

## CALCULATION OF REGISTRATION FEE

<b>Title of each class of securities to be registered</b>	<b>Amount to be registered(1)</b>	<b>Proposed maximum offering price per security(2)</b>	<b>Proposed maximum aggregate offering price(2)</b>	<b>Amount of registration fee(3)</b>
Common stock, par value \$0.001 per share	17,803,031	\$3.88	\$69,075,760.28	\$8,966.03

- (1) All 17,803,031 shares of common stock registered pursuant to this registration statement are to be offered by the selling stockholders named herein. Pursuant to Rule 416 under the Securities Act of 1933, as amended, or the Securities Act, the shares being registered hereunder include such indeterminate number of shares of the common stock of Ziopharm Oncology, Inc., or the Company, as may be issuable with respect to the shares being registered hereunder to prevent dilution by reason of any stock dividend, stock split, recapitalization or other similar transaction.
- (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act. The offering price per share and aggregate offering price are based upon the average of the high and low prices per share of the Company's common stock, as reported on the Nasdaq Capital Market on October 18, 2019, which is a date within five business days prior to the filing of this prospectus supplement.
- (3) Calculated in accordance with Rule 457(r) of the Securities Act. Payment of the registration fee at the time of filing of the Company's automatically effective shelf registration statement on Form S-3, filed with the Securities and Exchange Commission, or the SEC, on June 21, 2019 (File No. 333-232283), or the Registration Statement, was deferred pursuant to Rules 456(b) and 457(r) under the Securities Act. This table shall be deemed to update the "Calculation of Registration Fee" table in the Registration Statement.

**PROSPECTUS SUPPLEMENT**  
**(To Prospectus dated June 21, 2019)**

**17,803,031 Shares**



**ZIOPHARM Oncology**

**Common Stock**

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This prospectus supplement registers for resale, from time to time, up to 17,803,031 shares of our common stock, par value \$0.001 per share, by the selling stockholders named herein upon the exercise of outstanding warrants. The prices at which such selling stockholders may dispose of their shares will be determined by the selling stockholders or their transferees. We will not receive any proceeds from the sale of shares of common stock by the selling stockholders; however, we have agreed to pay the registration expenses relating to such shares of common stock and we will receive the net proceeds of any warrants exercised for cash.

The selling stockholders from time to time may offer and sell the shares held directly to purchasers or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, commissions or concessions. For further information regarding the possible methods by which the shares may be distributed, see “Plan of Distribution.”

Our common stock is listed on The Nasdaq Capital Market under the symbol “ZIOP.” On October 22, 2019, the last reported sale price for our common stock on The Nasdaq Capital Market was \$4.34 per share.

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**Investing in our common stock involves a high degree of risk. See “[Risk Factors](#)” beginning on page S-5 of this prospectus supplement, beginning on page 9 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.**

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

TABLE OF CONTENTS

**Prospectus Supplement**

	<u>Page</u>
<a href="#">About This Prospectus Supplement</a>	S-1
<a href="#">Prospectus Supplement Summary</a>	S-2
<a href="#">Risk Factors</a>	S-5
<a href="#">Special Note Regarding Forward-Looking Statements</a>	S-6
<a href="#">Use of Proceeds</a>	S-8
<a href="#">Selling Stockholders</a>	S-9
<a href="#">Plan of Distribution</a>	S-12
<a href="#">Legal Matters</a>	S-14
<a href="#">Experts</a>	S-14
<a href="#">Where You Can Find More Information</a>	S-14
<a href="#">Incorporation of Certain Information by Reference</a>	S-14

**Prospectus**

	<u>Page</u>
<a href="#">ABOUT THIS PROSPECTUS</a>	1
<a href="#">PROSPECTUS SUMMARY</a>	2
<a href="#">RISK FACTORS</a>	9
<a href="#">SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</a>	9
<a href="#">USE OF PROCEEDS</a>	11
<a href="#">DILUTION</a>	12
<a href="#">DESCRIPTION OF CAPITAL STOCK</a>	13
<a href="#">DESCRIPTION OF DEBT SECURITIES</a>	16
<a href="#">DESCRIPTION OF WARRANTS</a>	23
<a href="#">CERTAIN PROVISIONS OF DELAWARE LAW, THE CERTIFICATE OF INCORPORATION AND BYLAWS</a>	25
<a href="#">LEGAL OWNERSHIP OF SECURITIES</a>	27
<a href="#">PLAN OF DISTRIBUTION</a>	31
<a href="#">LEGAL MATTERS</a>	33
<a href="#">EXPERTS</a>	33
<a href="#">WHERE YOU CAN FIND MORE INFORMATION</a>	33
<a href="#">INCORPORATION OF INFORMATION BY REFERENCE</a>	33

## ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Both this prospectus supplement and the accompanying prospectus include or incorporate by reference important information about us, our common stock and other information you should know before investing. You should read both this prospectus supplement and the accompanying prospectus and the documents incorporated herein and therein by reference (see the sections entitled “Incorporation of Certain Information by Reference”), as well as any additional information described under “Where You Can Find More Information” in this prospectus supplement before making an investment decision.

We and the selling stockholders have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, in the accompanying prospectus or in any free writing prospectus that we have authorized for use in connection with this offering. Neither we nor the selling stockholders take responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus supplement or an offer to sell or the solicitation of any offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus supplement and the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and in any related free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

This prospectus supplement may add to, update or change the information in the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date, the statement in the document having the later date modifies or supersedes the earlier statement.

Unless the context otherwise indicates, references in this prospectus supplement and accompanying prospectus to “Ziopharm,” “we,” “our,” “us” and “the Company” refer, collectively, to Ziopharm Oncology, Inc., a Delaware corporation, and its subsidiaries. Our principal executive offices are located at One First Avenue, Parris Building 34, Navy Yard Plaza, Boston, Massachusetts 02129.

