

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated May 18, 2020)**25,000,000 Shares****Common Stock**

We are offering 25,000,000 shares of our common stock.

We have granted the underwriters an option for a period of 30 days to purchase up to 3,750,000 additional shares of our common stock.

Our common stock is listed on the Nasdaq Capital Market under the symbol "ONTX." On February 9, 2021, the last reported sale price of our common stock on the Nasdaq Capital Market was \$1.20 per share.

Investing in our securities involves significant risks. Please read the information contained in or incorporated by reference under the heading "Risk Factors" beginning on page S-5 of this prospectus supplement, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

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

	PER SHARE	TOTAL
Public offering price	\$1.00	\$25,000,000
Underwriting discounts and commissions ⁽¹⁾	\$0.06	\$ 1,500,000
Proceeds, before expenses, to us	\$0.94	\$23,500,000

(1) We have agreed to reimburse the underwriters for certain expenses. We refer you to "Underwriting" beginning on page S-13 of this prospectus supplement for additional information regarding total underwriting compensation.

Delivery of the shares of common stock is expected to be made on or about February 16, 2021. We have granted the underwriters an option for a period of 30 days to purchase an additional 3,750,000 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$1,725,000, and the total proceeds to us, before expenses, will be \$27,025,000. Certain of our officers and directors have indicated they intend to purchase an aggregate of less than 1% of the shares of common stock to be sold in this offering at the offering price and on the same terms as the other purchasers in this offering.

Sole Book-Running Manager

Guggenheim Securities

Co-Managers

Maxim Group LLC**Noble Capital Markets**

The date of this prospectus supplement is February 11, 2021.

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Prospectus

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a shelf registration statement on Form S-3 (File No. 333-237844) that we filed with the Securities and Exchange Commission, or SEC, on April 24, 2020, which was amended on Form S-3/A that we filed with the Securities and Exchange Commission, or SEC, on May 15, 2020 and was declared effective by the SEC on May 18, 2020, pursuant to which we may from time to time offer various securities in one or more offerings.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein or therein. The second part, the accompanying prospectus, including the documents incorporated by reference into the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference herein or therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in the accompanying prospectus — the statement in the document having the later date modifies or supersedes the earlier statement.

Neither we nor the underwriters have authorized anyone to provide information different from that contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in this offering. If anyone provides you with different or inconsistent information, you should not rely on it. Neither we nor the underwriters take any responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. Neither the delivery of this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in this offering, nor the sale of our common stock means that information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in this offering, is correct after their respective dates. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering in making your investment decision.

This prospectus supplement does not contain all of the information that is important to you. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement. You should rely only on the information contained or incorporated by reference in this document. You should assume that the information in this prospectus supplement and the accompanying prospectus, as well as the information we have filed with the SEC and incorporated by reference in this document, is accurate only as of its date or the date which is specified in those documents.

We are offering to sell, and seeking offers to buy, and the underwriters are soliciting offers to buy, these securities only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the securities in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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 its subsidiary, 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.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained else-where in or incorporated by reference into this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of Onconova and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information referred to under the heading “Risk Factors” in this prospectus supplement beginning on page [S-5](#) and under similar headings in our public filings incorporated by reference herein, including, without limitation, our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q.

Our Company

We are a biopharmaceutical company focused on discovering and developing novel products for patients with cancer. The Company has proprietary targeted anti-cancer agents designed to disrupt specific cellular pathways that are important for cancer cell proliferation. 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: (i) ON 123300 in solid tumors; and (ii) oral rigosertib alone or in combination with PD-1 inhibitors for treatment of KRAS-mutated solid tumors.

Onconova’s novel, proprietary multi-kinase inhibitor ON 123300 is currently in a dose-escalation and expansion Phase 1 trial in China, and a dose-escalation and expansion Phase 1 trial is planned in the U.S. to commence in the first half of 2021. Onconova’s product candidate oral rigosertib is currently in a dose-escalation and expansion Phase 1 investigator-initiated study targeting patients with KRAS+ lung adenocarcinoma in combination with nivolumab.

We believe unmet medical need in advanced HR+/HER2- breast cancer and other tumor types warrants the development of the next (third) generation CDK4/6 inhibitors. Among the potential differentiating features from existing therapies of the multi kinase inhibitor ON 123300 is its targeting of ARK5. Activity of ARK5 is reported as crucial in promoting cancer cell migration and invasion (Kusaki, 2004). ON 123300 treatment may have an impact on cell migration. Preclinical studies with tumor cell lines suggest that several malignancies including HR positive breast cancer, colorectal carcinoma, hepatocellular carcinoma, mantle cell lymphoma and multiple myeloma, may be clinically responsive to ON 123300 exposure. Accordingly, we believe that the unmet medical need of the advanced cancers potentially targeted by ON 123300, its mechanism of action and anticipated safety profile, all support conducting a dose-escalation and expansion Phase 1 trial that is planned to commence in the U.S. in the first half of 2021.

We are currently supporting investigator-initiated studies that are exploring the use of rigosertib for other cancers (KRAS mutated non-small cell lung cancer (NSCLC) and metastatic melanoma) driven by mutated Ras genes, including a Phase 1 study of rigosertib in combination with a PD-1 inhibitor for patients with progressive K-Ras mutated NSCLC. A recommended Phase 2 dose for future studies is expected in 2021.

We plan to continue to focus on the development of our novel multi kinase inhibitor targeting CDK4/6 + ARK5, ON 123300, and oral rigosertib in KRAS mutated cancers. We will direct our efforts to these programs. We are also evaluating other compounds in our pipeline and potential compounds for 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.

