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

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**FORM S-3**  
**REGISTRATION STATEMENT**  
*UNDER*  
*THE SECURITIES ACT OF 1933*

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**ZIOPHARM ONCOLOGY, INC.**  
(Exact name of registrant as specified in its charter)

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

**84-1475642**  
(I.R.S. Employer  
Identification Number)

**One First Avenue, Parris Building 34, Navy Yard Plaza  
Boston, Massachusetts 02129  
(617) 259-1970**

(Address, including zip code, and telephone number, including area code of registrant's principal executive offices)

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**Laurence J.N. Cooper, M.D., Ph.D.**  
**Chief Executive Officer**  
**ZIOPHARM Oncology, Inc.**

**One First Avenue, Parris Building 34, Navy Yard Plaza  
Boston, Massachusetts 02129  
(617) 259-1970**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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*Copies to:*

**Robert Hadfield**  
**General Counsel**  
**ZIOPHARM Oncology, Inc.**  
**One First Avenue, Parris Building 34, Navy Yard Plaza**  
**Boston, Massachusetts 02129**  
**(617) 259-1970**

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

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**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this registration statement.

[Table of Contents](#)

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 Securities Act.

**CALCULATION OF REGISTRATION FEE**

Title of each class of securities to be registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Unit(2)	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee
Common Stock, par value \$0.001 per share	37,878,788	\$2.15	\$81,439,394.20	\$9,870.45

- (1) Includes 18,939,394 shares of common stock that may be issued upon the exercise of outstanding warrants. Pursuant to Rule 416 under the Securities Act of 1933, as amended, the shares of common stock being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares of common stock being registered hereunder as a result of stock splits, stock dividends or similar transactions.
- (2) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457 promulgated under the Securities Act. The offering price per share and the aggregate offering price are based upon the average of the high and low prices of the Registrant’s common stock as reported on the Nasdaq Capital Market on February 4, 2019.

**The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

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[Table of Contents](#)

The information in this prospectus is not complete and may be changed. The selling stockholders may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state where such offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED FEBRUARY 7, 2019

PROSPECTUS



**ZIOPHARM Oncology, Inc.**

**37,878,788 Shares**

**Common Stock**

This prospectus relates to the disposition from time to time of up to 37,878,788 shares of our common stock, which includes 18,939,394 shares of our common stock issuable upon the exercise of outstanding warrants, which are held by the selling stockholders named in this prospectus. We are not selling any common stock under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholders. We will, however, receive the net proceeds of any warrants exercised for cash.

The selling stockholders identified in this prospectus, or their permitted transferees or other successors-in-interest that may be identified in a supplement to this prospectus or, if required, a post-effective amendment to the registration statement of which this prospectus is a part, may offer the shares from time to time through public or private transactions at fixed prices, at prevailing market prices, at varying prices determined at the time of sale, or at privately negotiated prices. We provide more information about how the selling stockholders may sell their shares of common stock in the section titled “Plan of Distribution” beginning on page 11 of this prospectus. We have agreed to pay certain expenses incurred in connection with the registration of these shares, however, we will not be paying any underwriting discounts or commissions in connection with any offering of shares of common stock under this prospectus.

Our common stock is traded on the Nasdaq Capital Market under the symbol “ZIOP.” On February 6, 2019, the last reported sales price of our common stock was \$2.32 per share.

*Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties we have described under the heading “[Risk Factors](#)” on page 3 of this prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, including those filed after the date hereof.*

**NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.**

The date of this prospectus is \_\_\_\_\_, 2019.

**TABLE OF CONTENTS**

<a href="#">ABOUT THIS PROSPECTUS</a>	i
<a href="#">PROSPECTUS SUMMARY</a>	1
<a href="#">RISK FACTORS</a>	3
<a href="#">SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</a>	4
<a href="#">USE OF PROCEEDS</a>	6
<a href="#">SELLING STOCKHOLDERS</a>	7
<a href="#">PLAN OF DISTRIBUTION</a>	11
<a href="#">LEGAL MATTERS</a>	13
<a href="#">EXPERTS</a>	13
<a href="#">WHERE YOU CAN FIND MORE INFORMATION</a>	13
<a href="#">INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</a>	14

## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under this shelf registration process, the selling stockholders may from time to time, in one or more offerings, sell the common stock described in this prospectus.

We have not authorized anyone to provide you with information other than the information contained in or incorporated by reference into this prospectus (as supplemented or amended). This document may only be used where it is legal to sell these securities. The information contained in this prospectus (and in any supplement or amendment to this prospectus) is accurate only as of the date on the front of the document, and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates.