## PROSPECTUS SUPPLEMENT SUMMARY

*The following summary highlights selected information contained or incorporated by reference elsewhere in this prospectus supplement and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus supplement, the accompanying prospectus and any related free writing prospectus that we have authorized for use in connection with this offering, including the information under the caption “Risk Factors” herein and therein and under similar headings in the documents that are incorporated by reference herein or therein. You should also carefully read the other information incorporated by reference into this prospectus supplement, including our financial statements and the related notes, and the exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus is a part.*

### Ziopharm Oncology, Inc.

#### Business Overview

We are a clinical-stage biopharmaceutical company focused on discovering, acquiring, developing and commercializing next generation immunotherapy platforms that leverage cell- and gene-based therapies to treat patients with cancer. We are developing two immuno-oncology platform technologies that utilize the immune system by employing novel, controlled gene expression and innovative cell engineering technologies designed to deliver safe, effective, and scalable non-viral cell- and viral-based gene therapies for the treatment of multiple cancer types. Our first platform is referred to as *Sleeping Beauty* and is based on the genetic engineering of immune cells using a non-viral transposon/transposase system that is intended to stably reprogram T cells outside of the body for subsequent infusion. Our second platform is termed Controlled IL-12, which is designed to stimulate expression of interleukin 12, a master regulator of the immune system, in a controlled and safe manner to focus the patient’s immune system to attack cancer cells. We believe these two platforms have the potential to provide unique and powerful solutions to address the issues associated with (1) treating solid tumors with heterogeneous and unknown antigens and (2) providing cost-effective scalable manufacturing solutions for T cell receptor T cell, or TCR+ T, therapies for solid tumors and chimeric antigen receptor, or CAR T cell, or CAR+ T, therapies targeting CD19 on malignant B cells. These programs are being advanced in collaboration with MD Anderson and the National Cancer Institute.

#### 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 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 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. Our website address is [www.ziopharm.com](http://www.ziopharm.com). The information contained on, or that can be accessed through, our website is not

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[Table of Contents](#)

incorporated by reference into this prospectus supplement or the accompanying prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus supplement or the accompanying prospectus or in deciding whether to purchase our common stock.

“Ziopharm,” the Ziopharm logo, and other trademarks or service marks of Ziopharm Oncology, Inc. appearing in this prospectus supplement and the accompanying prospectus are the property of Ziopharm Oncology, Inc. This prospectus supplement and the accompanying prospectus contain additional trade names, trademarks and service marks of others, which are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this prospectus may appear without the ® or TM symbols.

**The Offering**

<b>Common stock offered by selling stockholders</b>	17,803,031 shares
<b>Use of proceeds</b>	We will not receive any proceeds from the sale of shares of common stock by the selling stockholders. However, with respect to the warrants issued to the selling stockholders pursuant to the securities issuance agreements dated July 26, 2019 and September 11, 2019, upon any exercise of these warrants for cash, the selling stockholders would pay us an exercise price of \$7.00 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.
<b>Risk factors</b>	See “Risk Factors” on page S-5 and the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
<b>Nasdaq Capital Market symbol</b>	“ZIOP”

**RISK FACTORS**

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties discussed under the heading “Risk Factors” in our quarterly report on Form 10-Q for the quarter ended June 30, 2019 filed with the SEC on August 8, 2019 and incorporated by reference in this prospectus supplement, together with all of the other information contained in this prospectus supplement, the accompanying prospectus and in our filings with the SEC that we have incorporated by reference in this prospectus supplement and the accompanying prospectus. If any of these risks actually occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment. Please also read carefully the section below titled “Special Note Regarding Forward-Looking Statements.”

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we may authorize for use 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.

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## [Table of Contents](#)

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 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. Forward-looking statements are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. 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 June 30, 2019 filed with the SEC on August 8, 2019 and incorporated by reference in this prospectus supplement and the accompanying 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 supplement. 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 read carefully this prospectus supplement, the accompanying prospectus and any related free writing prospectuses prepared by or on behalf of us or the selling stockholders or to which we or the selling stockholders have referred you, together with the information incorporated herein and therein by reference as described in the section titled “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, 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 supplement. However, with respect to the warrants issued to the selling stockholders pursuant to the securities issuance agreements dated July 26, 2019 and September 11, 2019, upon any exercise of these warrants for cash, the selling stockholders would pay us an exercise price of \$7.00 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

The selling stockholders named in this prospectus supplement may offer and sell up to 17,803,031 shares of our common stock, par value \$0.001 per share.

On July 26, 2019, we entered into a securities issuance agreement with certain selling stockholders pursuant to which we issued and sold in a private placement warrants to purchase up to 15,015,152 shares of common stock, which we refer to in this prospectus supplement as the July 2019 Warrants. Separately, on September 11, 2019, we entered into a securities issuance agreement with a certain selling stockholder pursuant to which we issued and sold in a private placement warrants to purchase up to 2,787,879 shares of common stock, which we refer to in this prospectus supplement as the September 2019 Warrants. In this prospectus supplement, we refer to the July 2019 Warrants and the September 2019 Warrants collectively as the 2019 Warrants.

In connection with the private placements mentioned above, we also entered into registration rights agreements with the selling stockholders, pursuant to which we agreed to cover the resale of the shares underlying the 2019 Warrants. Our registration obligations under the registration rights agreements will continue in effect for up to two years from the date of closing of the private placements, August 6, 2021 with respect to the July 2019 Warrants and September 13, 2021 with respect to the September 2019 Warrants. The 2019 Warrants, which have a five-year term expiring on August 6, 2024 with respect to the July 2019 Warrants and September 13, 2024 with respect to the September 2019 Warrants, have a per share exercise price of \$7.00. The exercise price and number of shares of common stock issuable upon exercise of the 2019 Warrants may be adjusted in certain circumstances, including stock splits, stock dividends, reclassifications or similar event. The shares issuable upon exercise of the 2019 Warrants will become eligible for sale by the selling stockholders under this prospectus supplement only as the 2019 Warrants are exercised. We cannot predict when or whether any of the selling stockholders will exercise their 2019 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 supplement or, if required, a post-effective amendment to the registration statement of which this prospectus supplement is a part, to resell or otherwise dispose of the shares in the manner contemplated under “Plan of Distribution” in this prospectus supplement (as may be supplemented and amended). This prospectus supplement covers the sale or other disposition by the selling stockholders of up to the total number of shares of common stock issuable upon exercise of the 2019 Warrants issued to the selling stockholders. Throughout this prospectus supplement, when we refer to the shares of our common stock being registered on behalf of the selling stockholders, we are referring to the shares underlying the 2019 Warrants issued to the selling stockholders pursuant to the securities issuance agreements, and when we refer to the selling stockholders in this prospectus supplement, we are referring to the purchasers under the securities issuance agreements and, as applicable, their permitted transferees or other successors-in-interest that may be identified in a supplement to this prospectus supplement or, if required, a post-effective amendment to the registration statement of which this prospectus supplement 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 September 30, 2019, the number of shares of our common stock that may be offered under this prospectus supplement, 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”

[Table of Contents](#)

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 supplement.

