

19,551,124 Shares of Common Stock



We are offering an aggregate of 19,551,124 shares of common stock, or the Purchase Shares, at a price of \$0.445 per share, directly to certain investors pursuant to a purchase agreement between us and such investors dated January 7, 2021, or the Purchase Agreement.

The Purchase Shares are being offered and sold by us directly to the investors without a placement agent, underwriter, broker or dealer. We are not paying underwriting discounts or commissions in connection with this offering. The gross proceeds to us before expenses will be \$8,700,250. We estimate the total expenses of this offering will be approximately \$200,000.

Our common stock is listed on the Nasdaq Capital Market under the symbol "ONTX." The last reported sale price of our common stock on the Nasdaq Capital Market on January 6, 2021 was \$0.65 per share.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-3 and in the documents incorporated by reference in this prospectus supplement.

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

Delivery of the Purchase Shares is expected to be made on or about January 11, 2021, or the Closing Date, subject to the satisfaction of certain conditions set forth in the Purchase Agreement.

The date of this prospectus supplement is January 7, 2021

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the “prospectus,” we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein and therein, and any related free writing prospectus that we have authorized for use in connection with this offering.

You should rely only on the information that we have included or incorporated by reference in this prospectus supplement, the accompanying prospectus, and any related free writing prospectus that we may authorize to be provided to you. We have not 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 supplement, the accompanying prospectus, or any related free writing prospectus that we may authorize to be provided to you. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus supplement, the accompanying prospectus, or any related free writing prospectus.

This prospectus supplement, the accompanying prospectus, and any related free writing 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 supplement, the accompanying prospectus, or any related free writing 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.

You should not assume that the information contained in this prospectus supplement, the accompanying prospectus, or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference herein or therein is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus supplement, accompanying prospectus, or any related free writing prospectus is delivered, or securities are sold, on a later date.

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

Unless otherwise stated or the context requires otherwise, references in this prospectus to “Onconova,” the “company,” or the “Company,” “we,” “us,” or “our” refer to Onconova Therapeutics, Inc. and our subsidiaries, taken together. The Onconova logo and other trademarks or service marks of the Company appearing in this prospectus supplement or in the accompanying prospectus or incorporated by reference into this prospectus supplement and the accompanying prospectus are the property of Onconova Therapeutics, Inc. All other brand names or trademarks appearing in this prospectus supplement or in the accompanying prospectus or incorporated by reference into this prospectus supplement and the accompanying prospectus are the property of their respective owners.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein 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, contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein 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 supplement, the accompanying 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 supplement, the accompanying 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 from our forward-looking statements due to a number of factors, including risks related to:

- our need for additional financing for our research and development, trials 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 securities 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
- the impact of the novel coronavirus disease, COVID-19, to the global economy and capital markets, and to our business and our financial results.

Any forward-looking statements that we make in this prospectus supplement, the accompanying 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 supplement, the accompanying 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 supplement, the accompanying 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 supplement 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 supplement.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained in other parts of this prospectus supplement. Because it is only a summary, it does not contain all of the information that you should consider before investing in our securities and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus supplement, the accompanying prospectus, any applicable free writing prospectus and the documents incorporated by reference herein and therein. You should read all such documents carefully, especially the risk factors and our consolidated financial statements and the related notes included or incorporated by reference herein or therein, before deciding to buy shares of our common stock. Unless the context requires otherwise, references in this prospectus to “Onconova,” “we,” “us,” and “our” refer to Onconova Therapeutics, Inc.

Company Overview

We are a clinical-stage biopharmaceutical company focused on discovering and developing novel small molecule product candidates primarily to treat cancer. We have proprietary targeted agents designed to inhibit cellular pathways important to cancer cells. In August 2020, our Phase 3 INSPIRE trial concluded after the primary endpoint failed to demonstrate an improvement in survival. We are currently evaluating other compounds in our pipeline and potential compounds for in-licensing opportunities. We believe that the product candidates in our pipeline have the potential to be efficacious in a variety of cancers with unmet medical need. We have the following two clinical-stage programs: 1. ON 123300 in solid tumors; and 2. oral rigosertib alone or in combination with PD-1 inhibitors for treatment of KRAS-mutated solid tumors.