We urge you to read carefully this prospectus (as supplemented and amended), together with the information incorporated herein by reference as described under the heading “Incorporation of Certain Information by Reference” before deciding whether to invest in any of the common stock being offered.

This prospectus incorporates by reference market data, industry statistics and other data that have been obtained from, or compiled from, information made available by third parties. We have not independently verified their data. This prospectus and the information incorporated herein by reference includes trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus are the property of their respective owners.

## PROSPECTUS SUMMARY

*This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus (as supplemented and amended), including the financial data and related notes, risk factors and other information incorporated by reference in this prospectus before making an investment decision.*

*Unless the context indicates otherwise, as used in this prospectus, the terms “Ziopharm,” “the Company,” “we,” “us” and “our” refer to Ziopharm Oncology, Inc., a Delaware corporation. This prospectus or information incorporated by reference in this prospectus contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to or incorporated by reference in this prospectus, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies’ trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.*

### About Ziopharm Oncology

We are a biopharmaceutical company focused on discovering, acquiring, developing and commercializing next generation immunotherapy platforms that leverage gene- and cell-based therapies to treat patients with cancer. We are developing two immuno-oncology platform technologies designed to utilize the patient’s immune system by employing novel, controlled gene expression and innovative cell engineering technologies to deliver safe, effective, and scalable cell- and viral-based therapies for the treatment of multiple cancer types. Our first platform is Controlled IL-12, which is designed to deliver interleukin 12 or IL-12, a master regulator of the immune system, in a controlled and safe manner to focus the patient’s immune system to cancer. Our second platform is referred to as *Sleeping Beauty* and is based on the genetic engineering of immune cells using the *Sleeping Beauty* system to rapidly reprogram T cells outside of the body for subsequent infusion. We believe these two platforms provide or will provide unique and powerful solutions intended to advance the field of immuno-oncology and address the issues associated with (1) treating heterogenous solid tumors and unknown antigens therein through control of IL-12 and (2) providing rapid and cost-effective manufacturing solutions for CAR and TCR-based cell therapies for hematologic malignancies and solid tumors against known antigens.

We are developing a gene therapy that delivers Controlled IL-12 to treat patients with solid tumors including brain cancer. Based on technology licensed from MD Anderson Cancer Center, we are developing CAR T-cell or CAR+ T targeting CD19, and T-cell receptor T-cell, or TCR+ T, therapies. These programs are being advanced in collaboration with MD Anderson and the National Cancer Institute, or NCI.

### Corporate Information

We originally incorporated in Colorado in September 1998 (under the name Net Escapes, Inc.) and later changed our name to “EasyWeb, Inc.” in February 1999. We re-incorporated in Delaware on May 16, 2005 under the same name. On September 13, 2005, we completed a “reverse” acquisition of privately held Ziopharm, Inc., a Delaware corporation. To affect this transaction, we caused ZIO Acquisition Corp., our wholly-owned subsidiary, to merge with and into Ziopharm, Inc., with Ziopharm, Inc. surviving as our wholly owned subsidiary. In accordance with the terms of the merger, the outstanding common stock of Ziopharm, Inc. automatically converted into the right to receive an aggregate of approximately 97.3% of our outstanding common stock (after giving effect to the transaction). Following the merger, we caused Ziopharm, Inc. to merge

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[Table of Contents](#)

with and into us and we changed our name to “Ziopharm Oncology, Inc.” Although EasyWeb, Inc. was the legal acquirer in the transaction, we accounted for the transaction as a reverse acquisition under generally accepted accounting principles. As a result, Ziopharm, Inc. became the registrant with the Securities and Exchange Commission, or the SEC, and the historical financial statements of Ziopharm, Inc. became our historical financial statements.

Our principal executive offices are located at One First Avenue, Parris Building 34, Navy Yard Plaza, Boston, Massachusetts 02129, and our telephone number is (617) 259-1970.

### **The Offering**

The selling stockholders named in this prospectus may offer and sell up to 37,878,788 shares of our common stock, which includes 18,939,394 shares of our common stock issuable upon the exercise of outstanding warrants. The shares issuable upon exercise of the warrants will become eligible for sale by the selling stockholders under this prospectus only as the warrants are exercised. Our common stock is currently listed on the Nasdaq Capital Market under the symbol “ZIOP.” Shares of common stock that may be offered under this prospectus, when issued and paid for in the case of shares issuable upon exercise of the outstanding warrants, will be fully paid and non-assessable. We will not receive any of the proceeds of sales by the selling stockholders of any of the common stock covered by this prospectus. Throughout this prospectus, when we refer to the shares of our common stock being registered on behalf of the selling stockholders, we are referring to the shares and the shares underlying the warrants issued to the selling stockholders pursuant to the securities purchase agreement we entered into with the selling stockholders on November 11, 2018, and when we refer to the selling stockholders in this prospectus, we are referring to the purchasers under the securities purchase agreement and, as applicable, their permitted transferees or other successors-in-interest that may be identified in a supplement to this prospectus or, if required, a post-effective amendment to the registration statement of which this prospectus is a part.