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 2019 Warrants in full pursuant to cash exercises and further assumes the sale of all shares being offered by the selling stockholders under this prospectus supplement. The percentage of shares owned prior to and after the offering is based on 181,030,020 shares of common stock outstanding as of September 30, 2019 and, with respect to the percentage of shares owned after the offering, on the assumption that all of the selling stockholders have exercised the 2019 Warrants in full pursuant to cash exercises and therefore that all shares of common stock issuable upon exercise of the 2019 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	18,410,468 <sup>(3)</sup>	9.9	7,575,758	10,834,710	5.5
<b>Miller Opportunity Trust, a series of Trust for Advised Portfolios</b> One South Street, Suite 2550 Baltimore, Maryland 21202	14,087,879 <sup>(4)</sup>	7.6	3,787,879	10,300,000	5.2
<b>White Rock Capital Partners, L.P.</b> 3131 Turtle Creek Blvd., Suite 800 Dallas, Texas 75219	13,601,174 <sup>(5)</sup>	7.4	3,787,879	9,813,295	4.9
<b>Level One Partners, LLC</b> 210 Ridge McIntire Rd., Suite 350 Charlottesville, Virginia 22903	7,997,663 <sup>(6)</sup>	4.4	1,893,940	6,103,723	3.1
<b>WJD Investment Partners LLC</b> 2305 SW 18th Avenue Ft. Lauderdale, Florida 33315	1,515,150 <sup>(7)</sup>	*	757,575	757,575	*

\* Less than one percent.

(1) Under the terms of the 2019 Warrants, the number of shares of our common stock that may be acquired by a selling stockholder upon any exercise of a 2019 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 supplement 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 days prior to the expiration of the respective 2019 Warrant. If the operation of the

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## [Table of Contents](#)

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 issuable upon exercise of the 2019 Warrants issued to such selling stockholder. The shares issuable upon exercise of the 2019 Warrants will become eligible for sale by the selling stockholders under this prospectus supplement only as the 2019 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 2019 Warrants without regard to Exercise Limitation described in footnote (1) above.
- (3) Represents (i) 15,151,516 outstanding shares of common stock and (ii) 3,258,952 shares of common stock issuable upon exercise of 2019 Warrants. The beneficial ownership of 2019 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. Fuhrman, 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) 10,300,000 outstanding shares of common stock and (ii) 3,787,879 shares of common stock issuable upon exercise of 2019 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.
- (5) Represents (i) 9,813,295 outstanding shares of common stock and (ii) 3,787,879 shares of common stock issuable upon exercise of 2019 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.
- (6) Represents (i) 6,103,723 outstanding shares of common stock and (ii) 1,893,940 shares of common stock issuable upon exercise of 2019 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) 757,575 outstanding shares of common stock and (ii) 757,575 shares of common stock issuable upon exercise of 2019 Warrants. Donald Kleckner is the manager of, and may be deemed to beneficially own the securities held by, WJD Investment Partners LLC.

### **Relationships with the Selling Stockholders**

Each of the selling stockholders previously entered into a securities purchase agreement with us in November 2018, pursuant to which we sold and issued in a private placement immediately separable units comprised of shares of our common stock and warrants to purchase our common stock. Other than such transaction, 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

We are registering the shares of common stock to permit the resale from time to time of these shares of common stock by the selling stockholders named herein upon the exercise of outstanding warrants. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of common stock. However, with respect to the warrants issued to the selling stockholders pursuant to the securities issuance agreements dated July 26, 2019 and September 11, 2019, upon any exercise of these warrants for cash, the selling stockholders would pay us an exercise price of \$7.00 per share of common stock, subject to any adjustment pursuant to the terms of the warrants.

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 supplement 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 supplement and accompanying 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 supplement and accompanying prospectus, or under an amendment to this prospectus supplement 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 supplement. 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 supplement.

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

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## Table of Contents

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 supplement, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus supplement and accompanying prospectus (as supplemented or amended to reflect such transaction).

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.

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 supplement and accompanying prospectus (as each 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 will bear all reasonable fees and expenses in connection with the registration of the shares of common stock, other than any commissions, discounts or other fees payable to underwriters or broker-dealers in connection with any sale of shares, which will be borne by the selling stockholder selling such shares of common stock.

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 supplement and accompanying prospectus.

We have agreed with the selling stockholders to keep a registration statement covering the resale of the shares of common stock effective until the earlier to occur of (i) (A) August 6, 2021 with respect to the July 2019 Warrants and (B) September 13, 2021 with respect to the September 2019 Warrants 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.

Our common stock is listed on The Nasdaq Capital Market under the symbol “ZIOP.”

There can be no assurance that any selling stockholder will sell any or all of the shares of common stock registered pursuant to this prospectus supplement.

## LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Cooley LLP, Boston, Massachusetts.

## EXPERTS

The financial statements of Ziopharm Oncology, Inc. as of December 31, 2018 and 2017 and for each of the years in the three-year period ended December 31, 2018 and the effectiveness of internal control over financial reporting as of December 31, 2018, incorporated in this prospectus supplement by reference from the Ziopharm Oncology, Inc. Annual Report on Form 10-K for the year ended December 31, 2018, have been audited by RSM US LLP, an independent registered public accounting firm, as stated in their report thereon incorporated herein by reference, and have been incorporated in this prospectus supplement, the accompanying 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

We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet ([www.sec.gov](http://www.sec.gov)).

This prospectus supplement and the accompanying prospectus are part of an automatically effective registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus supplement or the accompanying prospectus for a copy of such contract, agreement or other document.

## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than Current Reports or portions furnished under Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K), including all filings made after the date of this prospectus supplement and prior to the termination of the offering of the common stock covered by this prospectus supplement:

- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2018 and filed with the SEC on March 5, 2019;

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## Table of Contents

- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 filed with the SEC on [May 8, 2019](#) and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 filed with the SEC on [August 8, 2019](#);
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2018 from our definitive proxy statement on [Schedule 14A](#) (other than information furnished rather than filed) filed with the SEC on April 29, 2019;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on [January 10, 2019](#), [February 4, 2019](#), [April 29, 2019](#), [May 28, 2019](#), [June 17, 2019](#), [July 24, 2019](#), [August 1, 2019](#), [September 13, 2019](#), [September 26, 2019](#), [October 1, 2019](#) and [October 15, 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 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

PROSPECTUS



From time to time, we may offer and sell any combination of the securities described in this prospectus, either individually or in combination, at prices and on terms described in one or more supplements to this prospectus. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable anti-dilution provisions.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered.

**This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.**

Our common stock is listed on the Nasdaq Capital Market under the symbol “ZIOP.” On June 20, 2019, the closing price of our common stock, as reported on the Nasdaq Capital Market, was \$5.82. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the Nasdaq Capital Market or other securities exchange of the securities covered by the prospectus supplement.

Securities may be sold to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section titled “Plan of Distribution” in this prospectus and in the applicable prospectus supplement. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and options to purchase additional shares will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

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**Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading “[Risk Factors](#)” on page 9 of this prospectus and any similar section contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the other documents that are incorporated by reference into this prospectus.**

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

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The date of this prospectus is June 21, 2019.

TABLE OF CONTENTS

	<u>Page</u>
<a href="#">ABOUT THIS PROSPECTUS</a>	1
<a href="#">PROSPECTUS SUMMARY</a>	2
<a href="#">RISK FACTORS</a>	9
<a href="#">SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</a>	9
<a href="#">USE OF PROCEEDS</a>	11
<a href="#">DILUTION</a>	12
<a href="#">DESCRIPTION OF CAPITAL STOCK</a>	13
<a href="#">DESCRIPTION OF DEBT SECURITIES</a>	16
<a href="#">DESCRIPTION OF WARRANTS</a>	23
<a href="#">CERTAIN PROVISIONS OF DELAWARE LAW, THE CERTIFICATE OF INCORPORATION AND BYLAWS</a>	25
<a href="#">LEGAL OWNERSHIP OF SECURITIES</a>	27
<a href="#">PLAN OF DISTRIBUTION</a>	31
<a href="#">LEGAL MATTERS</a>	33
<a href="#">EXPERTS</a>	33
<a href="#">WHERE YOU CAN FIND MORE INFORMATION</a>	33
<a href="#">INCORPORATION OF INFORMATION BY REFERENCE</a>	33

## ABOUT THIS PROSPECTUS

This prospectus is part of an automatic registration statement on FormS-3 that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration statement, we may sell common stock, preferred stock, various series of debt securities, or warrants to purchase any of such securities, either individually or in combination with other securities described in this prospectus, in one or more offerings from time to time. Selling stockholders may offer and sell, in one or more offerings, shares of common stock as described in this prospectus or the applicable prospectus supplement. There is no limit on the aggregate amount of the securities that we or selling stockholders may offer pursuant to the registration statement of which this prospectus is a part. This prospectus provides you with a general description of the securities we, and the common stock selling stockholders, may offer.

Each time we sell any type or series of securities, or selling stockholders offer common stock, under this prospectus, we will provide a prospectus supplement that will include more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference into this prospectus. This prospectus, together with the applicable prospectus supplement, any related free writing prospectus and the documents incorporated by reference into this prospectus and the applicable prospectus supplement, will include all material information relating to the applicable offering. Before buying any of the securities being offered, we urge you to carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectuses we have authorized for use in connection with a specific offering, together with the additional information incorporated herein by reference as described under the heading “Incorporation of Certain Information by Reference.”

**This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.**

You should rely only on the information contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different or additional information. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

The information appearing in this prospectus, any applicable prospectus supplement and any related free writing 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, the prospectus supplement or any related free writing prospectus, or the time of any sale of a security.

This prospectus includes summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described under the heading “Where You Can Find More Information.”

Unless the context otherwise indicates, references in this prospectus to “Ziopharm,” our “Company,” “we,” “us,” “our” and similar terms refer to Ziopharm Oncology, Inc.

## PROSPECTUS SUMMARY

*This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference into 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, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.*

### Ziopharm Oncology, Inc.

#### Company Overview

We are a clinical-stage biopharmaceutical company focused on discovering, acquiring, developing and commercializing next generation immunotherapy platforms that leverage cell- and gene-based therapies to treat patients with cancer. We are developing two immuno-oncology platform technologies that utilize the immune system by employing novel, controlled gene expression and innovative cell engineering technologies designed to deliver safe, effective, and scalable non-viral cell- and viral-based gene therapies for the treatment of multiple cancer types. Our first platform is referred to as *Sleeping Beauty* and is based on the genetic engineering of immune cells using a non-viral transposon/transposase system that is intended to stably reprogram T cells outside of the body for subsequent infusion. Our second platform is termed Controlled IL-12, which is designed to stimulate expression of 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 attack cancer cells. We believe these two platforms have the potential to provide unique and powerful solutions to address the issues associated with (1) treating solid tumors with heterogeneous and unknown antigens, and (2) providing cost-effective scalable manufacturing solutions for T cell receptor T cell, or TCR<sup>+</sup> T, therapies for solid tumors and chimeric antigen receptor, or CAR T cell, or CAR<sup>+</sup> T, therapies targeting CD19 on malignant B cells. We expect programs from our two platform technologies to be in the clinic in 2019.

