

PROSPECTUS SUPPLEMENT
(To Prospectus dated December 28, 2017)

\$5,000,000



Common Stock

We have entered into a sales agreement with Roth Capital Partners, LLC, or Roth, relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$5,000,000 from time to time through or to Roth acting as our sales agent or principal.

Our common stock is listed on the Nasdaq Capital Market under the symbol "ONTX." On May 16, 2019, the last reported sale price of our common stock on the Nasdaq Capital Market was \$3.75 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made in sales deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Roth is not required to sell any specific amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Roth and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Roth for sales of common stock sold pursuant to the sales agreement will be an amount equal to 3.0% of the gross proceeds of any shares of common stock sold under the sales agreement. In connection with the sale of the common stock on our behalf, Roth will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Roth will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Roth with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended.

As of May 16, 2019, the aggregate market value of our outstanding common stock held by non-affiliates, which we may refer to as the public float, was \$24,621,367, which was calculated based on 5,725,899 shares of outstanding common stock held by non-affiliates and on a price per share of \$4.30, the closing price of our common stock on May 8, 2019. In no event will we sell our common stock in a public primary offering with a value exceeding more than one-third of our public float in any 12 calendar month period so long as our public float remains below \$75.0 million. Other than the shares of common stock offered pursuant to this prospectus supplement, we have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to and including the date of this prospectus supplement.

Investing in our common stock involves risks. See the section entitled "Risk Factors" beginning on page S-4 of this prospectus supplement and in the documents we incorporate by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement and the accompanying prospectus. Any representation to the contrary is a criminal offense.

Roth Capital Partners

The date of this prospectus supplement is May 17, 2019

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document contains two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also supplements and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which provides more general information, some of which may not apply to this offering. If the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus, you should rely on the information set forth in this prospectus supplement.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and Roth has not, authorized anyone else to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any permitted free writing prospectuses we have authorized for use in connection with this offering.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement and the accompanying prospectus is accurate only as of the date of this prospectus supplement or the date of the accompanying prospectus, and the information in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of those respective documents, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates. It is important for you to read and consider all information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus in making your investment decision. You should read both this prospectus supplement and the accompanying prospectus, as well as the documents incorporated by reference into this prospectus supplement and the accompanying prospectus and the additional information described under “Where You Can Find More Information” in this prospectus supplement and in the accompanying prospectus, before investing in our common stock.

All references in this prospectus supplement to “Onconova,” the “company,” “we,” “us” and “our” refer to Onconova Therapeutics, Inc. and its consolidated subsidiaries, except where the context otherwise requires or as otherwise indicated.

This prospectus supplement, the accompanying prospectus, and the information incorporated by reference herein and therein include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us and this offering. Because it is a summary, it does not contain all of the information that you should consider before investing. Before investing in our common stock, you should read this entire prospectus supplement and the accompanying prospectus carefully, including the “Risk Factors,” and the financial statements and accompanying notes and other information incorporated by reference in this prospectus supplement and the accompanying prospectus.

Our Company

We are a clinical-stage biopharmaceutical company focused on discovering and developing novel small molecule product candidates primarily to treat cancer. Using our proprietary chemistry platform, we have created an extensive library of targeted agents designed to work against cellular pathways important to cancer cells. We believe that the product candidates in our pipeline have the potential to be efficacious in a variety of cancers. We have one Phase 3 clinical-stage product candidate and two other clinical-stage product candidates (one of which has been studied for treatment of acute radiation syndromes) and several preclinical programs. Substantially all of our current effort is focused on our lead product candidate, rigosertib. Rigosertib has been tested in an intravenous formulation as a single agent for patients with higher-risk myelodysplastic syndromes (“MDS”), and an oral formulation in lower risk MDS as a single agent or in combination with azacitidine for patients with higher-risk MDS.

In December 2015, we enrolled the first patient into our INSPIRE trial, a randomized controlled Phase 3 clinical trial of intravenous rigosertib (“rigosertib IV”) in a population of patients with higher-risk MDS after failure of hypomethylating agent (“HMA”) therapy. The primary endpoint of INSPIRE is overall survival. An interim analysis of the trial was performed in January 2018 and we anticipate completion of enrollment of the INSPIRE trial in the second half of 2019.

Our net losses were \$7.6 million and \$5.1 million for the three months ended March 31, 2019 and 2018, respectively. As of March 31, 2019, we had an accumulated deficit of \$389.5 million.

Corporate Information

We were incorporated in Delaware in December 1998 and commenced operations in January 1999. Our principal executive offices are located at 375 Pheasant Run, Newtown, Pennsylvania 18940, and our telephone number is (267) 759-3680. Our website address is www.onconova.com. The information on, or that can be accessed through, our website is not part of this prospectus.

THE OFFERING

Common stock offered	Shares of our common stock having an aggregate offering price of up to \$5,000,000.
Manner of offering	“At the market offering” that may be made from time to time through Roth Capital Partners, LLC, as sales agent or principal. See “Plan of Distribution” on page S-10 of this prospectus supplement.
Use of proceeds	We anticipate that the net proceeds from our sale of any securities will be used to fund the development of our clinical and preclinical programs, for other research and development activities and for general corporate purposes, which may include capital expenditures and funding our working capital needs. We expect from time to time to evaluate the acquisition of businesses, products and technologies for which a portion of the net proceeds may be used, although we currently are not planning or negotiating any such transactions. Pending such uses, we may invest the net proceeds in investment grade interest-bearing securities. See “Use of Proceeds” on page S-8 of this prospectus supplement.
Risk factors	See “Risk Factors” beginning on page S-4 of this prospectus supplement, and under similar headings in other documents incorporated by referenced into this prospectus supplement and the accompany prospectus, for a discussion of factors you should consider carefully before deciding to invest in our common stock.
Nasdaq Capital Markets symbol	“ONTX”

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and in our Annual Report on Form 10-K for the year ended December 31, 2018, and our Quarterly Report on Form 10-Q for the quarter end March 31, 2019 incorporated by reference in this prospectus supplement and the accompanying prospectus, any amendment or update thereto reflected in our subsequent filings with the SEC, and all of the other information in this prospectus supplement and the accompanying prospectus, including our financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus. If any of these risks is realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the trading price of our common stock could decline and you could lose part or all of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also materially harm our business, operating results and financial condition and could result in a complete loss of your investment.

Risks related to this offering

Purchasers in this offering will experience immediate and substantial dilution in the book value of their investment.

The common stock sold in this offering from time to time will be sold at various prices; however, we expect the price per share of common stock will be substantially higher than the net tangible book value of our common stock. Therefore, purchasers of our common stock in this offering will experience immediate dilution in the net tangible book value of the common stock purchased in this offering. Assuming that an aggregate of 1,333,333 shares of common stock are sold at a public offering price of \$3.75 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on May 16, 2019, for an aggregate gross proceeds of \$5,000,000 and after deducting estimated commissions and estimated offering expenses payable by us, our adjusted net tangible book value as of March 31, 2019 would have been approximately \$3.18 million, or approximately \$0.44 per share of our common stock. As a result, if you purchase shares of common stock in this offering at that assumed public offering price, you would suffer immediate and substantial dilution of \$3.31 per share with respect to the net tangible book value of the common stock. See “Dilution” in this prospectus supplement for a detailed illustration of the dilution you will incur if you purchase shares in this offering.

We will have broad discretion in how we use the net proceeds of this offering. We may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

Although we currently intend to use the net proceeds from this offering in the manner described in the section entitled “Use of Proceeds” in this prospectus supplement, we will have considerable discretion in the application of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

If we raise additional capital in the future, your ownership in us could be diluted.

Any issuance of equity we may undertake in the future to raise additional capital could cause the price of our common stock to decline, or require us to issue shares at a price that is lower than that paid by holders of our common stock in the past, which would result in those newly issued shares being dilutive. If we obtain funds through a credit facility or through the issuance of debt or preferred securities, these securities would likely have rights senior to your rights as a common stockholder, which could impair the value of our common stock.