## **RISK FACTORS**

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading “Risk Factors” contained in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018 filed with the SEC on November 9, 2018, as updated by our subsequent annual, quarterly and other reports and documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled “Special Note Regarding Forward-Looking Statements.”



## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements are based on our management's beliefs and assumptions and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the sections titled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. All statements, other than statements of historical facts, are forward-looking statements for purposes of these provisions, including, without limitation, any statements relating to:

- our ability to raise substantial additional capital to fund our planned operations in the near term and to continue as a going concern;
- our estimates regarding expenses, use of cash, timing of future cash needs and capital requirements;
- the development of our product candidates, including statements regarding the timing of initiation, completion and the outcome of clinical studies or trials and related preparatory work and the period during which the results of the trials will become available;
- our ability to advance our product candidates through various stages of development, especially through pivotal safety and efficacy trials;
- the risk that final trial data may not support interim analysis of the viability of our product candidates;
- our expectation regarding the safety and efficacy of our product candidates, the progress and timing of our research and development programs;
- the timing, scope or likelihood of regulatory filings and approvals from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies for our product candidates and for which indications;
- our ability to license additional intellectual property relating to our product candidates from third parties and to comply with our existing license agreements;
- our ability to achieve the results contemplated by our collaboration agreements and the benefits to be derived from relationships with collaborators;
- developments and projections relating to competition from other pharmaceutical and biotechnology companies or our industry;
- our estimates regarding the potential market opportunity for our product candidates;
- the anticipated rate and degree of market acceptance of our product candidates for any indication if approved;
- the anticipated amount, timing and accounting of contract liability (formerly deferred revenue), milestones and other payments under licensing, collaboration or acquisition agreements, research and development costs and other expenses;
- our intellectual property position, including the strength and enforceability of our intellectual property rights;
- our ability to attract and retain qualified employees and key personnel; and
- the impact of government laws and regulations in the United States and foreign countries.

In some cases, you can identify forward-looking statements by terms such as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "project," "target," "will" and other words and terms

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## [Table of Contents](#)

of similar meaning. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance, time frames or achievements to be materially different from the information expressed or implied by these forward-looking statements. While we believe that we have a reasonable basis for each forward-looking statement, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. We discuss many of these risks, uncertainties and other factors in greater detail under the heading “Risk Factors” contained in our quarterly report on Form 10-Q for the quarter ended September 30, 2018 filed with the SEC on November 9, 2018 and incorporated by reference in this prospectus, as the same may be amended, supplemented or superseded by the risks and uncertainties described under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus, together with the information incorporated herein by reference as described under the heading “Incorporation of Certain Information by Reference,” completely and with the understanding that our actual future results may be materially different from what we expect. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our business, results of operations and financial condition. We hereby qualify all of our forward-looking statements by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

### **USE OF PROCEEDS**

The selling stockholders will receive all of the net proceeds from sales of the common stock pursuant to this prospectus. However, in the case of warrants issued to the selling stockholders pursuant to the securities purchase agreement dated November 11, 2018, upon any exercise of these warrants for cash, the selling stockholders would pay us an exercise price of \$3.01 per share of common stock, subject to any adjustment pursuant to the terms of the warrants. We expect to use any such warrant exercise proceeds primarily for working capital and general corporate purposes. These warrants are also exercisable on a cashless basis by net exercise under certain conditions contained therein. If any of these warrants are exercised on a cashless basis, we would not receive any cash payment from the applicable selling stockholder upon any such cashless exercise of a warrant.

## SELLING STOCKHOLDERS

On November 11, 2018, we entered into a securities purchase agreement with the selling stockholders pursuant to which we issued and sold in a private placement an aggregate of 18,939,394 immediately separable units, comprised of an aggregate of 18,939,394 shares of our common stock and warrants to purchase up to 18,939,394 additional shares of common stock, which warrants we refer to in this prospectus as the 2018 Warrants, for an aggregate purchase price of approximately \$50.0 million. Pursuant to the securities purchase agreement, we agreed to file the registration statement of which this prospectus is a part to cover the resale of the shares of our common stock and the shares underlying the 2018 Warrants, and to keep such registration statement effective with respect to each selling stockholder until the earlier to occur of (i) November 13, 2020 or (ii) the date on which all of the shares of our common stock registered for resale under the registration statement have been disposed of in accordance with such registration statement, disposed of pursuant to Rule 144 under the Securities Act or can be resold pursuant to Rule 144 without restriction or limitation (including without the requirement to be in compliance with Rule 144(c)(1)) or another similar exemption under the Securities Act. The 2018 Warrants, which have a five-year term expiring on November 13, 2023, have a per share exercise price of \$3.01. The exercise price and number of shares of common stock issuable upon exercise of the 2018 Warrants may be adjusted in certain circumstances, including stock splits, stock dividends, reclassifications and the like. The shares issuable upon exercise of the 2018 Warrants will become eligible for sale by the selling stockholders under this prospectus only as the 2018 Warrants are exercised. We cannot predict when or whether any of the selling stockholders will exercise their 2018 Warrants.