Using our *Sleeping Beauty* platform, we are developing TCR<sup>+</sup> T therapies initially to target solid tumors. Our T cell receptor, or TCR, program designs and manufactures T cells that are intended to target tumor-specific antigens, thereby delivering personalized therapy that can attack an individual patient's cancer. These antigens are referred to as neoantigens as they are only expressed by the tumor, reducing the potential for toxicity upon targeting normal cells. A minority of neoantigens are shared between patients and between classes of tumors and are referred to as "hotspots". The *Sleeping Beauty* system uses DNA plasmids to reprogram T cells to express introduced TCRs on a patient-by-patient basis (addressing inter-tumor heterogeneity) and possibly to express more than one TCR for each patient (addressing intra-tumor heterogeneity). The genetic modification of patient-derived T cells using the *Sleeping Beauty* system enables us to target neoantigens unique to a patient's tumor infusing recipient-derived (autologous) TCRs and shared neoantigens in hotspots using allogeneic TCRs derived from third parties. We believe the scalability of our approach provides a competitive advantage to alternative viral-based approaches to T cell manufacturing. Under our Cooperative Research and Development Agreement, or CRADA, the National Cancer Institute, or the NCI, intends to initiate a clinical trial in patients with a variety of solid tumors using the *Sleeping Beauty* platform to genetically modify T cells to target patient-specific neoantigens in mid-2019. The clinical trial will be under the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI.

We are also developing CAR<sup>+</sup> T therapies using our *Sleeping Beauty* platform. Our CAR<sup>+</sup> T program seeks to solve the complex and costly manufacturing limitations of existing CD19-specific CAR<sup>+</sup> T therapies that we

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[Table of Contents](#)

believe will continue limiting their commercial potential. We believe using DNA plasmids in the *Sleeping Beauty* system to express CAR and our proprietary membrane-bound interleukin 15, or mbIL15, in resting T cells obtained from peripheral blood will enable infused T cells to propagate within the patient to target leukemia and lymphoma, thus avoiding the need to numerically expand T cells for weeks in bioreactors before patient administration. The mbIL15 is co-expressed with a “kill switch” to conditionally eliminate infused T cells. We expect the lower cost of DNA plasmids compared with the virus used by other CAR<sup>+</sup> T programs, together with the avoidance of lengthy *ex vivo* manufacturing, will reduce the cost and complexity of manufacturing CAR<sup>+</sup> T cells. These technologies should enable T cells to be infused within two days of gene transfer in a process we refer to as rapid personalized manufacture, or RPM. We are advancing our CAR<sup>+</sup> T therapies in the United States in collaboration with The University of Texas MD Anderson Cancer Center, or MD Anderson, to target CD19 on malignant B cells. In 2019, we hope to resolve our clinical hold with the U.S. Food and Drug Administration, or FDA, and initiate a Phase 1 clinical trial in the United States of our third-generation *Sleeping Beauty* modified CAR<sup>+</sup> T cells, co-expressing CAR and mbIL15, manufactured and infused into the patient in less than two days from gene transfer. In addition, in a joint venture with TriArm Therapeutics, Ltd., or TriArm, we are forming Eden BioCell, Ltd., or Eden BioCell, to lead clinical development and commercialization of *Sleeping Beauty*-generated CD19-specific CAR-T therapies in the People’s Republic of China, Taiwan and Korea. Eden BioCell will be owned equally by us and TriArm and the parties will share decision-making authority. TriArm has committed up to \$35.0 million to this joint venture and will manage all clinical development to execute trials in the territory. We expect our joint venture with TriArm to close in mid-2019 and we may evaluate additional programs to pursue in this joint venture.

Our Controlled IL-12 platform uses virotherapy based on an engineered replication-incompetent adenovirus(Ad-RTS-hIL-12) plus veledimex as a gene delivery system to conditionally produce IL-12, a potent, naturally occurring anti-cancer protein, to treat patients with solid tumors where a specific target is unknown, including brain cancer. Our Controlled IL-12 platform allows us to deliver IL-12 in a tunable dose, which is critical for this potent cytokine. In a Phase 1 clinical trial of patients with recurrent glioblastoma multiforme, or rGBM, a subset of patients (n=6) who received low-dose steroids along with 20 mg of veledimex plus Ad-RTS-hIL-12, achieved 17.8 months median overall survival, or OS, compared with five to eight months OS established in historical controls. Thirty-six additional patients with rGBM have been recruited into a sub study designed to encourage use of low-dose steroids and 20 mg veledimex to further understand the potential of Controlled IL-12 as a monotherapy. We are also developing our Controlled IL-12 platform in combination with immune checkpoint inhibitors. In June 2018, we began enrolling patients with rGBM to receive Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab) in a phase 1 dose-escalation trial. In November 2018, we announced a clinical supply agreement with Regeneron Pharmaceuticals, Inc., or Regeneron, to evaluate Ad-RTS-hIL-12 plus veledimex in combination with Regeneron’s PD-1 antibody Libtayo® (cemiplimab-rwlc) for the treatment of patients with rGBM. We currently expect to initiate a phase 2 clinical trial in the first half of 2019 in approximately 30 patients with rGBM to measure preliminary safety and efficacy of Ad-RTS-hIL-12 plus veledimex in combination with Libtayo.

As of March 31, 2019, we had cash and cash equivalents of approximately \$51.5 million. We expect that our existing cash and cash equivalents will be sufficient to fund our current operations into the second quarter of 2020, and we have no committed sources of additional capital at this time. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors.

We have not generated significant revenue and have incurred significant net losses in each year since our inception. For the three months ended March 31, 2019, we had a net loss of \$13.4 million, and, as of March 31, 2019, we have incurred approximately \$579.8 million of accumulated deficit since our inception in 2003. We

expect to continue to incur significant operating expenditures and net losses. Further development of our product candidates will likely require substantial increases in our expenses as we:

- continue to undertake clinical trials for product candidates;
- seek regulatory approvals for product candidates;
- work with regulatory authorities to identify and address program-related inquiries;
- implement additional internal systems and infrastructure;
- hire additional personnel; and
- scale-up the formulation and manufacturing of our product candidates.

We continue to seek additional financial resources to fund the further development of our product candidates. If we are unable to obtain sufficient additional capital, one or more of these programs could be delayed, and we may be unable to continue our operations at planned levels and be forced to reduce our operations. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability.

### **Recent Developments**

#### *Changes to Board of Directors*

On June 13, 2019, Heidi Hagen was appointed to our board of directors. Also on June 13, 2019, Scott Braunstein, M.D., Laurence Cooper, M.D., Ph.D., Elan Ezickson, Douglas Pagán, and Scott Tarriff were elected to our board at our 2019 annual meeting of stockholders. James Cannon stepped down from our board when his term expired at our 2019 annual meeting of stockholders.