We have never paid dividends on our capital stock and we do not anticipate paying dividends in the foreseeable future.

We have never paid dividends on any of our capital stock and currently intend to retain any future earnings to fund the growth of our business. Any determination to pay dividends in the future will be at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general

business conditions and other factors that our board of directors may deem relevant. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for the foreseeable future.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. In addition, the sale of substantial amounts of our common stock could adversely impact its price. As of March 31, 2019, we had outstanding 5,895,004 shares of our common stock, outstanding options to purchase 345,794 shares of our common stock and warrants to purchase 5,504,722 shares of our common stock. The sale or the availability for sale of a large number of shares of our common stock in the public market could cause the price of our common stock to decline.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering 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. We may, in some cases, use terms such as “believes,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should,” “approximately” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, protection of our intellectual property portfolio, the degree of clinical utility of our products, particularly in specific patient populations, our ability to develop commercial and manufacturing functions, expectations regarding clinical trial data, our results of operations, cash needs, financial condition, liquidity, collaborations, partnerships, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for such forward-looking statements, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this report. In addition, even if our results of operations, financial condition and liquidity, and events in the industry in which we operate are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods.

Actual results could differ materially from our forward-looking statements due to a number of factors, including risks related to:

- our need for additional financing for our INSPIRE trial and other operations, and our ability to obtain sufficient funds on acceptable terms when needed, and our plans and future needs to scale back operations if adequate financing is not obtained;
- our ability to continue as a going concern;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the success and timing of our preclinical studies and clinical trials, including site initiation and patient enrollment, and regulatory approval of protocols for future clinical trials;
- our ability to enter into, maintain and perform collaboration agreements with other pharmaceutical companies, for funding and commercialization of our clinical drug product candidates or preclinical compounds, and our ability to achieve certain milestones under those agreements;
- the difficulties in obtaining and maintaining regulatory approval of our product candidates, and the labeling under any approval we may obtain;
- our plans and ability to develop, manufacture and commercialize our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;

- the rate and degree of market acceptance of any of our product candidates;
- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;
- the successful development of our commercialization capabilities, including sales and marketing capabilities;
- recently enacted and future legislation and regulation regarding the healthcare system;
- the success of competing therapies and products that are or may become available;
- our ability to maintain the listing of our securities on a national securities exchange;
- the potential for third party disputes and litigation; and
- the performance of third parties, including contract research organizations and third-party manufacturers.

Any forward-looking statements that we make speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after such date or to reflect the occurrence of unanticipated events. Comparisons of results for current and any prior periods are not intended to express any future trends or indications of future performance, unless expressed as such, and should only be viewed as historical data.

You should also read carefully the factors described in the “Risk Factors” in this prospectus supplement, the accompanying prospectus, our Annual Report on Form 10-K for the year ended December 31, 2018 and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, to better understand significant risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements and you should not place undue reliance on any forward-looking statements.

USE OF PROCEEDS

We may issue and sell shares of common stock having aggregate sales proceeds of up to \$5,000,000 from time to time in this offering. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and net proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with Roth as a source of financing.

We anticipate that the net proceeds from our sale of any securities will be used to fund the development of our clinical and preclinical programs, for other research and development activities and for general corporate purposes, which may include capital expenditures and funding our working capital needs. We expect from time to time to evaluate the acquisition of businesses, products and technologies for which a portion of the net proceeds may be used, although we currently are not planning or negotiating any such transactions. Pending such uses, we may invest the net proceeds in investment grade interest-bearing securities.

The amounts actually expended for each purpose may vary significantly depending upon numerous factors, including the amount and timing of the proceeds from this offering and progress with our clinical development programs. Expenditures will also depend upon the establishment of collaborative arrangements with other companies, the availability of additional financing and other factors. Investors will be relying on the judgment of our management regarding the application of the proceeds of any sale of securities.

DILUTION

If you purchase our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock immediately after this offering. Net tangible book value per share is determined by dividing the number of shares of common stock outstanding as of March 31, 2019 into our total tangible assets less total liabilities.

Our net tangible book value as of March 31, 2019 was \$(1,536,000), or \$(0.26) per share, based on 5,895,004 shares of our common stock outstanding as of that date. After giving effect to the sale of 1,333,333 shares of common stock by us at an assumed public offering price of \$3.75 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on May 16, 2019, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2019 would have been \$3,184,000, or \$0.44 per share. This represents an immediate increase in net tangible book value of \$0.70 per share to existing stockholders and immediate dilution of \$3.31 per share to investors in this offering, as illustrated by the following table:

Assumed public offering price per share		\$	3.75
Net tangible book value per share as of March 31, 2019	\$	(0.26)	
Increase in net tangible book value per share attributable to investors participating in this offering		0.70	
As adjusted net tangible book value per share after giving effect to this offering			0.44
Dilution per share to investors in this offering		\$	3.31

The table above assumes for illustrative purposes that an aggregate of 1,333,333 shares of our common stock are sold at a price of \$3.75 per share, the last reported sale price of our common stock on the Nasdaq Stock Market on May 16, 2019, for aggregate gross proceeds of \$5,000,000. The shares sold in this offering, if any, will be sold from time to time at various prices. A \$0.50 increase or decrease in the price at which the shares are sold from the assumed public offering price of \$3.75 per share, would increase or decrease our as adjusted net tangible book value by approximately \$0.01 per share, and the dilution per share to investors in this offering by approximately \$0.49 per share, after deducting estimated commissions and estimated offering expenses payable by us. The as adjusted information provided above is illustrative only. The common stock sold in this offering, if any, will be sold from time to time at various prices.

The number of shares of common stock to be outstanding immediately after this offering is based on 5,895,004 shares outstanding as of March 31, 2019 and excludes:

- 345,794 shares of common stock issuable upon the exercise of stock options outstanding at March 31, 2019 with a weighted average exercise price of approximately \$77.75 per share;
- 5,504,722 shares of common stock issuable upon the exercise of outstanding or issuable warrants at March 31, 2019 with a weighted average exercise price of approximately \$9.11 per share (includes common stock issuable for warrants which are exercisable for our Series A or Series B Convertible Preferred Stock, each of which is convertible to common stock); and
- 118,890 shares of common stock reserved for future issuance under our 2018 Omnibus Incentive Compensation Plan at March 31, 2019.

As of May 17, 2019, the total number of our outstanding shares of Common Stock was 5,998,524.

To the extent that additional shares are issued pursuant to the foregoing, investors purchasing our common stock in this offering will experience further dilution. In addition, we may offer other securities in other offerings due to market conditions or strategic considerations. To the extent we issue such securities, investors may experience further dilution.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Roth Capital Partners, LLC, or Roth, under which we may issue and sell shares of our common stock from time to time through or to Roth acting as sales agent or principal, subject to certain limitations, having an aggregate gross sales price of up to \$5,000,000. Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be “at the market offerings” as defined in Rule 415 promulgated under the Securities Act. We may instruct Roth not to sell our common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Roth may suspend the offering of our common stock upon notice and subject to other conditions. As an agent, Roth will not engage in any transactions that stabilize the price of our common stock.

Each time we wish to issue and sell common stock under the sales agreement, we will notify Roth of the number or dollar value of shares to be sold, the dates on which such sales are anticipated to be made, any minimum price below which sales may not be made and other sales parameters as we deem appropriate. Once we have so instructed Roth, unless Roth declines to accept the terms of the notice, Roth has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligation of Roth under the sales agreement to sell shares of our common stock is subject to a number of conditions that we must meet.

We will pay Roth a commission equal to 3.0% of the gross proceeds we receive from the sales of our common stock under the sales agreement. Because there is no minimum offering amount required as a condition to closing this offering, the actual total public offering amount, Roth’s commission and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Roth for its reasonable documented out-of-pocket expenses, including fees and disbursements of its counsel, in an amount not to exceed \$50,000 in the aggregate. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Roth under the sales agreement, will be approximately \$80,000.