We are registering the resale of the above-referenced shares to permit each of the selling stockholders identified below, or their permitted transferees or other successors-in-interest that may be identified in a supplement to this prospectus or, if required, a post-effective amendment to the registration statement of which this prospectus is a part, to resell or otherwise dispose of the shares in the manner contemplated under “Plan of Distribution” in this prospectus (as may be supplemented and amended). This prospectus covers the sale or other disposition by the selling stockholders of up to the total number of shares of common stock issued to the selling stockholders pursuant to the securities purchase agreement, plus the total number of shares of common stock issuable upon exercise of the 2018 Warrants issued to the selling stockholders. Throughout this prospectus, when we refer to the shares of our common stock being registered on behalf of the selling stockholders, we are referring to the shares of our common stock and the shares underlying the 2018 Warrants issued to the selling stockholders pursuant to the securities purchase agreement, and when we refer to the selling stockholders in this prospectus, we are referring to the purchasers under the securities purchase agreement and, as applicable, their permitted transferees or other successors-in-interest that may be identified in a supplement to this prospectus or, if required, a post-effective amendment to the registration statement of which this prospectus is a part.

The selling stockholders may sell some, all or none of their shares. We do not know how long the selling stockholders will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale or other disposition of any of the shares. The shares of our common stock covered hereby may be offered from time to time by the selling stockholders.

The following table sets forth the name of each selling stockholder, the number and percentage of our common stock beneficially owned by the selling stockholders as of December 31, 2018, the number of shares of our common stock that may be offered under this prospectus, and the number and percentage of our common stock beneficially owned by the selling stockholders assuming all of the shares of our common stock registered hereunder are sold. Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our common stock. Generally, a person “beneficially owns” shares of our common stock if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days. The number of shares of our common stock in the column “Number of Shares Offered” represents all of the shares of our common stock that a selling stockholder may offer and sell from time to time under this prospectus.

[Table of Contents](#)

All information contained in the table below and the footnotes thereto is based upon information provided to us by the selling stockholders. The information in the table below and the footnotes thereto regarding shares of common stock to be beneficially owned after the offering assumes that all of the selling stockholders have exercised the 2018 Warrants in full pursuant to cash exercises and further assumes the sale of all shares being offered by the selling stockholders under this prospectus. The percentage of shares owned prior to and after the offering is based on 161,137,689 shares of common stock outstanding as of December 31, 2018 and, with respect to the percentage of shares owned after the offering, on the assumption that all of the selling stockholders have exercised the 2018 Warrants in full pursuant to cash exercises and therefore that all shares of common stock issuable upon exercise of the 2018 Warrants were outstanding as of that date. Unless otherwise indicated in the footnotes to this table, we believe that each of the selling stockholders named in this table has sole voting and investment power with respect to the shares of common stock indicated as beneficially owned. Except as otherwise indicated below, based on the information provided to us by the selling stockholders, none of the selling stockholders is a broker-dealer or an affiliate of a broker-dealer.

Name and Address	Prior to Offering		Number of Shares Offered(2)	After Offering	
	Number of Shares Beneficially Owned(1)	Percentage of Shares Beneficially Owned(1)		Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
<b>MSD Credit Opportunity Master Fund, L.P.</b> 645 Fifth Avenue, 21st Floor New York, New York 10022	16,664,957(3)	9.9	15,151,516	3,410,500	1.9
<b>White Rock Capital Partners, L.P.</b> 3131 Turtle Creek Blvd., Suite 800 Dallas, Texas 75219	12,375,758(4)	7.5	7,575,758	4,800,000	2.7
<b>Miller Opportunity Trust, a series of Trust for Advised Portfolios</b> One South Street, Suite 2550 Baltimore, Maryland 21202	11,380,658(5)	6.9	7,575,758	3,804,900	2.1
<b>Level One Partners, LLC</b> 210 Ridge McIntire Rd., Suite 350 Charlottesville, Virginia 22903	5,795,061(6)	3.6	3,787,880	2,007,181	1.1
<b>Robert W. Postma Roth IRA</b> 141 Mecox Road P.O. Box 207 Water Mill, New York 11976	1,896,352(7)	1.2	1,893,940	2,412	*
<b>WJD Investment Partners LLC</b> 2305 SW 18th Avenue Ft. Lauderdale, Florida 33315	1,515,150(8)	*	1,515,150	—	*
<b>Steven Denstman</b> 5235 Hidden Harbor Road Sarasota, Florida 34242	588,786(9)	*	378,786	210,000	*

\* Less than one percent.