Our recent efforts have been primarily focused on our product candidate, rigosertib, for patients with myelodysplastic syndromes (“MDS”). Rigosertib has been tested in an intravenous formulation as a single agent for patients with relapsed/refractory higher-risk MDS (“HR-MDS”), and an oral formulation as a single agent in lower risk MDS or in combination with azacitidine for patients with newly diagnosed or refractory HR-MDS.

On August 24, 2020, we announced topline results from the INSPIRE trial, a randomized controlled Phase 3 clinical trial of intravenous rigosertib (“rigosertib IV”) in a population of patients with HR-MDS after failure of hypomethylating agent (“HMA”) therapy, which commenced in December 2015 and assessed the efficacy and safety of IV rigosertib in HR-MDS patients.

The trial did not meet its primary endpoint of improved overall survival, comparing IV rigosertib plus best supportive care to physician's choice (“PC”) plus best supportive care in patients who had progressed on, failed to respond to, or relapsed after previous treatment with an HMA within nine cycles over the course of one year after initiation of HMA treatment. A pre-specified analysis in the very high risk (“VHR-MDS”) patient subgroup was also conducted. Results of INSPIRE demonstrated that in the intent-to-treat analysis patients randomized to IV rigosertib resulted in overall survival of 6.4 months, versus 6.3 months for PC (Hazard ratio 1.13, 95% Confidence interval 0.88-1.46; p=0.33) in the HR-MDS population. Overall survival in the pre-specified VHR-MDS subgroup of patients was identical in the two study arms (5.2 months) (Hazard ratio 1.12, 95% Confidence interval 0.83-1.51; p=0.47). Safety analysis indicates that IV rigosertib was generally well tolerated, with reported adverse events similar to those observed in previous clinical studies with IV rigosertib in MDS. Serious adverse events (“SAEs”) were uncommon, with a similar profile of SAEs in both study arms.

Currently, we are conducting genomics profiling of samples from patients enrolled in the INSPIRE trial. These data may provide new insights into the prognosis of HR MDS with mutations of the RAS pathway and importantly into the future treatment of RAS-mutated diseases such as inherited Rasopathies and Ras-mutated cancers.

Based on the results of the INSPIRE trial and the previously conducted ONTIME Phase 3 trial, we currently do not plan to further pursue intravenous rigosertib for treating HR-MDS. We plan to continue to focus on the other programs in our pipeline, including oral rigosertib in KRAS mutated cancers and our novel CDK4/6 + ARK5 multi kinase inhibitor ON 123300. We will direct our efforts to these programs and are also reviewing potential in-licensing opportunities.

Our net losses were \$18.7 million and \$15.8 million for the nine months ended September 30, 2020 and 2019, respectively. As of September 30, 2020, we had an accumulated deficit of \$422.1 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 by us	19,551,124 shares.
Total common stock to be outstanding after this offering	206,694,391 shares.
Use of proceeds	We intend to use the net proceeds from this offering to for working capital and general corporate purposes. See "Use of Proceeds."
Risk factors	You should read the "Risk Factors" section of this prospectus supplement beginning on page S-3 as well as those risk factors that are incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Capital Market symbol	ONTX.

The number of shares of our common stock that will be outstanding immediately after this offering is based on 184,548,267 shares of our common stock outstanding as of September 30, 2020. This calculation excludes:

- 1,003,990 shares of Common Stock issuable upon the exercise of stock options outstanding at September 30, 2020 with a weighted average exercise price of approximately \$24.96 per share;
- 11,619,215 shares of Common Stock issuable upon the exercise of outstanding or issuable warrants at September 30, 2020 with a weighted average exercise price of approximately \$1.99 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
- 50,194 shares of Common Stock reserved for future issuance under our 2018 Equity Compensation Plan, as amended, at September 30, 2020.

Unless otherwise indicated herein, all information in this prospectus supplement, including the number of shares that will be outstanding after this offering reflects and assumes no exercise of outstanding options or warrants after September 30, 2020.

Immediately prior to the offering on January 7, 2021, the number of the Company's total outstanding shares of common stock was 187,143,267.