Settlement for sales of our common stock will occur on the second trading day following the date on which any sales are made, in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf, Roth will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of Roth will be deemed to be underwriting commission or discount. We have agreed to provide indemnification and contribution to Roth against certain liabilities, including liabilities under the Securities Act.

The offering pursuant to the sales agreement will terminate upon the earlier of (i) the issuance and sale of all shares of our common stock subject to the sales agreement, or (ii) the termination of the sales agreement as permitted therein.

Roth and its affiliates may in the future provide various investment banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Roth will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement will be passed upon for us by Morgan, Lewis & Bockius LLP, Philadelphia, Pennsylvania. Roth Capital Partners, LLC is being represented by Duane Morris LLP, New York, New York, in connection with this offering.

EXPERTS

The consolidated financial statements of Onconova Therapeutics, Inc. appearing in Onconova Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2018 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements) included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus supplement and the accompanying prospectus is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site on the worldwide web is <http://www.sec.gov>. The information on the SEC's website is not part of this prospectus supplement and the accompanying prospectus, and any references to this website or any other website are inactive textual references only.

INCORPORATION BY REFERENCE

The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus supplement and the accompanying prospectus. Information that is incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus and you should read it with the same care that you read this prospectus supplement and the accompanying prospectus. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus supplement and the accompanying prospectus, and will be considered to be a part of this prospectus supplement and the accompanying prospectus from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus supplement and the accompanying prospectus:

- Our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2018 that we filed with the SEC on April 1, 2019, including the information required by Part III, Item 10 through 14, of Form 10-K, which is incorporated by reference to our definitive proxy statement on [Schedule 14A](#) for our 2019 annual meeting of stockholders filed with the SEC on April 29, 2019;
- Our Quarterly Report on [Form 10-Q](#) for the fiscal quarter ended March 31, 2019 that we filed with the SEC on May 15, 2019;
- Our Current Report on Form 8-Ks filed with the SEC on [January 15, 2019](#) and [May 16, 2019](#); and

- The description of our Common Stock contained in our registration statement on [Form 8-A](#) filed on July 23, 2013 (Registration no. 001-36020) with the SEC, including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference all additional documents that we file with the SEC under the terms of Section 13(a), 13(c), 14 or 15(d) of the Exchange Act that are made after the initial filing date of the registration statement of which this prospectus supplement and the accompanying prospectus is a part and the effectiveness of the registration statement, as well as between the date of this prospectus supplement and the termination of any offering of securities offered by this prospectus supplement and the accompanying prospectus. We are not, however, incorporating, in each case, any documents or information that we are deemed to furnish and not file in accordance with SEC rules

You may request a copy of any or all of the documents incorporated by reference but not delivered with this prospectus, at no cost, by writing or telephoning us at the following address and number: Onconova Therapeutics, Inc., 375 Pheasant Run, Newtown, Pennsylvania, 18940, (267) 759-3680, Attention: Suzanne Hutchison. We will not, however, send exhibits to those documents, unless the exhibits are specifically incorporated by reference in those documents.

We make available free of charge on our website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports, as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission, or SEC. You may obtain a free copy of these reports on our website, www.onconova.com.

PROSPECTUS



Onconova Therapeutics, Inc.

\$84,546,394

Common Stock, Preferred Stock,
Debt Securities, Warrants and Units
and

1,671 Shares of Common Stock Offered by Selling Stockholders

This prospectus covers our offer and sale from time to time of any combination of common stock, preferred stock, debt securities, warrants or units described in this prospectus in one or more offerings. This prospectus provides a general description of the securities we may offer and sell. Each time we offer and sell securities we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement will also describe the specific manner in which we will offer the securities and may also add, update or change information contained in this prospectus. The aggregate offering price of all securities sold by us under this prospectus may not exceed \$84,546,394.

In addition, the selling stockholders to be named in the applicable prospectus supplement may offer and sell up to an aggregate of 1,671 shares of our common stock from time to time, in amounts, at prices and on terms that will be determined at the time the shares of our common stock are offered. The prospectus supplement may also add, update or change information contained in this prospectus. We will not receive proceeds from the sale of shares of our common stock by the selling stockholders.

You should read this prospectus and any supplement carefully before you purchase any of our securities. **This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement.**

The securities may be offered and sold by us or the selling stockholders from time to time at fixed prices, at market prices or at negotiated prices, and may be offered and sold to or through one or more underwriters, dealers or agents or directly to purchasers on a continuous or delayed basis. See “Plan of Distribution.”

Our common stock is currently listed on the Nasdaq Capital Market under the symbol “ONTX.” On December 20, 2017, the last reported sale price of our common stock on the Nasdaq Capital Market was \$1.50 per share.

As of December 20, 2017, the aggregate market value of our outstanding common stock held by non-affiliates, or the public float, was \$21,659,846 which was calculated based on shares of our outstanding common stock held by non-affiliates and on a price of \$2.35 per share, the last reported sale price for our common stock, on October 24, 2017. During the 12 calendar month period that ends on, we have offered securities with an aggregate market value of approximately \$7,409,115 pursuant to General Instruction I.B.6 of Form S-3.

You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized any other person to provide you with different information.

Investing in these securities involves risks, including those set forth in the “Risk Factors” section of the applicable prospectus supplement and any related free writing prospectus and of our most recent Annual Report on Form 10-K, as revised or supplemented by our Quarterly Reports on Form 10-Q filed with the SEC since the filing of our most recent Annual Report on Form 10-K, each of which is incorporated by reference into this prospectus.

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

This prospectus is dated December 28, 2017.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC. This prospectus covers the primary offering by us of up to an aggregate offering price of \$84,546,394 of securities. In addition, under this prospectus, the selling stockholders, to be named in a prospectus supplement to this prospectus, may, from time to time, offer and sell up to an aggregate 1,671 shares of our common stock in one or more offerings. We may offer and sell any combination of the securities described in this prospectus and the selling stockholders may offer and sell shares of common stock in one or more offerings. This prospectus provides you with a general description of the securities we may offer and sell. Each time we offer and sell securities under this prospectus, we will provide a prospectus supplement that will contain 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 may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading “Where You Can Find More Information,” before investing in any of the securities offered.

We have filed or incorporated by reference exhibits to the registration statement of which this prospectus forms a part. You should read the exhibits carefully for provisions that may be important to you.

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

Neither we nor any selling stockholder has authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying supplement to this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or any accompanying prospectus supplement. This prospectus and any accompanying supplement to this prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and any accompanying supplement to this prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any document we file with the SEC at the SEC’s public reference room at 100 F Street NE, Room 1580, Washington, D.C. 20549. You may obtain information on the operation of the SEC’s public reference facilities by calling the SEC at 1-800-SEC-0330. You can request copies of these documents, upon payment of a duplicating fee, by writing to the SEC at its principal office at 100 F Street NE, Room 1580, Washington, D.C. 20549-1004. The SEC maintains an Internet website at <http://www.sec.gov> that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. Our SEC filings are accessible through the Internet at that website. Our reports on Forms 10-K, 10-Q and 8-K, and amendments to those reports, are also available for download, free of charge, as soon as reasonably practicable after these reports are filed with the SEC, at our website at www.onconova.com. The content contained in, or that can be accessed through, our website is not a part of this prospectus.

Unless the context indicates otherwise, as used in this prospectus, the terms “Onconova,” “Onconova Therapeutics,” “Company,” “we,” “us” and “our” refer to Onconova Therapeutics, Inc. and its consolidated subsidiaries.

INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below:

- Our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2016 that we filed with the SEC on March 29, 2017, including the information required by Part III, Items 10 through 14, of Form 10-K, which is incorporated by reference to our definitive [proxy statement for our 2017 annual meeting of stockholders filed on April 12, 2017](#);
- Our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017, June 30, 2017 and September 30, 2017 that we filed with the SEC on [May 15, 2017](#), [August 14, 2017](#) and [November 9, 2017](#), respectively;
- Our Current Reports on Form 8-K filed with the SEC on [April 20, 2017](#), [April 24, 2017](#), [May 18, 2017](#), [May 25, 2017](#), [August 18, 2017](#), [November 13, 2017](#) and [November 17, 2017](#);
- The description of our common stock contained in our registration statement on [Form 8-A](#) filed on July 23, 2013 (Registration no. 001-36020) with the SEC, including any amendment or report filed for the purpose of updating such description;
- All documents filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is a part and prior to the effectiveness of such registration statement; and
- All documents filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and before we stop offering the securities under this prospectus.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon his or her written or oral request, a copy of any or all documents referred to above which have been or may be incorporated by reference into this prospectus but not delivered with this prospectus excluding exhibits to those documents unless they are specifically incorporated by reference into those documents. You can request those documents from us, at no cost, by writing or telephoning us at: Onconova Therapeutics, Inc., 375 Pheasant Run, Newtown, Pennsylvania, 18940, (267) 759-3680, Attention: Suzanne Hutchison.

The most recent information that we file with the SEC automatically updates and supersedes older information. The information contained in any such filing will be deemed to be a part of this prospectus, commencing on the date on which the filing is made.

Information furnished under Items 2.02 or 7.01 (or corresponding information furnished under Item 9.01 or included as an exhibit) in any past or future Current Report on Form 8-K that we file with the SEC, unless otherwise specified in such report, is not incorporated by reference in this prospectus.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain, and any prospectus supplement may 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. All statements, other than statements of historical facts, included or incorporated in this prospectus or any prospectus supplement regarding our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. We may, in some cases, use terms such as “believes,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should,” “approximately” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements appear in a number of places throughout this prospectus and the documents incorporated by reference herein, and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, protection of our intellectual property portfolio, the degree of clinical utility of our products, particularly in specific patient populations, our ability to develop commercial and manufacturing functions, expectations regarding clinical trial data, our results of operations, cash needs, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus and in documents incorporated by reference herein, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this prospectus.

Actual results could differ materially and adversely from our forward-looking statements due to a number of factors, including, without limitation, risks related to:

- our need for additional financing for our INSPIRE trial and other operations, and our ability to obtain sufficient funds on acceptable terms when needed, and our plans and future needs to scale back operations if adequate financing is not obtained;
- our ability to continue as a going concern;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the success and timing of our preclinical studies and clinical trials, including site initiation and patient enrollment, and regulatory approval of protocols for future clinical trials;
- our ability to enter into, maintain and perform collaboration agreements with other pharmaceutical companies, for funding and commercialization of our clinical product candidates or preclinical compounds, and our ability to achieve certain milestones under those agreements;
- the difficulties in obtaining and maintaining regulatory approval of our product candidates, and the labeling under any approval we may obtain;
- our plans and ability to develop, manufacture and commercialize our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any of our product candidates;

- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;
- the successful development of our commercialization capabilities, including sales and marketing capabilities;
- recently enacted and future legislation and regulation regarding the healthcare system;
- the success of competing therapies and products that are or become available;
- our ability to maintain the listing of our Common Stock on a national securities exchange;
- the potential for third party disputes and litigation;
- the performance of third parties, including contract research organizations (“CROs”) and third-party manufacturers; and
- our expectations regarding CRO transition.

Any forward-looking statements that we make in this prospectus and the documents incorporated by reference herein speak only as of the date of such statement, and we undertake no obligation to update such statements whether as a result of any new information, future events, changed circumstances or otherwise. Comparisons of results for current and any prior periods are not intended to express any future trends or indications of future performance, unless expressed as such, and should only be viewed as historical data.

You should also read carefully the factors described in the “Risk Factors” section of this prospectus and in documents incorporated by reference herein, to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus and in documents incorporated by reference herein will prove to be accurate. 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 timeframe, or at all.

We obtained the industry, market and competitive position data in this prospectus and in documents incorporated by reference herein from our own internal estimates and research as well as from industry and general publications and research surveys and studies conducted by third parties. Industry publications and surveys generally state that the information contained therein has been obtained from sources believed to be reliable. We believe this data is accurate in all material respects as of the date of this prospectus.

RISK FACTORS

Our business is influenced by many factors that are difficult to predict, and that involve uncertainties that may materially affect actual operating results, cash flows and financial condition. Before making an investment decision, you should carefully consider these risks set forth in the “Risk Factors” section of our Annual Report on Form 10-K, as filed with the SEC on March 29, 2017, and our Quarterly Reports on Form 10-Q for the quarter ended September 30, 2017, as filed with the SEC on November 9, 2017, which are incorporated by reference into this prospectus, as well as any amendment or update to our risk factors reflected in subsequent filings with the SEC and any applicable prospectus supplement or any free writing prospectus. You should also carefully consider any other information we include or incorporate by reference in this prospectus. Any such risk could cause our business, financial condition or operating results to suffer. The market price of our common stock could decline if one or more of these risks and uncertainties develop into actual events. You could lose all or part of your investment.

ONCONOVA THERAPEUTICS, INC.**Overview**

We are a clinical-stage biopharmaceutical company focused on discovering and developing novel small molecule product candidates primarily to treat cancer. Using our proprietary chemistry platform, we have created a library of targeted agents designed to work against cellular pathways important to cancer cells. We believe that the product candidates in our pipeline have the potential to be efficacious in a variety of cancers. We have one Phase 3 clinical-stage product candidate and two other clinical-stage product candidates (one of which is being developed for treatment of acute radiation syndromes) and several preclinical programs. Substantially all of our current effort is focused on our lead product candidate, rigosertib. Rigosertib is being tested in an intravenous formulation as a single agent, and an oral formulation in combination with azacitidine, in clinical trials for patients with higher-risk myelodysplastic syndromes (“MDS”). The Company has and may continue to delay, scale-back, or eliminate certain of its research and development activities and other aspects of its operations until such time as the Company is successful in securing additional funding.

In December 2015, we enrolled the first patient in a randomized controlled Phase 3 clinical trial of intravenous rigosertib “rigosertib IV” in a population of patients with higher-risk MDS after failure of hypomethylating agent (“HMA”) therapy. The trial, which we refer to as INSPIRE, is expected to enroll approximately 225 patients at more than 170 sites globally. The primary endpoint of INSPIRE is overall survival.

Our net losses were \$17.9 million and \$14.2 million for the nine months ended September 30, 2017 and 2016, respectively. As of September 30, 2017, we had an accumulated deficit of \$356.1 million.

Rigosertib

Rigosertib is a small molecule which we believe blocks cellular signaling by targeting RAS effector pathways. This is believed to be mediated by the interaction of rigosertib to the RAS-binding domain (“RBD”), found in many RAS effector proteins, including the Raf and PI3K kinases. We believe this mechanism of action provides a new approach to block the interactions between RAS and its targets containing RBD sites. Rigosertib is currently being tested in clinical trials as a single agent, and in combination with azacitidine, in patients with MDS. We have enrolled more than 1,300 patients in rigosertib clinical trials for MDS and other conditions. We were a party to a license and development agreement with Baxalta (as defined below), which granted Baxalta certain rights to commercialize rigosertib in Europe. The Baxalta agreement was terminated on August 30, 2016, at which time the European rights reverted to us at no cost. We are party to a collaboration agreement with Symbio, which grants Symbio certain rights to commercialize rigosertib in Japan and Korea. We have retained development and commercialization rights to rigosertib in the rest of the world, including in the United States and Europe, although we could consider licensing commercialization rights to other territories as we continue to seek additional funding.

Rigosertib IV for higher-risk MDS

In early 2014, we announced topline survival results from our “ONTIME” trial, a multi-center Phase 3 clinical trial of rigosertib IV as a single agent versus best supportive care including low dose Ara-C. The ONTIME trial did not meet its primary endpoint of an improvement in overall survival in the intent-to-treat population, although improvements in median overall survival were observed in various pre-specified and exploratory subgroups of higher-risk MDS patients. As a result, additional clinical work is on-going.