#### *Clinical and Regulatory Developments*

- On April 1, 2019, we announced that the FDA has granted Fast Track Designation for our Controlled IL-12 program which consists of Ad-RTS-hIL-12 plus veledimex, for the treatment of recurrent or progressive glioblastoma multiforme in adults. The FDA's Fast Track program is designed to facilitate the development and expedite the review of drugs that treat serious conditions and fill an unmet medical need.
- Enrollment continues in our Phase 1 clinical trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab). The Data and Safety Monitoring Board for the clinical trial has authorized escalation to the third dosing cohort for this clinical trial.
- Under our CRADA, the NCI is undertaking a clinical trial with enrollment expected to begin in mid-2019. NCI is developing autologous peripheral blood lymphocytes genetically modified with the *Sleeping Beauty* system to express TCRs that recognize neoantigens expressed by patients' solid tumors. On June 11, 2019, we announced that the FDA had cleared the investigational new drug application submitted by the NCI for this clinical trial.
- Patients are being followed in a Phase 1 investigator-led trial at MD Anderson to infuse CD19-specific CAR<sup>+</sup>T cells based on genetic modification with the *Sleeping Beauty* system for patients with B-cell leukemias and lymphomas. This second-generation trial explores T cell dosing and time to manufacture.
- On June 2, 2019, we announced the presentation of new interim analyses of clinical data from Ad-RTS-hIL-12 plus veledimex, both as monotherapy and in combination with a PD-1 inhibitor, for

the treatment of recurrent or progressive glioblastoma multiforme in adults, at the American Society for Clinical Oncology (ASCO) Annual Meeting.

*Patent License Agreement with the NCI*

On May 28, 2019, we entered into a patent license agreement, or the License, with the NCI. Pursuant to the License, we hold an exclusive, worldwide license to certain intellectual property to develop and commercialize patient-derived (autologous), peripheral blood T cell therapy products engineered by transposon-mediated gene transfer to express TCRs reactive to mutated KRAS, p53 and EGFR. In addition, pursuant to the License, we hold an exclusive, worldwide license to certain intellectual property for manufacturing technologies to develop and commercialize autologous, peripheral blood T cell therapy products engineered by non-viral gene transfer to express TCRs, as well as a non-exclusive, worldwide license to certain additional manufacturing technologies.

Pursuant to the terms of the License, we are required to pay the NCI a cash payment in the aggregate amount of \$1,500,000, with a \$500,000 payment due within sixty days of the execution date of the License and additional \$500,000 payments due on the six- and twelve-month anniversaries of the License. We also agreed to reimburse the NCI for past patent expenses in the aggregate amount of approximately \$46,000.

The terms of the License also require us to pay the NCI minimum annual royalties in the amount of \$250,000, which amount will be reduced to \$100,000 once the aggregate minimum annual royalties paid by us equals \$1,500,000. The first minimum annual royalty payment is payable on the date that is eighteen months following the date of the License.

We are also required to make performance-based payments upon successful completion of clinical and regulatory benchmarks relating to the licensed products. The aggregate potential benchmark payments are \$4.3 million, of which aggregate payments of \$3.0 million are due only after marketing approval in the United States or in Europe, Japan, Australia, China or India. The first benchmark payment of \$100,000 will be due upon the initiation of our first sponsored Phase 1 clinical trial of a licensed product or licensed process in the field of use licensed under the License.

In addition, we are required to pay the NCI one-time benchmark payments following aggregate net sales of licensed products at certain net sales up to \$1.0 billion. The aggregate potential amount of these benchmark payments is \$12.0 million. We must also pay the NCI royalties on net sales of products covered by the License at rates in the low to mid-single digits depending upon the technology included in a licensed product. To the extent we enter into a sublicensing agreement relating to a licensed product, we are required to pay the NCI a percentage of all consideration received from a sublicensee, which percentage will decrease based on the stage of development of the licensed product at the time of the sublicense.

The License will expire upon expiration of the last patent contained in the licensed patent rights, unless terminated earlier. The NCI may terminate or modify the License in the event of a material breach, including if we do not meet certain milestones by certain dates, or upon certain insolvency events that remain uncured following the date that is 90 days following written notice of such breach or insolvency event. We may terminate the License, or any portion thereof, in our sole discretion at any time upon 60 days' written notice to the NCI. In addition, the NCI has the right to require us to sublicense the rights to the product candidates covered by the License upon certain conditions, including if we are not reasonably satisfying required health and safety needs or if we are not satisfying requirements for public use as specified by federal regulations.

**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 effect 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 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 Commission 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. Our internet site is [www.ziopharm.com](http://www.ziopharm.com). Information found on, 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 or part of any prospectus supplement.

### **The Securities We May Offer**

We may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- important U.S. federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

**This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.**

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the estimated net proceeds to us.

**Common Stock.** We may issue shares of our common stock from time to time. Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders and does not have cumulative voting rights. Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock. Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future. In this prospectus, we have summarized certain general features of our common stock under the heading “Description of Capital Stock—Common Stock.” We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

**Preferred Stock.** We may issue shares of our preferred stock from time to time, in one or more series. Under our certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to designate up to 30,000,000 shares of preferred stock in one or more series and to determine the designations, voting powers, preferences and rights of each series of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series, any or all of which may be greater than the rights of the common stock. Any convertible preferred stock we may issue will be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at the holder’s option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under the heading “Description of Capital Stock—Preferred Stock.” We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

**Debt Securities.** We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or preferred stock. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities under the heading "Description of Debt Securities." We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. We have filed a form of indenture as an exhibit to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will be incorporated by reference from reports that we file with the SEC, supplemental indentures and forms of debt securities containing the terms of the debt securities being offered.

**Warrants.** We may issue warrants for the purchase of common stock, preferred stock or debt securities, in one or more series, from time to time. We may issue warrants independently or in combination with common stock, preferred stock or debt securities. In this prospectus, we have summarized certain general features of the warrants under the heading "Description of Warrants." We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that we may offer as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will be incorporated by reference from reports that we file with the SEC, the form of warrant or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants may be issued under a warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

## 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 the applicable prospectus supplement and any related free writing prospectus, and under similar headings in our Annual Report on Form 10-K for the year ended December 31, 2018 and in our most recent Quarterly Report on Form 10-Q, as updated by our subsequent filings, which 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, results of operations, financial condition and cash flows, 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.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements. These are based on our management’s current beliefs, expectations and assumptions about future events, conditions and results 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, as well as any amendments thereto, filed with the SEC.