- (1) Under the terms of the 2018 Warrants, the number of shares of our common stock that may be acquired by a selling stockholder upon any exercise of a 2018 Warrant is generally limited to the extent necessary to ensure that, following such exercise, such selling stockholder would not, together with its affiliates and any other persons or entities whose beneficial ownership of our common stock would be aggregated with such selling stockholder for purposes of Section 13(d) of the Exchange Act, beneficially own in excess of 9.99% of the total number of shares of our common stock then issued and outstanding and/or the then combined voting power of all of our voting securities, which we refer to in this prospectus as the Exercise Limitation. The Exercise Limitation (i) may be increased, decreased or terminated, in each selling stockholder's sole discretion, upon at least 61 days' prior notice to us and (ii) terminates automatically on the date that is 15

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## Table of Contents

days prior to the expiration of the 2018 Warrant. If the operation of the Exercise Limitation currently limits the beneficial ownership of a selling stockholder, such limitation is noted in the footnotes that follow. In addition, as noted in footnote (2), the number of shares shown under the column titled “Number of Shares Offered” is shown without regard to the Exercise Limitation.

- (2) The number of shares offered hereby, for each selling stockholder, consists solely of the shares issued to such selling stockholder pursuant to the securities purchase agreement and the shares issuable upon exercise of the 2018 Warrants issued to such selling stockholder. The shares issuable upon exercise of the 2018 Warrants will become eligible for sale by the selling stockholders under this prospectus only as the 2018 Warrants are exercised. In addition, the number of shares offered hereby shown under the column titled “Number of Shares Offered” includes the maximum number of shares issuable upon the exercise of the 2018 Warrants without regard to Exercise Limitation described in footnote (1) above.
- (3) Represents (i) 10,986,258 outstanding shares of common stock and (ii) 5,678,699 shares of common stock issuable upon exercise of 2018 Warrants. The beneficial ownership of 2018 Warrants held by the selling stockholder is currently limited by the Exercise Limitation. MSD Partners, L.P. is the investment manager of, and may be deemed to beneficially own the securities held by, MSD Credit Opportunity Master Fund, L.P. MSD Partners (GP), LLC is the general partner of, and may be deemed to beneficially own the securities beneficially owned by, MSD Partners, L.P. Each of Glenn R. Fuhman, John C. Phelan and Marc R. Lisker is a manager of, and may be deemed to beneficially own the securities beneficially owned by, MSD Partners (GP), LLC.
- (4) Represents (i) 8,587,879 outstanding shares of common stock and (ii) 3,787,879 shares of common stock issuable upon exercise of 2018 Warrants. White Rock Management, L.P. is the general partner of, and may be deemed to beneficially own the securities held by, White Rock Capital Partners, L.P. White Rock Capital (TX), Inc. is the general partner of, and may be deemed to beneficially own the securities beneficially owned by, White Rock Management, L.P. Thomas U. Barton and Joseph U. Barton are the shareholders of, and may be deemed to beneficially own the securities beneficially owned by, White Rock Capital (TX), Inc.
- (5) Represents (i) 7,592,779 outstanding shares of common stock and (ii) 3,787,879 shares of common stock issuable upon exercise of 2018 Warrants. Miller Value Partners, LLC is the investment manager of, and may be deemed to beneficially own the securities held by, Miller Opportunity Trust, a series of Trust for Advised Portfolios. William H. Miller III is the managing member of, and may be deemed to beneficially own the securities beneficially owned by, Miller Value Partners, LLC.
- (6) Represents (i) 3,901,121 outstanding shares of common stock and (ii) 1,893,940 shares of common stock issuable upon exercise of 2018 Warrants. Robert D. Hardie has voting and investment control over, and may be deemed to beneficially own, the securities held by Level One Partners, LLC.
- (7) Represents (i) 949,382 outstanding shares of common stock and (ii) 946,970 shares of common stock issuable upon exercise of 2018 Warrants. Robert W. Postma has voting and investment control over, and may be deemed to beneficially own, the securities held by Robert W. Postma Roth IRA.
- (8) Represents (i) 757,575 outstanding shares of common stock and (ii) 757,575 shares of common stock issuable upon exercise of 2018 Warrants. Donald Kleckner is the manager of, and may be deemed to beneficially own the securities held by, WJD Investment Partners LLC.
- (9) Represents (i) 399,393 outstanding shares of common stock and (ii) 189,393 shares of common stock issuable upon exercise of 2018 Warrants.