During 2014 and 2015, we held meetings with the U.S. Food and Drug Administration (“FDA”) European Medicines Agency (“EMA”) and several European national regulatory authorities to discuss and seek guidance on a path for approval of rigosertib IV in higher-risk MDS patients whose disease had failed HMA therapy. After discussions with the FDA and EMA, we refined our patient eligibility criteria by defining what we believe to be a more homogenous patient population. After regulatory feedback, input from key opinion leaders in the U.S. and Europe and based on learnings from the ONTIME study, we designed a new randomized controlled Phase 3 trial, referred to as INSPIRE. The INSPIRE trial is enrolling higher-risk MDS patients under 82 years of age who have progressed on, relapsed, or failed to respond to, previous treatment with HMAs within nine months or nine cycles over the course of one year after initiation of HMA therapy, and had their last dose of HMA within six months prior to enrollment in the trial. The primary endpoint of this study is overall survival of all randomized patients in the intent-to-treat (“ITT”) population and the International Prognostic Scoring System- Revised (IPSS-R) Very High Risk subgroup. This randomized trial of approximately 225 patients is expected to be conducted at more than 170 sites globally.

The first patient in the INSPIRE trial was enrolled at the MD Anderson Cancer Center in December 2015, the first patient in Europe was enrolled in March, 2016, and the first patient in Japan was enrolled in July, 2016.

Enrollment for the INSPIRE Phase 3 trial for second-line higher-risk MDS patients is highly selective and required us to search extensively to identify appropriate candidates meeting the stringent entry criteria. Accordingly, this trial has been opened at more than 175 sites on four continents. Our partner, SymBio Pharmaceuticals, has opened more than 30 sites in Japan for the INSPIRE protocol. As of October 31, 2017, the trial is active at approximately 170 sites in 22 countries. The selection of countries and trial sites is carefully undertaken to ensure availability of appropriate patients meeting eligibility criteria. Since these criteria are purposely designed to be narrow and selective, extensive screening and trial site education is integral to our plan. INSPIRE trial outcome is measured by overall survival and includes a pre-planned interim analysis which is triggered by 88 events (deaths). The timing of interim analysis is difficult to precisely define. Based on our statistical analysis plan, the enrollment rate, and the expected survival in a comparable patient subgroup from the ONTIME trial, we expect the interim analysis to occur late in the fourth quarter of 2017. The interim analysis involves an initial analysis of efficacy by an independent statistical consultant. These results will be submitted to the independent data monitoring committee (DMC). The interim analysis may result in the trial stopping due to futility, trial continuation as planned without any changes, or continuation with changes according to the preset criteria for trial expansion or continued randomization only for the Very High Risk subgroup. The adaptive design element has been reviewed by regulatory agencies in the US and Europe. The actual timing of the interim analysis and its outcome will permit better estimates for complete enrollment and top-line analysis. Since the date of the interim analysis is tied to the unpredictability of reaching a pre-identified number of death events, the precise time of completing the interim analysis, which will be roughly a couple of weeks after reaching the number of events, cannot be forecast precisely, and could occur early next year.

In an attempt to optimize enrollment, we have taken proactive measures to increase enrollment including the addition of trial sites in three new countries, replacement of the principal CRO and addition of another CRO to our trial management group. Due to these changes full enrollment may take longer than initially expected. Since the interim analysis could potentially change the required number of patients to be randomized for the trial, a better estimate of these timelines can be provided after this analysis is completed. Should enrollment not return to desired levels, full enrollment may be delayed even if the adaptive design is not required as per the statistical analysis plan.

As called for in the INSPIRE Charter, the DMC has previously conducted two periodic safety reviews, and after each review, the trial continued per plan.

Safety and Tolerability of rigosertib in MDS and other hematologic malignancies

A comprehensive analysis of IV and oral rigosertib safety in patients with Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML) was presented in December 2016 at the American Society of Hematology (ASH) Annual Meeting. The most commonly reported treatment-emergent adverse events (TEAEs) in $\geq 10\%$ of patients with MDS/AML receiving rigosertib intravenous (IV) monotherapy were fatigue (33%), nausea (33%), diarrhea (27%), constipation (25%), anaemia (24%) and pyrexia (24%). The most common \geq Grade 3 AEs were anaemia (21%), febrile neutropenia (13%), pneumonia (12%) and thrombocytopenia (11%). The most common serious AEs were febrile neutropenia (10%), pneumonia (9%), and sepsis (7%). The most common AEs leading to discontinuation of IV rigosertib were sepsis and pneumonia (3% each).

Rigosertib oral in combination with azacitidine for higher-risk MDS

In December 2016, at the American Society of Hematology (ASH) Annual Meeting, we presented Phase 1/2 data from an oral rigosertib and azacitidine combination trial in higher-risk MDS. 33 of 40 MDS patients enrolled were evaluable for response at the time of the analysis. The median age of patients was 66, with 73% being male. The IPSS-R distribution was: 7.5% Low, 12.5% Intermediate, 37.5% High, 32.5% Very High and 10% unknown. 76% of patients responded per 2006 International Working Group (IWG) criteria. Responses were as follows:

Response per IWG 2006

	Overall Evaluable (N=33)	No prior HMA (N=20)	Prior HMA (N=13)
Complete remission (CR)	8 (24)%	7 (35)%	1 (8)%
Marrow CR + hematologic improvement	10 (30)%	6 (30)%	4 (31)%
Marrow CR alone	6 (18)%	3 (15)%	3 (23)%
Hematologic improvement alone	1 (3)%	1 (5)%	0
Stable disease	8 (24)%	3 (15)%	5 (38)%
Overall IWG response	25 (76)%	17 (85)%	8 (62)%
Clinical benefit response	19 (58)%	14 (70)%	5 (38)%

The median duration of response was 8 months for CR, 12.3 months for marrow CR.

Safety/Tolerability of the Combination:

Oral rigosertib (560 mg qAM, 280 mg qPM) was administered on Day 1-21 of a 28-day cycle. Azacitidine 75 mg/m²/day SC or IV was administered for 7 days starting on Day 8. The combination of oral rigosertib and azacitidine was well tolerated. The most common TEAEs in ≥ 10% of patients were nausea (41%), fatigue (39%), diarrhea (37%), constipation (37%) and dysuria (28%). The most common serious AEs were pneumonia (11%) and febrile neutropenia (7%). The most common AEs leading to discontinuation were AML (4%) and pneumonia (4%).

Next steps for rigosertib oral in combination with azacitidine for higher-risk MDS

Following an end of Phase 2 meeting with the Food and Drug Administration (FDA) in September 2016, we began development of a Phase 3 protocol. The Phase 3 trial will be designed as a global 1:1 randomized, placebo-controlled trial of oral rigosertib plus azacitidine compared to azacitidine plus placebo. Based on the results of the Phase 1/2 Study, we plan to use the full dose of azacitidine, as defined in the product insert. The patient population studied in this trial will be first-line (HMA naïve) higher-risk MDS patients. The primary endpoint for assessment of efficacy will be the composite Response Rate of complete remission (CR) + partial remission (PR,) as per the IWG 2006 Response Criteria. Formal FDA review will be sought via the Special Protocol Assessment (SPA) mechanism. We will not commence the Phase 3 trial without additional financing.

While the Phase 3 trial is being designed, we have expanded the Phase 1/2 trial cohort by up to 40 subjects. Under a protocol expansion, we plan to use the expanded cohorts to explore dose optimization by increasing the dose of rigosertib and varying the dose administration scheme of rigosertib oral to identify an optimal dose and schedule. After amendments were filed with the regulatory agencies, we started the expansion phase of this trial in the U.S. sites that participated in the initial trial. The first patient was enrolled in April and since then, more than half of the planned patients have been enrolled in the expansion trial. We plan to add more sites in the U.S. to complete enrollment of the expanded trial.