RISK FACTORS

An investment in our common stock or securities convertible or exercisable into our common stock involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully consider the risks described below and those discussed under the caption entitled “Risk Factors” in our Annual Reports on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference in this prospectus supplement and the accompanying prospectus, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference herein and therein, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to This Offering

We may be required to raise additional financing by issuing new securities with terms or rights superior to those of our existing securityholders, which could adversely affect the market price of shares of common Stock and our business.

We will require additional financing to fund future operations, including expansion in current and new markets, development and acquisition, capital costs and the costs of any necessary implementation of technological innovations or alternative technologies. We may not be able to obtain financing on favorable terms, if at all. If we raise additional funds by issuing equity securities, the percentage ownership of our current stockholders will be reduced, and the holders of the new equity securities may have rights superior to those of our existing securityholders, which could adversely affect the market price of common stock and the voting power of shares of common stock. If we raise additional funds by issuing debt securities, the holders of these debt securities would similarly have some rights senior to those of our existing securityholders, and the terms of these debt securities could impose restrictions on operations and create a significant interest expense for us which could have a materially adverse effect on our business.

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion with respect to the use of proceeds of this offering, including for any of the purposes described in the section of this prospectus supplement entitled “Use of Proceeds.” You will be relying on the judgment of our management regarding the application of the proceeds of this offering. The results and effectiveness of the use of proceeds are uncertain, and we could spend the proceeds in ways that you do not agree with or that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates, and cause the price of our common stock to decline.

You will experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

Since the offering price for our securities in this offering is substantially higher than the net tangible book value per share of our common stock outstanding prior to this offering, you will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the offering price of \$0.445 per share, if you purchase securities in this offering, you will suffer immediate dilution of \$0.344 per share in the net tangible book value of the common stock. See the section entitled “Dilution” below for a more detailed discussion of the dilution you will incur if you purchase shares in this offering.

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

Our business requires significant funding, and we currently invest available funds and earnings in product development. Therefore, we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We currently plan to invest all available funds and future earnings in the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of potential gain for the foreseeable future.

We may not comply with the Nasdaq continued listing requirements. If we are unable to comply with the continued listing requirements of the Nasdaq Capital Market, our common stock could be delisted, which could affect our common stock's market price and liquidity and reduce our ability to raise capital.

We are required to meet certain qualitative and financial tests to maintain the listing of our securities on the Nasdaq Capital Market.

On October 6, 2020, we received a letter from the Nasdaq Capital Market indicating that we failed to comply with the minimum bid price requirement of Nasdaq Listing Rule 5550(a)(2). Nasdaq Listing Rule 5550(a) (2) requires that companies listed on the Nasdaq Capital Market maintain a minimum closing bid price of at least \$1.00 per share.

Under Nasdaq Listing Rule 5810(c)(3)(A), we have a 180 calendar day grace period, or until April 5, 2021, to regain compliance by meeting the continued listing standard. The continued listing standard will be met if the Company's common stock has a minimum closing bid price of at least \$1.00 per share for a minimum of ten consecutive business days during the 180 calendar day grace period.

If we are not in compliance by April 5, 2021, we may be afforded a second 180 calendar day period to regain compliance. To qualify, we would be required to meet the continued listing requirement for market value of publicly held shares and all other initial listing standards for the Nasdaq Capital Market, except for the minimum bid price requirement. In addition, we would be required to notify the Nasdaq Capital Market of our intention to cure the minimum bid price deficiency during the second compliance period, by effecting a reverse stock split, if necessary.

If we do not regain compliance within the allotted compliance period(s), including any extensions that may be granted by the Nasdaq Capital Market, we will be provided notice that the Company's common stock will be subject to delisting. At that time, we may appeal the Nasdaq Staff's determination to a Nasdaq Hearings Panel.

There can be no assurance that we will be able to regain compliance with the minimum bid price requirement or will otherwise be in compliance with other the Nasdaq Capital Market listing criteria.

If we are unable to maintain compliance with the continued listing requirements of the Nasdaq Capital Market, our common stock could be delisted, making it could be more difficult to buy or sell our securities and to obtain accurate quotations, and the price of our securities could suffer a material decline. Delisting could also impair our ability to raise capital.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the securities that we are offering will be approximately \$8.5 million, based on the offering price of \$0.445 per share, after deducting estimated offering expenses payable by us.

