for which registration statements filed on Form S-8 relating to the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (the “2012 Plan”) are already effective. Pursuant to Instruction E to Form S-8, we incorporate by reference into this Registration Statement the contents of (i) the registration statement that we filed on Form S-8 (File No. 333-185433) with the Securities and Exchange Commission on December 12, 2012 in its entirety and including exhibits thereto, relating to the registration of 4,000,000 shares of our common stock, par value \$0.001 per share, authorized for issuance under the 2012 Plan, and (ii) the registration statement that we filed on Form S-8 (File No. 333-199304) with the Securities and Exchange Commission on October 14, 2014 in its entirety and including exhibits thereto, relating to the registration of an additional 5,000,000 shares of our common stock, par value \$0.001 per share, authorized for issuance under the 2012 Plan. This Registration Statement provides for the registration of an additional 5,000,000 shares of common stock to be issued under the 2012 Plan. These 5,000,000 shares represent an increase in the number of shares of common stock reserved for issuance under the 2012 Plan, which increase was approved by the registrant’s stockholders on September 18, 2018 at the registrant’s 2018 Annual Meeting of Stockholders.

---

## EXHIBITS

<u>Exhibit No.</u>	<u>Description of Document</u>
4.1	<a href="#"><u>Amended and Restated Certificate of Incorporation, as filed with the Delaware Secretary of State on April 26, 2006 (incorporated by reference to Exhibit 3.1 to the registrant's Current Report on Form 8-K (SEC File No. 000-32353) filed April 26, 2006).</u></a>
4.2	<a href="#"><u>Bylaws, as amended to date (incorporated by reference to Exhibit 3.3 to the registrant's Current Report on Form 8-K (SEC File No. 000-32353) filed September 19, 2005).</u></a>
4.3	<a href="#"><u>Specimen common stock certificate (incorporated by reference to Exhibit 4.1 to the registrant's Registration Statement on Form SB-2 (SEC File No. 333-129020) filed October 14, 2005).</u></a>
5.1	<a href="#"><u>Opinion of Cooley LLP.</u></a>
23.1	<a href="#"><u>Consent of RSM US LLP.</u></a>
23.2	<a href="#"><u>Consent of Cooley LLP (included as part of Exhibit 5.1 and incorporated herein by reference).</u></a>
24.1	<a href="#"><u>Power of Attorney (included on the signature page to this Registration Statement).</u></a>
99.1	<a href="#"><u>ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K (SEC File No. 001-33038) filed September 24, 2018).</u></a>
99.2	<a href="#"><u>Form of Restricted Stock Agreement Granted Under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K (SEC File No. 001-33038) filed June 26, 2012).</u></a>
99.3	<a href="#"><u>Form of Option Agreement Granted Under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the registrant's Current Report on Form 8-K (SEC File No. 001-33038) filed June 26, 2012).</u></a>





Marc A. Recht  
T: +1 617 937 2316  
mrecht@cooley.com

November 9, 2018

ZIOPHARM Oncology, Inc.  
One First Avenue, Parris Building 34, Navy Yard Plaza  
Boston, Massachusetts 02129

Ladies and Gentlemen:

You have requested our opinion with respect to certain matters in connection with the filing by ZIOPHARM Oncology, Inc., a Delaware corporation (the "**Company**"), of a Registration Statement on Form S-8 (the "**Registration Statement**") with the Securities and Exchange Commission under the Securities Act of 1933, as amended, covering the offering of up to 5,000,000 shares of the Company's common stock, \$0.001 par value per share (the "**Shares**"), pursuant to the Company's 2012 Equity Incentive Plan (the "**Plan**").

In connection with this opinion, we have examined and relied upon the Registration Statement and related prospectus, the Company's Restated Certificate of Incorporation and Amended and Restated By-Laws, each as currently in effect, the Plan, and originals, or copies certified to our satisfaction, of such other documents, records, certificates, memoranda and other instruments as we deemed necessary or appropriate to enable us to render the opinion expressed below. We have assumed the genuineness and authenticity of all documents submitted to us as originals, the conformity to originals of all documents submitted to us as copies thereof, and the due execution and delivery of all documents where due execution and delivery are a prerequisite to the effectiveness thereof. As to certain factual matters, we have relied upon a certificate of an officer of the Company and have not sought independently to verify such matters.

Our opinion is expressed only with respect to the General Corporation Law of the State of Delaware. We express no opinion to the extent that any other laws are applicable to the subject matter hereof and express no opinion and provide no assurance as to compliance with any federal or state securities law, rule or regulation.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares, when issued and sold in accordance with the Plan, the Registration Statement and the related prospectus, will be validly issued, fully paid and nonassessable (except as to Shares issued pursuant to certain deferred payment arrangements, which will be fully paid and nonassessable when such deferred payments are made in full).

We consent to the filing of this opinion as an exhibit to the Registration Statement.

Very truly yours,

COOLEY LLP

By: /s/ Marc A. Recht  
Marc A. Recht

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in the Registration Statement on Form S-8 of ZIOPHARM Oncology, Inc. of our report dated March 1, 2018, relating to the financial statements and the effectiveness of internal control over financial reporting of ZIOPHARM Oncology, Inc., appearing in the Annual Report on Form 10-K of ZIOPHARM Oncology, Inc. for the year ended December 31, 2017.

/s/ RSM US LLP

Boston, Massachusetts  
November 9, 2018