In June 2017, at the Congress of the European Hematology Association Meeting, we updated the data from the Phase 1/2 trial and highlighted results in AML patients included in this study. Response data was presented on eight evaluable patients with AML who were tested with the rigosertib and azacitidine combination. For the eight evaluable patients with AML, the combination was well tolerated and the safety profile was similar to single-agent azacitidine, based on safety information in the azacitidine FDA approved label. Based on the presented results of the combination studies, the authors

concluded that continued study in AML was warranted. We will not commence further development of rigosertib oral in combination with azacitidine for AML without additional financing.

Rigosertib oral for lower-risk MDS

Higher-risk MDS patients suffer from a shortfall in normal circulating blood cells, or cytopenias, as well as elevated levels of cancer cells, or blasts in their bone marrow and sometimes in their peripheral blood. Lower-risk MDS patients suffer mainly from cytopenias, that is low levels of red blood cells, white blood cells or platelets. Thus, lower-risk MDS patients depend on transfusions and growth factors or other therapies to improve their low blood counts.

We have explored single agent rigosertib oral as a treatment for lower-risk MDS in two Phase 2 clinical trials, 09-05 and 09-07. In December 2013, we presented data at the Annual ASH Meeting from the 09-05 Phase 2 trial. To date, Phase 2 clinical data has indicated that further study of single agent oral rigosertib in transfusion-dependent, lower-risk MDS patients is warranted. Rigosertib has been generally well tolerated, except for urinary side effects at higher dose levels. Future clinical trials will be needed to evaluate dosing and schedule modifications and their impact on efficacy and safety results of oral rigosertib in lower-risk MDS patients.

Data presented from the 09-05 trial also suggested the potential of a genomic methylation assessment of bone marrow cells to prospectively identify lower-risk MDS patients likely to respond to oral rigosertib. We therefore expanded the 09-05 trial by adding an additional cohort of 20 patients to advance the development of this genomic methylation test. To date, a biomarker which would predict response has not been identified. Further testing and development of oral rigosertib for lower-risk MDS will be required. We will not commence further development of rigosertib oral for lower-risk MDS without additional financing.

Safety and Tolerability of rigosertib oral in MDS and other hematologic malignancies

Oral rigosertib as a monotherapy was evaluated in four Phase 1 and 2 studies in MDS and other hematologic malignancies. One study is completed and a clinical study report is available. The most common TEAEs in $\geq 10\%$ of patients were pollakiuria (increased urinary frequency) (35%), fatigue (32%), diarrhea (26%), dysuria (29%) and haematuria (24%). The most common \geq Grade 3 AEs were anaemia (17%), thrombocytopenia (5%), haematuria (4%) and urinary tract infection (4%). The most common serious AE was pneumonia (6%). The most common AEs leading to discontinuation of patients receiving oral rigosertib as monotherapy were dysuria (8%), urinary tract pain (7%), haematuria (5%) and urinary frequency (5%).

In addition to the above described clinical trials, we are continuing the preclinical and chemistry, manufacturing, and control work for IV and oral rigosertib.

Other Programs

The vast majority of the Company's efforts are now devoted to the advanced stage development of rigosertib for unmet medical needs of MDS patients. Other programs are either paused, inactive or require only minimal internal resources and efforts.

Briciclib

Briciclib, another of our product candidates, is a small molecule targeting an important intracellular regulatory protein, Cyclin D1, which is often found at elevated levels in cancer cells. Cyclin D1 expression is regulated through a process termed cap-dependent translation, which requires the function of eukaryotic initiation factor 4E protein. In vitro evidence indicates briciclib binds to eukaryotic initiation factor 4E protein, blocking cap-dependent translation of Cyclin D1 and other cancer proteins, such as c-MYC, leading to tumor cell death. We have been conducting a Phase 1 multi-site dose-escalation trial of briciclib in patients with advanced solid tumors refractory to current therapies. Safety and efficacy assessments are complete in six of the seven dose-escalation cohorts of patients in this trial. As of December 2015, the Investigational New Drug ("IND") for briciclib is on full clinical hold following a drug product lot testing failure. We will be required to undertake appropriate remedial actions prior to re-initiating the clinical trial and completing the final dose-escalation cohort.

Recilisib

Recilisib is a product candidate being developed in collaboration with the U.S. Department of Defense for acute radiation syndromes. We have completed four Phase 1 trials to evaluate the safety and pharmacokinetics of recilisib in healthy

human adult subjects using both subcutaneous and oral formulations. We have also conducted animal studies and clinical trials of recilisib under the FDA's Animal Rule, which permits marketing approval for new medical countermeasures for which conventional human efficacy studies are not feasible or ethical, by relying on evidence from adequate and well-controlled studies in appropriate animal models to support efficacy in humans when the results of those studies establish that the drug is reasonably likely to produce a human clinical benefit. Human safety data, however, is still required. Ongoing studies of recilisib, focusing on animal models and biomarker development to assess the efficacy of recilisib are being conducted by third parties with government funding. We anticipate that any future development of recilisib beyond these ongoing studies would be conducted solely with government funding or by collaboration. Use of government funds to finance the research and development in whole or in part means any future effort to commercialize recilisib will be subject to federal laws and regulations on U.S. government rights in intellectual property. Additionally, we are subject to laws and regulations governing any research contracts, grants, or cooperative agreements under which government funding was provided.

Preclinical Product Candidates

In addition to our three clinical-stage product candidates, we have several product candidates that target kinases, cellular metabolism or cell division in preclinical development. We may explore additional collaborations to further the development of these product candidates as we focus internally on our more advanced programs.

Positive preclinical data was announced at the American Association for Cancer Research (AACR) annual meeting, which took place April 1-5 in Washington, DC, for ON 123300, a first-in-class dual inhibitor of CDK4/6 + ARK5, and for ON 150030, a novel Type 1 inhibitor of FLT3 and Src pathways. We believe our CDK inhibitor is differentiated from other agents in the market (Palbociclib, Ribociclib and Abemaciclib) or in development (such as the compounds being developed by G1 Therapeutics) by its dual inhibition of CDK4/6 + ARK5. We continue to carry out research to enhance the pre-clinical data package for this compound in an attempt to seek partners for co-development of this novel compound.

In a preclinical Rb+ve xenograft model for breast cancer, ON 123300 activity was shown to be similar to Palbociclib (Pfizer's Ibrance®). Moreover, based on the same preclinical model, the new molecule may have the potential advantage of reduced neutropenia when compared to Palbociclib. Whereas both compounds resulted in decreased RBC and platelet counts in this preclinical model system, Palbociclib was found to have a more prominent and statistically significant ($P < 0.05$) inhibitory effect on neutrophil counts when compared to ON 123300.

CORPORATE INFORMATION

We were incorporated in Delaware in December 1998 and commenced operations in January 1999. Our principal executive offices are located at 375 Pheasant Run, Newtown, Pennsylvania 18940, and our telephone number is (267) 759-3680. Our website address is www.onconova.com. The information on, or that can be accessed through, our website is not part of this prospectus.

USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, we anticipate that the net proceeds from our sale of any securities will be used to fund the development of our clinical and preclinical programs, for other research and development activities and for general corporate purposes, which may include capital expenditures and funding our working capital needs. We expect from time to time to evaluate the acquisition of businesses, products and technologies for which a portion of the net proceeds may be used, although we currently are not planning or negotiating any such transactions. Pending such uses, we may invest the net proceeds in investment grade interest-bearing securities.

The amounts actually expended for each purpose may vary significantly depending upon numerous factors, including the amount and timing of the proceeds from this offering and progress with our clinical development programs. Expenditures will also depend upon the establishment of collaborative arrangements with other companies, the availability of additional financing and other factors. Investors will be relying on the judgment of our management regarding the application of the proceeds of any sale of securities.

In the case of sales by selling stockholders, we will not receive any of the proceeds of such sales.