We currently intend to use the net proceeds from the offering for working capital and general corporate purposes. Pending the use of the net proceeds, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities.

DILUTION

If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the offering price per share you will pay in this offering and the as adjusted net tangible book value per share of our common stock after this offering. Net tangible book value per share represents our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding.

As of September 30, 2020, our net tangible book value was \$12,215,000, or \$0.066 per share of common stock. After giving effect to our issuance and sale of 19,551,124 shares of common stock in this offering at the offering price of \$0.445 per share, after deducting estimated offering expenses payable by us, the as adjusted net tangible book value as of September 30, 2020 would have been \$20,715,000, or \$0.101 per share. This represents an immediate increase in as adjusted net tangible book value to existing stockholders of \$0.035 per share and an immediate dilution to new investors purchasing common stock in this offering of \$0.344 per share.

The following table illustrates this per share dilution to the new investors purchasing securities in this offering:

Offering price per share	\$	0.445
Net tangible book value per share at September 30, 2020	0.066	
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering	0.035	
As adjusted net tangible book value per share after this offering		0.101
Dilution per share to new investors in this offering	\$	0.344

The foregoing table and discussion are based on 184,548,267 shares outstanding as of September 30, 2020, and excludes:

- 1,003,990 shares of Common Stock issuable upon the exercise of stock options outstanding at September 30, 2020 with a weighted average exercise price of approximately \$24.96 per share;
- 11,619,215 shares of Common Stock issuable upon the exercise of outstanding or issuable warrants at September 30, 2020 with a weighted average exercise price of approximately \$1.99 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
- 50,194 shares of Common Stock reserved for future issuance under our 2018 Equity Compensation Plan, as amended, at September 30, 2020.

PLAN OF DISTRIBUTION

We have entered into the Purchase Agreement with certain investors pursuant to which we have agreed to issue and sell directly to such investors, and such investors have agreed to purchase directly from us, an aggregate of 19,551,124 Purchase Shares, at a price of \$0.445 per Purchase Share. We currently anticipate that the closing of the sale of the Purchase Shares will take place on or about January 11, 2021, subject to the satisfaction of certain conditions set forth in the Purchase Agreement, at which time we expect to deliver the Purchase Shares to the investors against payment of the purchase price therefor. The gross proceeds to us before expenses will be \$8,700,250.

The Purchase Shares are being offered and sold by us directly to the investors without a placement agent, underwriter, broker or dealer. We are not paying underwriting discounts or commissions in connection with this offering.

Under the Purchase Agreement, subject to certain exceptions, we are subject to company lock-up restrictions on the issuance and sale of our securities for 60 days following the closing of this offering. Additionally, under the Purchase Agreement, subject to certain exceptions, we are prohibited from effecting or entering into an agreement to effect any "variable rate transactions" as defined in the Purchase Agreement for a period of 5 years following the closing of this offering.

In addition, each investor has agreed that such investor will not, during the period commencing on the date of this prospectus supplement and ending on the earlier of (i) the calendar day immediately following the date established by our board of directors as the record date for the Company's special meeting of stockholders to be held on March 4, 2021 and (ii) January 21, 2021, offer, pledge, sell, contract to sell, grant, lend, or otherwise transfer or dispose of, directly or indirectly, any of the shares such investor purchased in the offering. Each investor has also agreed to vote all of the shares of our common stock beneficially owned by such investor and its affiliates and entitled to vote at the special meeting of stockholders to be held on March 4, 2021 in favor of each Company proposal that is submitted by the Company to its stockholders for a vote at the special meeting.

In connection with the offering, we have agreed to pay Lincoln Park Capital Fund, LLC, as the lead investor, an aggregate of \$100,000 as the full and complete expense reimbursement of Lincoln Park's expenses in connection with the offering, including any due diligence expenses and legal fees. Furthermore, under the Purchase Agreement, we have granted Lincoln Park certain rights to participate in up to 50% of the amount of any future offerings of our common stock or securities exercisable for or convertible into our common stock that we seek to complete within one year after the closing of this offering, other than a firm commitment public offering.