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[Table of Contents](#)

**Relationships with the Selling Stockholders**

Neither the selling stockholders nor any of the persons that control them has had any material relationships with us or our affiliates within the past three years.

## PLAN OF DISTRIBUTION

The selling stockholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of common stock previously issued and the shares of common stock issuable upon exercise of the warrants or interests in shares of common stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. The selling stockholders may sell their shares of our common stock pursuant to this prospectus at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock or warrants owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).



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## [Table of Contents](#)

The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our common stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to keep the registration statement of which this prospectus constitutes a part effective until such time as the shares offered by the selling stockholders have been effectively registered under the Securities Act and disposed of in accordance with such registration statement, the shares offered by the selling stockholders have been disposed of pursuant to Rule 144 under the Securities Act or the shares offered by the selling stockholders may be resold pursuant to Rule 144 without restriction or limitation (including without the requirement to be in compliance with Rule 144(c)(1)) or another similar exemption under the Securities Act.

## LEGAL MATTERS

The validity of the common stock being offered hereby has been passed upon for us by Cooley LLP, Boston, Massachusetts.

## EXPERTS

The financial statements of Ziopharm Oncology, Inc. as of December 31, 2017 and 2016 and for each of the years in the three-year period ended December 31, 2017 and the effectiveness of internal control over financial reporting as of December 31, 2017, incorporated in this prospectus by reference from the Ziopharm Oncology, Inc. Annual Report on Form 10-K for the year ended December 31, 2017, have been audited by RSM US LLP, an independent registered public accounting firm, as stated in their report thereon (which report expresses an unqualified opinion and includes an explanatory paragraph related to the Company's ability to continue as a going concern) incorporated herein by reference, and have been incorporated in this prospectus and registration Statement in reliance upon such report and upon the authority of such firm as experts in accounting and auditing.

## WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the common stock we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of common stock in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of common stock offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us. The address of the SEC website is [www.sec.gov](http://www.sec.gov).

We maintain a website at [www.ziopharm.com](http://www.ziopharm.com). Information contained in, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus.

## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 and filed with the SEC on March 1, 2018, as amended on April 30, 2018;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018 filed with the SEC on May 10, 2018, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 filed with the SEC on August 8, 2018 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018 filed with the SEC on November 9, 2018;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed) filed with the SEC on August 8, 2018;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on January 9, 2018, February 5, 2018, February 6, 2018, February 22, 2018, March 13, 2018, June 18, 2018, July 27, 2018, September 24, 2018, October 9, 2018, October 11, 2018, October 16, 2018, November 13, 2018, December 14, 2018, January 10, 2019 and February 4, 2019; and
- the description of our common stock which is registered under Section 12 of the Exchange Act, in our registration statement on Form 8-A, filed with the SEC on September 20, 2006, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the common stock made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered a copy of any or all of the documents that are incorporated by reference in this prospectus but not delivered with this prospectus, including exhibits that are specifically incorporated by reference in such documents. You may request a copy of such documents at no cost, by writing or telephoning us at the following address or telephone number:

Ziopharm Oncology, Inc.  
One First Avenue, Parris Building 34, Navy Yard Plaza  
Boston, Massachusetts 02129  
Attention: General Counsel  
(617) 259-1970

**PART II**

**INFORMATION NOT REQUIRED IN THE PROSPECTUS**

**Item 14. Other Expenses of Issuance and Distribution**

The following table sets forth the estimated costs and expenses, other than underwriting discounts and commissions, payable by us in connection with the offering of common stock being registered. The selling stockholders will not bear any portion of such expenses. All the amounts shown are estimates, except for the SEC registration fee.

	<u>Amount</u>
SEC registration fee	\$ 9,870
Accounting fees and expenses	15,000
Legal fees and expenses	25,000
Printing and miscellaneous fees and expenses	2,000
<b>Total</b>	<u><u>\$51,870</u></u>

**Item 15. Indemnification of Directors and Officers**

Under Article 6 of the registrant's bylaws, each director and officer of the registrant will be indemnified to the fullest extent permitted by applicable law as it presently exists or may hereafter be amended, who was or is made or is threatened to be made a party or is otherwise involved in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he or she, or a person for whom he or she is the legal representative, is or was a director or officer of the registrant or, while a director or officer of the registrant, is or was serving at the request of the registrant as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust, enterprise or nonprofit entity, including service with respect to employee benefit plans, against all liability and loss suffered and expenses (including attorneys' fees) reasonably incurred by such director or officer. However, the registrant shall be required to indemnify a director or officer in connection with a proceeding commenced by such director or officer only if the commencement of such proceeding (or part thereof) by the director or officer was authorized by the Board. The registrant's Amended and Restated Certificate of Incorporation also eliminates the liability of directors of the registrant for monetary damages to the fullest extent permissible under Delaware law.