DESCRIPTION OF SECURITIES

We may offer shares of our common stock and preferred stock, various series of debt securities, warrants or units to purchase any of such securities, with a total value of up to \$84,546,394, from time to time in one or more offerings under this prospectus at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities that we may offer. In connection with each offering, we will provide a prospectus supplement that will describe the specific amounts, prices and terms of the securities being offered, including, to the extent applicable:

- designation or classification;
- aggregate offering price;
- rates and times of payment of dividends;
- redemption, conversion or exchange terms;
- conversion or exchange prices or rates and 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;
- restrictive covenants;
- voting or other rights; and
- important federal income tax considerations.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement will offer a security that is not included in the Registration Statement at the time of its effectiveness or offer a security of a type that is not described in this prospectus.

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

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 75,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share. As of December 20, 2017, 10,771,163 shares of our common stock, and no shares of our preferred stock, were outstanding.

Common Stock

Subject to the preferences that may be applicable to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that may be declared by our board of directors out of funds legally available for that purpose. Holders of our common stock are entitled to one vote for each share on all matters voted on by stockholders, including the election of directors. Holders of our common stock do not have any conversion, redemption, sinking fund or preemptive rights. In the event of our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in any assets remaining after the satisfaction in full of the prior rights of creditors and the aggregate liquidation preference of any preferred stock then outstanding. 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 preferred stock that we may designate and issue in the future. All outstanding shares of our common stock are, and any shares of common stock that we may issue in the future will be, fully paid and non-assessable.

Preferred Stock

We may issue any class of preferred stock in any series. Our board of directors has the authority, subject to limitations

prescribed under Delaware law, to issue preferred stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations and restrictions. Our board of directors can also increase or decrease the number of shares of any series, but not below the number of shares of that series then outstanding. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of our company and may adversely affect the market price of our common stock and the voting and other rights of the holders of common stock.

Delaware Anti-Takeover Law and Provisions in Our Certificate of Incorporation and Bylaws

Delaware Anti-Takeover Law

We are subject to Section 203 of the Delaware General Corporation Law. Section 203 generally prohibits a public Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years after the date of the transaction in which the person became an interested stockholder, unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon 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 specified shares; or
- at or subsequent to the date of the transaction, 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 66²/3% of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a “business combination” to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, lease, exchange, mortgage, pledge, transfer or other disposition of 10% or more of the assets of the corporation to or with the interested stockholder;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, 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 stockholder” as any person that is:

- the owner of 15% or more of the outstanding voting stock of the corporation;
- an affiliate or associate of the corporation who was the owner of 15% or more of the outstanding voting stock of the corporation at any time within three years immediately prior to the relevant date; or
- the affiliates and associates of the above.

Under specific circumstances, Section 203 makes it more difficult for an “interested stockholder” to effect various business combinations with a corporation for a three-year period, although the stockholders may, by adopting an amendment to the

corporation's certificate of incorporation or bylaws, elect not to be governed by this section, effective 12 months after adoption.

Our Tenth Amended and Restated Certificate of Incorporation, as amended, or our "certificate of incorporation," and our Amended and Restated Bylaws, or our "bylaws," do not exclude us from the restrictions of Section 203. We anticipate that the provisions of Section 203 might encourage companies interested in acquiring us to negotiate in advance with our board of directors since the stockholder approval requirement would be avoided if a majority of the directors then in office approve either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder.

Certificate of Incorporation and Bylaws

Provisions of our certificate of incorporation and bylaws may delay or discourage transactions involving an actual or potential change of control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our certificate of incorporation and bylaws will:

- permit our board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that all vacancies on our board of directors, including as a result of newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- not provide for cumulative voting rights, thereby allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election; and
- provide that special meetings of our stockholders may be called only by the board of directors or by such person or persons requested by a majority of the board of directors to call such meetings.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Wells Fargo Shareowner Services.

Listing

Our common stock is listed on the Nasdaq Capital Market under the symbol "ONTX."

DESCRIPTION OF DEBT SECURITIES

This prospectus describes certain general terms and provisions of our debt securities. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. The following description of debt securities will apply to the debt securities offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of debt securities may specify different or additional terms.

We may offer under this prospectus up to \$84,546,394 aggregate principal amount of secured or unsecured debt securities, or if debt securities are issued at a discount, or in a foreign currency or composite currency, such principal amount as may be sold for an initial public offering price of up to \$84,546,394. The debt securities may be either senior debt securities, senior

subordinated debt securities or subordinated debt securities. The debt securities offered hereby will be issued under an indenture between us and a trustee. A form of indenture, which will be qualified under, subject to, and governed by, the Trust Indenture Act of 1939, as amended, is filed as an exhibit to the registration statement.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and detailed or determined in the manner provided in a board of directors' resolution, an officers' certificate or by an indenture. The particular terms of each series of debt securities will be described in a prospectus supplement relating to the series, including any pricing supplement.

We can issue debt securities that may be in one or more series with the same or various maturities, at par, at a premium or at a discount. We will set forth in a prospectus supplement, including any pricing supplement, relating to any series of debt securities being offered, the initial offering price, the aggregate principal amount and the following terms of the debt securities:

- the title of the debt securities;
- the price or prices (expressed as a percentage of the aggregate principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which we will pay the principal on the debt securities;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where the principal of, and premium and interest on, the debt securities will be payable;
- the terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities;
- the dates on which and the price or prices at which we will repurchase the debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities;
- the designation of the currency, currencies or currency units in which payment of principal of, and premium and interest on, the debt securities will be made;
- if payments of principal of, and premium or interest on, the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, and premium or interest on, the debt securities will

be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;

- any provisions relating to any security provided for the debt securities;
- any addition to or change in the events of default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any other terms of the debt securities, which may modify or delete any provision of the indenture as it applies to that series; and
- any depositories, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities.

We may issue debt securities that are exchangeable and/or convertible into shares of our common stock or any class or series of preferred stock. The terms, if any, on which the debt securities may be exchanged and/or converted will be set forth in the applicable prospectus supplement. Such terms may include provisions for conversion, either mandatory, at the option of the holder or at our option, in which case the number of shares of common stock, preferred stock or other securities to be received by the holders of debt securities would be calculated as of a time and in the manner stated in the prospectus supplement.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Payment of Interest and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, as Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a book-entry debt security), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a certificated debt security), as described in the applicable prospectus supplement.

Certificated Debt Securities

You may transfer or exchange certificated debt securities at the trustee's office or paying agencies in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

You may transfer certificated debt securities and the right to receive the principal of, and premium and interest on, certificated debt securities only by surrendering the old certificate representing those certificated debt securities and either we or the trustee will reissue the old certificate to the new holder or we or the trustee will issue a new certificate to the new holder.

Book-Entry Debt Securities

We may issue the debt securities of a series in the form of one or more book-entry debt securities that would be deposited with

a depositary or its nominee identified in the prospectus supplement. We may issue book-entry debt securities in either temporary or permanent form. We will describe in the prospectus supplement the terms of any depositary arrangement and the rights and limitations of owners of beneficial interests in any book-entry debt security.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase debt securities, common stock, preferred stock or other securities or any combination of the foregoing. We may issue warrants independently or together with other securities. Warrants sold with other securities may be attached to or separate from the other securities. We will issue warrants under one or more warrant agreements between us and a warrant agent that we will name in the prospectus supplement.

The prospectus supplement relating to any warrants that we may offer will include specific terms relating to the offering. We will file the form of any warrant agreement with the SEC, and you should read the warrant agreement for provisions that may be important to you. The prospectus supplement will include some or all of the following terms:

- the title of the warrants;
- the aggregate number of warrants offered;
- the designation, number and terms of the debt securities, common stock, preferred stock or other securities purchasable upon exercise of the warrants, and procedures by which those numbers may be adjusted;
- the exercise price of the warrants;
- the dates or periods during which the warrants are exercisable;
- the designation and terms of any securities with which the warrants are issued;
- if the warrants are issued as a unit with another security, the date, if any, on and after which the warrants and the other security will be separately transferable;
- if the exercise price is not payable in U.S. dollars, the foreign currency, currency unit or composite currency in which the exercise price is denominated;
- any minimum or maximum amount of warrants that may be exercised at any one time;
- any terms, procedures and limitations relating to the transferability, exchange, exercise, amendment or termination of the warrants; and
- any adjustments to the terms of the warrants resulting from the occurrence of certain events or from the entry into or consummation by us of certain transactions.