Any statements in this prospectus, or incorporated herein, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. Within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, these forward-looking statements include statements regarding:

- our ability to raise substantial additional capital to fund our planned operations 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 agreement;
- 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;

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## [Table of Contents](#)

- 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 deferred revenues, 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 “may”, “will”, “should”, “could”, “would”, “expects”, “plans”, “anticipates”, “believes”, “estimates”, “projects”, “predicts”, “potential” and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading “Risk Factors” in the applicable prospectus supplement or free writing prospectus and in our reports filed from time to time under the Securities Act and/or the Exchange Act. We encourage you to read these filings as they are made. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement.

You should refer to the “Risk Factors” section contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Given these risks, uncertainties and other factors, many of which are beyond our control, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate, and you should not place undue reliance on these forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this prospectus, even if new information becomes available in the future.

## **USE OF PROCEEDS**

We will retain broad discretion over the use of the net proceeds from the sale of our securities offered by this prospectus. Unless we indicate otherwise in the applicable prospectus supplement or in any related free writing prospectus we have authorized for use in connection with a specific offering, we anticipate that any net proceeds will be used for working capital and general corporate purposes. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. Pending these uses, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

## **DILUTION**

We will set forth in a prospectus supplement the following information regarding any material dilution of the equity interests of investors purchasing securities in an offering under this prospectus:

- the net tangible book value per share of our equity securities before and after the offering;
- the amount of the increase in such net tangible book value per share attributable to the cash payments made by purchasers in the offering; and
- the amount of the immediate dilution from the public offering price which will be absorbed by such purchasers.

## DESCRIPTION OF CAPITAL STOCK

*The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries. You should also refer to the amended and restated certificate of incorporation and the amended and restated bylaws, which are filed as exhibits to the registration statement of which this prospectus is part.*

### General

As of the date of this prospectus, our authorized capital stock consists of 280,000,000 shares, comprised of 250,000,000 shares of common stock, par value \$0.001 per share, and 30,000,000 shares of preferred stock, par value \$0.001 per share. As of June 18, 2019, there were 161,319,096 shares of common stock and no shares of preferred stock issued and outstanding. Our common stock is traded on the Nasdaq Capital Market under the symbol “ZIOF”.

### Common Stock

*Voting Rights.* The holders of our common stock are entitled to one vote for each outstanding share of common stock owned by such stockholder on every matter properly submitted to the stockholders for their vote. Stockholders are not entitled to vote cumulatively for the election of directors. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. At any meeting of the stockholders, a quorum as to any matter shall consist of a majority of the votes entitled to be cast on the matter, except where a larger quorum is required by law, by our certificate of incorporation or by our bylaws.

*Dividend Rights.* Holders of our common stock are entitled to receive ratably dividends and other distributions of cash or any other right or property as may be declared by our board of directors out of our assets or funds legally available for such dividends or distributions. The dividend rights of holders of common stock are subject to the dividend rights of the holders of any series of preferred stock that may be issued and outstanding from time to time.

*Liquidation Rights.* In the event of any voluntary or involuntary liquidation, dissolution or winding up of our affairs, holders of our common stock would be entitled to share ratably in our assets that are legally available for distribution to stockholders after payment of liabilities. If we have any preferred stock outstanding at such time, the holders of such preferred stock may be entitled to distribution and/or liquidation preferences that require us to pay the applicable distribution to the holders of preferred stock before paying distributions to the holders of common stock.

*Rights and Preferences.* Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company.

See “Certain Provisions of Delaware Law, the Certificate of Incorporation and Bylaws” for a description of provisions of our certificate of incorporation and bylaws which may have the effect of delaying, deferring or preventing changes in our control.

### Preferred Stock

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority, without stockholder approval, subject to limitations prescribed by law, to provide for the issuance of up to

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## Table of Contents

30,000,000 shares of preferred stock in one or more series, and by filing a certificate pursuant to the applicable law of the State of Delaware, to establish from time to time the number of shares to be included in each such series, and to fix the designation, powers, preferences and rights of the shares of each series and any qualifications, limitations or restrictions thereof, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the Commission, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares offered;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate(s), period(s) and/or payment date(s) or method(s) of calculation for dividends;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provision for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price (or manner of calculation) and conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

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[Table of Contents](#)

Our board of directors could authorize the issuance of shares of preferred stock with terms and conditions that could have the effect of discouraging a takeover or other transaction that might involve a premium price for holders of the shares or which holders might believe to be in their best interests. The issuance of preferred stock could adversely affect the voting power, conversion or other rights of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation.

The laws of the state of Delaware, the state of our incorporation, provide that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of such preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

The transfer agent and registrar for any series of preferred stock will be set forth in the applicable prospectus supplement.

## DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

### General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

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## [Table of Contents](#)

- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depository for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

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## [Table of Contents](#)

- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

### **Conversion or Exchange Rights**

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

### **Consolidation, Merger or Sale**

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

### **Events of Default under the Indenture**

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

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## [Table of Contents](#)

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request,
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

### **Modification of Indenture; Waiver**

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;

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## [Table of Contents](#)

- to comply with the provisions described above under “Description of Debt Securities — Consolidation, Merger or Sale;”
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under “Description of Debt Securities — General” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

### **Discharge**

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;

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## [Table of Contents](#)

- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

### **Form, Exchange and Transfer**

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

### **Information Concerning the Trustee**

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

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[Table of Contents](#)

**Payment and Paying Agents**

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

**Governing Law**

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

## DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and in any related free writing prospectuses that we may authorize to be distributed to you, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and be issued in one or more series. Warrants may be offered independently or in combination with common stock, preferred stock or debt securities offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that describe the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

### General

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;

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## [Table of Contents](#)

- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special U.S. federal income tax considerations of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

### **Exercise of Warrants**

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

### **Governing Law**

Unless we otherwise specify in the applicable prospectus supplement, the warrants and any warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