We will pay all of the expenses incident to the registration, offering and sale of the Purchase Shares under this prospectus supplement and the accompanying base prospectus. We estimate that the total expenses for the offering will be approximately \$200,000.

Each of the investors has represented to us that at no time prior to the date of this prospectus supplement has such investor or its agents, representatives or affiliates engaged in or effected, in any manner whatsoever, directly or indirectly, any short sale (as such term is defined in Rule 200 of Regulation SHO of the Exchange Act) of our common stock or any hedging transaction, and that neither it nor its agents, representatives or affiliates will engage in any of the aforementioned transactions at any time beginning on the date of this prospectus supplement.

We have agreed to indemnify the investors and certain other persons against certain liabilities in connection with this offering of our common stock, including liabilities arising under the Securities Act and the Exchange Act or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities.

The representations, warranties and covenants contained in the Purchase Agreement were made solely for the benefit of us and the investors. In addition, such representations, warranties and covenants (i) are intended as a way of allocating the risk between us and the investors and not as statements of fact, and (ii) may apply standards of materiality in a way that is different from what may be viewed as material by stockholders of, or other investors in, our company. Moreover, information concerning the subject matter of the representations and warranties may change after the date of the Purchase Agreement, which subsequent information may or may not be fully reflected in public disclosures.

The offering of the Purchase Shares by us to the investors under the Purchase Agreement is registered pursuant to our shelf registration statement on Form S-3 (File No. 333-237844), as to which this prospectus supplement relates.

A copy of the Purchase Agreement will be filed with the SEC and incorporated by reference into the registration statement of which this prospectus supplement and the accompanying base prospectus form a part.

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

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

LEGAL MATTERS

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

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, 2019](#) have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, 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

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the SEC. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement and the exhibits to the registration statement or the documents incorporated by reference herein and therein. For further information with respect to us and the securities that we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement and the documents incorporated by reference herein and therein. You should rely only on the information contained in this prospectus supplement or the accompanying prospectus or incorporated by reference herein or therein. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of the securities offered hereby.

We file annual, quarterly, and other reports, proxy and information statements, and other information with the Securities and Exchange Commission. The SEC maintains a website that contains reports, proxy statements and other information regarding us. The address of the SEC website is www.sec.gov. We maintain a website at www.onconova.com. Information contained on our website is not incorporated into this prospectus supplement and you should not consider information contained on our website to be part of this prospectus supplement.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement and the accompanying prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus supplement and the accompanying prospectus.

The following documents are incorporated by reference into this document (other than the portions of these documents deemed to be “furnished” or not deemed to be “filed,” including the portions of these documents that are furnished under Item 2.02 or Item 7.01 of a Current Report on Form 8-K, including any exhibits included with such Items):

- (1) Our [Annual Report on Form 10-K for the fiscal year ended December 31, 2019 that we filed with the SEC on March 27, 2020](#), including the information required by Part III, Items 10 through 14, of Form 10-K, which we incorporate by reference to our [definitive proxy statement for our 2020 annual meeting of stockholders filed on April 23, 2020](#);
- (2) Our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2020, filed on [May 15, 2020](#), for the quarter ended June 30, 2020, filed on [August 12, 2020](#), and for the quarter ended September 30, 2020, filed on [November 16, 2020](#);
- (3) Our Current Reports on Form 8-K filed on [January 3, 2020](#), [January 17, 2020](#), [January 23, 2020](#), [June 2, 2020](#), [June 10, 2020](#), [July 2, 2020](#), [July 10, 2020](#), [August 4, 2020](#), [August 24, 2020](#) (Item 8.01 only), [August 31, 2020](#), [October 9, 2020](#), [November 23, 2020](#) (Item 8.01 only), [December 18, 2020](#), [December 21, 2020](#) (Item 8.01 only); and
- (4) [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 into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and until the completion or termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, as well as proxy statements.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

We make available, free of charge, through 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 filed or furnished pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. You may also obtain, free of charge, a copy of any of these documents (other than exhibits to these documents unless the exhibits are specifically incorporated by reference into these documents or referred to in this prospectus) by writing or calling us at the following address and telephone number:

Onconova Therapeutics, Inc.
375 Pheasant Run
Newtown, Pennsylvania, 18940
Attention: Suzanne Hutchinson
(267) 759-3680

PROSPECTUS



Onconova Therapeutics, Inc.