As of November 17, 2017, we had (i) non-tradable warrants with an expiration date of July 2021 to purchase 96,842 shares of common stock at an exercise price of \$11.50 per share, (ii) tradable warrants with an expiration date of July 2021 to purchase 3,192,022 shares of common stock at an exercise price of \$4.92 per share and (iii) non-tradable pre-funded warrants with an expiration date of July 2023 to purchase 5,907 shares of common stock at an exercise price of \$0.01 per share. Our tradable warrants are traded on the Nasdaq Capital Market under the symbol "ONTXW."

DESCRIPTION OF UNITS

As specified in any applicable prospectus supplement, we may issue units consisting of one or more warrants, debt securities, shares of preferred stock, shares of common stock or any combination of such securities.

SELLING STOCKHOLDERS**Selling Stockholders for the Secondary Offering of up to 1,671 Shares of Common Stock**

This prospectus also relates to the possible resale by certain of our stockholders of up to an aggregate of 1,671 shares of our common stock which were previously acquired by such stockholders through several private placements of our preferred stock completed by us prior to our initial public offering, which were all converted to shares of our common stock in connection with our initial public offering. In connection with such private placements, these persons have registration rights with respect to their shares as described further below under the heading “Certain Relationships and Related Party Transactions.”

Unless otherwise indicated, the selling stockholders have sole voting and investment power with respect to their shares of common stock. All of the information contained in the table below is based solely upon information provided to us by the selling stockholders or otherwise known by us. In addition to the shares offered hereby, the selling stockholders may otherwise beneficially own our shares of common stock as a result of, among others, open market purchases, which information is not obtainable by us without undue effort and expense. The selling stockholders may have sold, transferred or otherwise disposed of, or may sell, transfer or otherwise dispose of, at any time or from time to time since the date on which the information regarding the shares beneficially owned was last known by us, all or a portion of the shares beneficially owned in transactions exempt from the registration requirements of the Securities Act.

The number of shares outstanding and the percentages of beneficial ownership are based on 10,771,163 shares of our common stock outstanding as of December 20, 2017.

For the purposes of the following table, the number of shares of our common stock beneficially owned has been determined in accordance with Rule 13d-3 under the Exchange Act, and such information is not necessarily indicative of beneficial ownership for any other purpose. Under Rule 13d-3, beneficial ownership includes any shares as to which a selling stockholder has sole or shared voting power or investment power and also any shares which that selling stockholder has the right to acquire within 60 days of the date of this prospectus through the exercise of any stock option.

of Selling Stockholder	Number of Shares Beneficially Owned Prior to the Offering	Number of Shares Offered	Number of Shares Beneficially Owned After the Offering	% of Common Stock Beneficially Owned After the Offering
DKG Leasing-2000 LLC	119	119	0	0
Kathryn Jane McDonald	19	19	0	0
Utkarsh Palnitkar	1,533	1,533	0	0

Certain Relationships and Related Party Transactions

We entered into an Eighth Amended and Restated Stockholders’ Agreement on July 27, 2012, with certain holders of our common and preferred stock. Under the stockholders’ agreement, holders of shares of our preferred stock have been granted registration rights with respect to the shares of common stock issued upon conversion as further described below.

Demand Registration Rights

At any time, the holders of 25% or more of the shares having demand registration rights may request that we register all or a portion of their shares of common stock. We will effect the registration as requested, unless, in the good faith judgment of our board of directors, such registration would be materially detrimental to us and our stockholders and should be delayed. We have the right to defer the filing of such registration statement once for up to 120 days during any 12-month period. We are not obligated to file a registration statement pursuant to this provision on more than two occasions. In addition, when we are eligible for the use of Form S-3, or any successor form, holders of a majority of the shares having demand registration rights may make unlimited requests that we register all or a portion of their common stock for sale under the Securities Act on Form

S-3, or any successor form, so long as the aggregate price to the public in connection with any such offering is at least \$500,000. However, we are not obligated to file a Form S-3 pursuant to this provision on more than two occasions in any 12-month period.

Piggyback Registration Rights

In addition, if at any time we register any shares of our stock, the holders of all shares having registration rights are entitled to notice of the filing of the applicable registration statement and to include all or a portion of their common stock in the registration.

The secondary offering of up to 1,671 shares of our common stock is being made pursuant to the exercise of these piggyback registration rights.

Other Provisions

In the event that any registration in which the holders of registrable shares participate pursuant to the stockholders' agreement is an underwritten public offering, the number of registrable shares to be included may, in specified circumstances, be limited due to market conditions. The number of registrable shares to be excluded from registration pursuant to the above shall not be reduced below 20% of the shares to be offered.

We will pay all registration expenses, other than underwriting discounts and selling commissions, and the reasonable fees and expenses, other than underwriting discounts and selling commissions, and the reasonable fees and expenses of a single special counsel for the selling stockholders, related to any demand or piggyback registration.

PLAN OF DISTRIBUTION

We and/or the selling stockholders, if applicable, may sell the securities in one or more of the following ways (or in any combination) from time to time:

- to or through one or more underwriters or dealers in a public offering and sale by them;
- directly to a limited number of purchasers or to a single purchaser;
- through agents;
- through block trades in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction; or
- in any manner, as provided in the applicable prospectus supplement.

Each time we offer and sell securities under this prospectus, we will file a prospectus supplement. The prospectus supplement will state the terms of the offering of the securities, including:

- the name or names of any underwriters, dealers or agents;
- the purchase price of such securities and the proceeds to be received by us, if any;
- any underwriting discounts or agency fees and other items constituting underwriters' or agents' compensation;
- any public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchanges on which the securities may be listed.

Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

If we and/or the selling stockholders, if applicable, use underwriters in the sale, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including:

- negotiated transactions;
- at a fixed public offering price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to prevailing market prices; or
- at negotiated prices.

Unless otherwise stated in a prospectus supplement, the obligations of the underwriters to purchase any securities will be conditioned on customary closing conditions and the underwriters will be obligated to purchase all of such series of securities, if any are purchased.

We and/or the selling stockholders, if applicable, may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment.

We and/or the selling stockholders, if applicable, may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the 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. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

In offering the shares covered by this prospectus, the selling stockholders, and any broker-dealers and any other participating broker-dealers who may execute sales for the selling stockholders, may be deemed to be “underwriters” within the meaning of the Securities Act in connection with these sales. Any profits received by the selling stockholders and the compensation of such broker-dealers may be deemed to be underwriting discounts and commissions.

Underwriters and agents may be entitled under agreements entered into with us and/or the selling stockholders, if applicable, to indemnification by us and/or the selling stockholders, if applicable, against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the underwriters or agents may be required to make. Underwriters and agents may be customers of, engage in transactions with, or perform services for us and our affiliates in the ordinary course of business.

Each series of securities will be a new issue of securities and will have no established trading market other than the common stock which is listed on the Nasdaq Capital Market. Any underwriters to whom securities are sold for public offering and sale may make a market in the securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice. The securities, other than the common stock, may or may not be listed on a national securities exchange.

EXPERTS

The consolidated financial statements of Onconova Therapeutics, Inc. at December 31, 2016 and 2015, and for the years then ended, appearing in our Annual Report (Form 10-K) for the year ended December 31, 2016 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company’s ability to continue as a going concern as described in Note 1 to the consolidated financial statements) included therein and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Morgan, Lewis & Bockius LLP, Philadelphia, Pennsylvania.

\$5,000,000



Common Stock

PROSPECTUS SUPPLEMENT

Roth Capital Partners

May 17, 2019