### **Enforceability of Rights by Holders of Warrants**

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

**CERTAIN PROVISIONS OF DELAWARE LAW,  
THE CERTIFICATE OF INCORPORATION AND BYLAWS**

**Limitations on Directors' Liability**

Our amended and restated certificate of incorporation and our bylaws contain provisions indemnifying our directors and officers to the fullest extent permitted by law. In addition, as permitted by Delaware law, our amended and restated certificate of incorporation provides that no director will be liable to us or our stockholders for monetary damages for breach of certain fiduciary duties as a director. The effect of this provision is to restrict our rights and the rights of our stockholders in derivative suits to recover monetary damages against a director for breach of certain fiduciary duties as a director, except that a director will be personally liable for:

- the benefits to be derived from relationships with our collaborators;
- any breach of his or her duty of loyalty to the registrant or its stockholders;
- acts or omissions not in good faith which involve intentional misconduct or a knowing violation of law;
- the payment of dividends or the redemption or purchase of stock in violation of Delaware law; or
- any transaction from which the director derived an improper personal benefit.

This provision does not affect a director's liability under the federal securities laws.

To the extent that our directors, officers and controlling persons are indemnified under the provisions contained in our amended and restated certificate of incorporation, Delaware law or contractual arrangements against liabilities arising under the Securities Act, we have 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.

**Provisions that May Have an Anti-Takeover Effect**

Certain provisions set forth in our amended and restated certificate of incorporation, bylaws and in Delaware law, which are summarized below, are intended to enhance the likelihood of continuity and stability in the composition of our board of directors and in the policies formulated by our board of directors and to discourage certain types of transactions that may involve an actual or threatened change of control. In that regard, these provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they also may inhibit fluctuations in the market price of our common stock that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in our management.

*Blank Check Preferred Stock.* Our amended and restated certificate of incorporation contains provisions that permit our board of directors to issue, without any further vote or action by the stockholders, up to 30,000,000 shares of preferred stock in one or more series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting powers (if any) of the shares of the series, and the preferences and relative, participating, optional and other special rights, if any, and any qualifications, limitations or restrictions, of the shares of such series. As a result, our board of directors could authorize the issuance of shares of preferred stock with terms and conditions that could have the effect of delaying, deferring or preventing a transaction or a change in control that might involve a premium price for holders of the registrant's common stock or otherwise be in their best interest.

*Special Meetings of Stockholders.* Our bylaws provide that special meetings of stockholders may be called only by the board of directors. Stockholders are not permitted to call a special meeting of stockholders or to require that the board of directors call such a special meeting.

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[Table of Contents](#)

*Delaware Takeover Statute.*

We are subject to Section 203 of the Delaware General Corporation Law, or DGCL, which regulates acquisitions of some Delaware corporations. In general, Section 203 prohibits, with some exceptions, a Delaware corporation that is a public company from engaging in any “business combination” with any “interested stockholder” for a period of three years following the date that such stockholder became an interested stockholder, unless:

- prior to such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- on consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding those shares owned (x) by persons who are directors and also officers and (y) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 of the DGCL defines “business combination” to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an “interested shareholder” as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with such entity or person.

## LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depository or warrant agent maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

### **Book-Entry Holders**

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depository or its participants. Consequently, for securities issued in global form, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

### **Street Name Holders**

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depository will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any applicable trustee or depository will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

### **Legal Holders**

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

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## [Table of Contents](#)

For example, once we make a payment or give a notice to the legal holder, we have no further responsibility for the payment or notice even if that legal holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the legal holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

### **Special Considerations for Indirect Holders**

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

### **Global Securities**

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under "Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

### **Special Considerations for Global Securities**

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We

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## [Table of Contents](#)

do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank, broker or other financial institution for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your bank, broker or other financial institution may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

### **Special Situations When a Global Security Will Be Terminated**

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks, brokers or other financial institutions to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

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[Table of Contents](#)

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

## PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the times of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We may also sell equity securities covered by this registration statement in an “at the market offering” as defined in Rule 415 under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

- on or through the facilities of Nasdaq or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- other than on Nasdaq or such other securities exchanges or quotation or trading services.

Such at the market offerings, if any, may be conducted by underwriters acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

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## [Table of Contents](#)

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any underwriters who are qualified market makers on Nasdaq may engage in passive market making transactions in the securities on Nasdaq in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

## LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon by Cooley LLP. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

## EXPERTS

The financial statements of ZIOPHARM Oncology, Inc. as of December 31, 2018 and 2017 and for each of the years in the three-year period ended December 31, 2018 and the effectiveness of internal control over financial reporting as of December 31, 2018, incorporated in these Prospectuses by reference from the ZIOPHARM Oncology, Inc. Annual Report on Form 10-K for the year ended December 31, 2018, 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) incorporated herein by reference, and have been incorporated in these Prospectuses 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 on Form S-3 we filed with the SEC under the Securities Act. 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 securities 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. You should rely only on the information contained in this prospectus or incorporated by reference. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities 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 the securities 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 found on, 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 or part of any prospectus supplement.

## INCORPORATION OF 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. The SEC file number for the documents incorporated by reference in this prospectus is 001-33038. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this document:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2018, filed with the SEC on March 5, 2019;

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## Table of Contents

- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2018 from our definitive proxy statement on [Schedule 14A](#) (other than information furnished rather than filed), which was filed with the SEC on April 29, 2019;
- our Quarterly Report on [Form 10-Q](#) for the fiscal quarter ended March 31, 2019, filed with the SEC on May 8, 2019;
- our Current Reports on Form 8-K filed with the SEC on [January 10, 2019](#), [February 4, 2019](#), [April 29, 2019](#), [May 28, 2019](#) and [June 17, 2019](#) to the extent the information in such reports is filed and not furnished; and
- the description of our common stock set forth in the registration statement on [Form 8-A](#) registering our common stock under Section 12 of the Exchange Act, which was filed with the SEC on September 20, 2006, including any amendments or reports filed for purposes 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, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into 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

**17,803,031 Shares**



**ZIOPHARM Oncology**

**Common Stock**

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**Prospectus Supplement**

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October 23, 2019

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