Section 145 of the Delaware General Corporation Law states:

(a) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that the person's conduct was unlawful.

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[Table of Contents](#)

(b) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

(c) To the extent that a present or former director or officer of a corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding referred to in subsections (a) and (b) of this section, or in defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection therewith.

(d) Any indemnification under subsections (a) and (b) of this section (unless ordered by a court) shall be made by the corporation only as authorized in the specific case upon a determination that indemnification of the present or former director, officer, employee or agent is proper in the circumstances because the person has met the applicable standard of conduct set forth in subsections (a) and (b) of this section. Such determination shall be made, with respect to a person who is a director or officer of the corporation at the time of such determination:

- (1) By a majority vote of the directors who are not parties to such action, suit or proceeding, even though less than a quorum; or
- (2) By a committee of such directors designated by majority vote of such directors, even though less than a quorum; or
- (3) If there are no such directors, or if such directors so direct, by independent legal counsel in a written opinion; or
- (4) By the stockholders.

(e) Expenses (including attorneys' fees) incurred by an officer or director of the corporation in defending any civil, criminal, administrative or investigative action, suit or proceeding may be paid by the corporation in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of such director or officer to repay such amount if it shall ultimately be determined that such person is not entitled to be indemnified by the corporation as authorized in this section. Such expenses (including attorneys' fees) incurred by former directors and officers or other employees and agents of the corporation or by persons serving at the request of the corporation as directors, officers, employees or agents of another corporation, partnership, joint venture, trust or other enterprise may be so paid upon such terms and conditions, if any, as the corporation deems appropriate.

(f) The indemnification and advancement of expenses provided by, or granted pursuant to, the other subsections of this section shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in such person's official capacity and as to action in another capacity while holding such office. A right to indemnification or to advancement of expenses arising under a provision of the certificate of incorporation or a bylaw shall not be eliminated or impaired by an amendment to the certificate of incorporation or the bylaws after the occurrence of the act or omission that is the subject of the civil, criminal, administrative or investigative action, suit or proceeding for which indemnification or advancement of expenses is sought, unless the provision in effect at the time of such act or omission explicitly authorizes such elimination or impairment after such action or omission has occurred.

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[Table of Contents](#)

(g) A corporation shall have power to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the corporation would have the power to indemnify such person against such liability under this section.

(h) For purposes of this section, references to "the corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under this section with respect to the resulting or surviving corporation as such person would have with respect to such constituent corporation if its separate existence had continued.

(i) For purposes of this section, references to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on a person with respect to any employee benefit plan; and references to "serving at the request of the corporation" shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner such person reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the corporation" as referred to in this section.

(j) The indemnification and advancement of expenses provided by, or granted pursuant to, this section shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

(k) The Court of Chancery is hereby vested with exclusive jurisdiction to hear and determine all actions for advancement of expenses or indemnification brought under this section or under any bylaw, agreement, vote of stockholders or disinterested directors, or otherwise. The Court of Chancery may summarily determine a corporation's obligation to advance expenses (including attorneys' fees).

The registrant maintains insurance on behalf of its officers and directors, insuring them against liabilities that they may incur in such capacities or arising out of this status.

The above discussion of the registrant's Amended and Restated Certificate of Incorporation and Bylaws and of Section 145 of the Delaware General Corporation Law is not intended to be exhaustive and is respectively qualified in its entirety by such Amended and Restated Certificate of Incorporation, Bylaws and statute.

The registrant has entered into indemnity agreements with each of its current directors and its executive officers to give such directors and officers additional contractual assurances regarding the scope of the indemnification set forth in the registrant's certificate of incorporation and bylaws and to provide additional procedural protections. At present, there is no pending litigation or proceeding involving any of the registrant's directors, officers or employees for which indemnification is sought, nor is the registrant aware of any threatened litigation that may result in claims for indemnification.

The securities purchase agreement that the registrant entered into with the selling stockholders identified in the prospectus included in this registration statement provides for cross indemnification in connection with registration of the registrant's common stock on behalf of such selling stockholder, including for certain liabilities arising under the Securities Act.