\$150,000,000

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

113 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 \$150,000,000.

In addition, the selling stockholders to be named in the applicable prospectus supplement may offer and sell up to an aggregate of 113 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 April 23, 2020, the last reported sale price of our common stock on the Nasdaq Capital Market was \$0.3014 per share.

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 in the documents 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 May 18, 2020.

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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 \$150,000,000 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 113 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. 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, 2019](#) that we filed with the SEC on March 27, 2020, including the information required by Part III, Items 10 through 14, of Form 10-K, which we incorporate by reference to our definitive proxy statement for our 2020 annual meeting of stockholders filed on [April 23, 2020](#);
- Our Current Reports on Form 8-K filed with the SEC on [January 3, 2020](#), [January 17, 2020](#) and [January 23, 2020](#);
- 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 the 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 limitations, risks related to:

- our need for additional financing for our rigosertib trials 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 (“CROs”) and third-party manufacturers.

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 27, 2020](#), 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. We have proprietary 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 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 as a single agent in lower risk MDS 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 improvement in overall survival. An interim analysis of the trial was performed in January 2018. We completed enrollment of the required 360 randomized patients in March 2020. As of March 2020, more than 85% of the required death events have been reported. Based on survival events and trends to date, we anticipate reporting topline survival data in the second half of 2020, following at least 288 confirmed death events.

Our net losses were \$21.5 million and \$20.4 million for the year ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of \$403.4 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.

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 \$150,000,000, 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 250,000,000 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 April 24, 2020, 167,416,070 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.

In 2018, our board of directors designated 1,044,488 shares of preferred stock as Series A Convertible Preferred Stock and 1,796,875 shares of preferred stock as Series B Convertible Preferred Stock, As of April 24, 2020, we had no shares of preferred stock outstanding.

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 66 2/3% 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 (as of April 24, 2020, 1,044,488 shares have been designated as Series A Convertible Preferred Stock and 1,796,875 shares have been designated as Series B Convertible Preferred Stock);
- 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 EQ 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 \$150,000,000 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 \$150,000,000. 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 depositaries, 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 depository 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 depository 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 April 24, 2020, we had (i) non-tradable warrants with an expiration date ranging from March 2021 to December 2024 to purchase 23,612,454 shares of common stock at a weighted average exercise price of \$0.3290 per share, (ii) tradable warrants with an expiration date of July 27, 2021 to purchase 212,801 shares of common stock at an exercise price of \$73.80 per share, and (iii) non-tradable pre-funded warrants with no expiration date to purchase 1,377,451 shares of common stock at an exercise price of \$0.014 per share. Our tradable warrants are traded on the Nasdaq Capital Market under the symbol "ONTXW."

Additionally, as of April 24, 2020, we had (i) non-tradable warrants with an expiration date of December 31, 2022 to purchase 261,890 shares of Series A Preferred Stock at an exercise price of \$0.10667 per 0.1 preferred share (or 392,834 shares of common stock at an exercise price of \$1.60 per common share on an as-converted basis) and (ii) non-tradable warrants with an expiration date of December 31, 2022 to purchase 677,289 shares of Series B Preferred Stock at an exercise price of \$0.425 per 0.025 preferred share (or 1,806,104 shares of common stock at an exercise price of \$1.60 per common share on an as-converted basis).

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 113 Shares of Common Stock

This prospectus also relates to the possible resale by certain of our stockholders of up to an aggregate of 113 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 167,416,070 shares of our common stock outstanding as of April 24, 2020.

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	8	8	0	0
Kathryn Jane McDonald	2	2	0	0
Utkarsh Palnitkar	103	103	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 113 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 reallocated 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. appearing in Onconova Therapeutics, Inc.’s [Annual Report \(Form 10-K\) for the year ended December 31, 2019](#) have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, 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.

LEGAL MATTERS

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

19,551,124 Shares of Common Stock



Prospectus Supplement
January 7, 2021