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## Table of Contents

### **Item 16. Exhibits**

<u>Exhibit Number</u>	<u>Description of Document</u>
3.1	<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>
3.2	<a href="#"><u>Bylaws, as amended to date (incorporated by reference to Exhibit 3.3 to the Registrant's Form 8-K, SEC File No. 000-32353, filed September 19, 2005).</u></a>
4.1	<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>
4.2	<a href="#"><u>Form of Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed November 13, 2018).</u></a>
4.3	<a href="#"><u>Securities Purchase Agreement, dated November 11, 2018, between the Registrant and the purchasers identified in Exhibit A therein (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed November 13, 2018).</u></a>
4.4	<a href="#"><u>Registration Rights Agreement, dated November 11, 2018, between the Registrant and the purchasers identified in Schedule 1 therein (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed November 13, 2018).</u></a>
5.1*	<a href="#"><u>Opinion of Cooley LLP</u></a>
23.1*	<a href="#"><u>Consent of RSM US LLP, Independent Registered Public Accounting Firm</u></a>
23.2*	<a href="#"><u>Consent of Cooley LLP (included in Exhibit 5.1)</u></a>
24.1*	<a href="#"><u>Power of Attorney (included on signature page)</u></a>

\* Filed herewith.

### **Item 17. Undertakings**

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
  - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
  - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;
  - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

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## [Table of Contents](#)

*provided, however*, that the undertakings set forth in paragraphs (1)(i), (1)(ii) and (1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in this registration statement or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

- (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
- (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser: (i) any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424; (ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant; (iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and (iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities



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[Table of Contents](#)

Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Boston, Commonwealth of Massachusetts, on the 7th day of February, 2019.

**ZIOPHARM ONCOLOGY, INC.**

By: /s/ Laurence J.N. Cooper  
Laurence J.N. Cooper, M.D., Ph.D.  
Chief Executive Officer

**POWER OF ATTORNEY**

**KNOW ALL PERSONS BY THESE PRESENTS**, that each person whose signature appears below constitutes and appoints Laurence J.N. Cooper and Robert Hadfield, and each or any one of them, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and re-substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments and registration statements filed pursuant to Rule 462 under the Securities Act) to this Registration Statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Laurence J.N. Cooper</u> Laurence J.N. Cooper	Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	February 7, 2019
<u>/s/ Kevin G. Lafond</u> Kevin G. Lafond	Senior Vice President, Finance, Chief Accounting Officer and Treasurer <i>(Principal Financial and Accounting Officer)</i>	February 7, 2019
<u>/s/ Scott Braunstein</u> Scott Braunstein	Director	February 7, 2019
<u>/s/ James A. Cannon</u> James A. Cannon	Director	February 7, 2019
<u>/s/ Elan Z. Ezickson</u> Elan Z. Ezickson	Director	February 7, 2019
<u>/s/ Douglas W. Pagán</u> Douglas W. Pagán	Director	February 7, 2019
<u>/s/ Scott Tarriff</u> Scott Tarriff	Director	February 7, 2019



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

February 7, 2019

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

Ladies and Gentlemen:

You have requested our opinion, as counsel to ZIOPHARM Oncology, Inc., a Delaware corporation (the "**Company**"), with respect to certain matters in connection with the filing by the Company of a Registration Statement on Form S-3 (the "**Registration Statement**") with the Securities and Exchange Commission, including a related prospectus filed with the Registration Statement (the "**Prospectus**"), covering the registration for resale of up to 37,878,788 shares of the Common Stock, \$0.001 par value, of the Company on behalf of certain selling stockholders, including 18,939,394 currently outstanding shares of Common Stock (the "**Shares**") and up to 18,939,394 shares of Common Stock (the "**Warrant Shares**") issuable upon the exercise of certain warrants held by such selling stockholders (the "**Warrants**").

In connection with this opinion, we have examined and relied upon the Registration Statement, the Prospectus, the Warrants, the Company's Amended and Restated Certificate of Incorporation, its By-Laws, and the originals or copies certified to our satisfaction of such records, documents, certificates, memoranda and other instruments as in our judgment are 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 and the conformity to originals of all documents submitted to us as copies thereof. As to certain factual matters, we have relied upon a certificate of an officer of the Company and have not independently sought to verify such matters.

Our opinion is expressed only with respect to the federal laws of the United States of America and the General Corporation Law of the State of Delaware.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that (i) the Shares are validly issued, fully paid and nonassessable, and (ii) the Warrant Shares, when issued and sold in accordance with the terms of the Warrants, will be validly issued, fully paid and nonassessable.

We consent to the reference to our firm under the caption "Legal Matters" in the Prospectus and 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 this Registration Statement on Form S-3 and related Prospectus 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.

We also consent to the reference to our firm under the heading “Experts” in such Prospectus.

/s/ RSM US LLP

Boston, Massachusetts

February 7, 2019