Recent Developments

On December 18, 2020, Onconova received permission from the FDA for a Phase 1 study to proceed under an Investigational New Drug application that the Company submitted on November 20, 2020 for its product candidate ON 123300. Patient enrollment has continued in the ongoing dose-escalation and expansion

Phase 1 trial for ON 123300 in China, and the ongoing dose-escalation and expansion Phase 1 investigator-initiated study targeting patients with KRAS+ lung adenocarcinoma in combination with nivolumab.

On January 7, 2021, the Company raised \$8.5 million net of expense by selling 19,551,124 shares of Common Stock to certain institutional investors.

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	25,000,000 shares.
Option to purchase additional shares	We have granted the underwriters an option for a period of up to 30 days from the date of this prospectus supplement to purchase up to an additional 3,750,000 shares of our common stock at the public offering price less the underwriting discounts and commissions.
Common stock to be outstanding after this offering	209,548,267 shares (213,298,267 shares assuming the underwriters exercise in full their option to purchase additional shares).
Use of proceeds	We intend to use the net proceeds from this offering for working capital and general corporate purposes. See “Use of Proceeds.”
Risk factors	An investment in our common stock involves a high degree of risk. You should read the risk factors found in this prospectus supplement, the accompanying prospectus, and in the documents incorporated herein and therein by reference, as well as the other cautionary statements throughout this prospectus supplement and the accompanying prospectus, to ensure you understand the risks associated with an investment in our common stock. See “Risk Factors” beginning on page S-5 of this prospectus supplement, the accompanying prospectus and page 5 of the accompanying prospectus.
Nasdaq Capital Market symbol	“ONTX”

Outstanding Shares

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 (the “2018 Equity Compensation Plan”), 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.

On January 7, 2021, the Company sold 19,551,124 shares of Common Stock to certain institutional investors and, immediately prior to this offering, the number of the Company’s total outstanding shares of common stock was 207,762,391 (including warrant and option exercises after September 30, 2020).

Except as otherwise indicated herein, all information in this prospectus supplement, including the number of shares of our common stock that will be outstanding after this offering, does not assume or give effect to the exercise of the underwriters’ option to purchase additional shares in this offering.

Insider Participation

Certain of our officers and directors have indicated they intend to purchase an aggregate of less than 1% of the shares of common stock to be sold in this offering at the offering price and on the same terms as the other purchasers in this offering.

RISK FACTORS

An investment in 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 Our Business and Industry

We recently changed the focus of our product development efforts and may not be successful in our revised strategy.

On August 24, 2020, we announced topline results from the INSPIRE trial, which assessed the efficacy and safety of IV rigosertib in HR-MDS patients. The trial did not meet its primary endpoint of improved survival for patients randomized to IV rigosertib compared to the control arm. 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 multi kinase inhibitor targeting CDK4/6 + ARK5, ON 123300. We are also reviewing potential in-licensing opportunities.

Although, we believe that there are opportunities for us to develop oral rigosertib in KRAS mutated cancers and our novel multi kinase inhibitor targeting CDK4/6 + ARK5, ON 123300, in indications such as metastatic breast cancer, mantle cell lymphoma and multiple myeloma, clinical drug development is expensive, can take many years to complete, and its outcome is inherently uncertain. There can be no assurance that our new focus on oral rigosertib and ON 123300 will be successful, and that we will be able to successfully develop a product candidate or, even if we do, that we will be able to successfully commercialize such candidate.

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. 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.

On January 13, 2021, we filed a definitive proxy statement on Schedule 14A for our Special Meeting of Stockholders to be held on March 4, 2021 (the Special Meeting"). One of the proposals our stockholders will vote upon at the Special Meeting is a reverse stock split proposal, under which we will combine our outstanding shares of common stock into a lesser number of outstanding shares by a ratio of not less than one-for-five and not more than one-for-fifteen, with the exact ratio to be set within this range by our board of directors in its sole discretion. There can be no assurance that our stockholders will approve the reverse stock split proposal at the Special Meeting.

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.

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;
- the impact of the novel coronavirus disease, COVID-19, to the global economy and capital markets, and to our business and our financial results; and
- our new focus on oral rigosertib and ON 123300.

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.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 25,000,000 shares of our common stock in this offering will be approximately \$23.2 million, or approximately \$26.7 million if the underwriters exercise their option to purchase additional shares in full, after deducting the estimated underwriting discounts and commissions and the 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

Purchasers of our common stock in this offering will experience immediate dilution to the extent of the difference between the public offering price per share of our common stock, and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

We calculate net tangible book value (deficit) per share by dividing our net tangible book value (deficit), which is tangible assets less total liabilities, by the number of outstanding shares of our common stock.

As of September 30, 2020, our net tangible book value was \$12,215,000, or \$0.066 per share of common stock.

Our pro forma net tangible book value as of September 30, 2020 was \$20,715,000, or \$0.101 per share of our common stock. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the pro forma number of shares of our common stock outstanding, after giving effect to our issuance and sale of 19,551,124 shares of our common stock in the registered direct offering closed on January 11, 2021.

Dilution per share to new investors represents the difference between the amount per share paid by purchasers for our common stock in this offering and the pro forma as adjusted net tangible book value per share of our common stock immediately following the completion of this offering.

After giving effect to the sale of 25,000,000 shares of our common stock in this offering at the public offering price of \$1.00 per share, and after deducting the underwriting discounts and commissions and the estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of September 30, 2020 would have been approximately \$43,875,000, or approximately \$0.191 per share of our common stock. This represents an immediate increase in pro forma net tangible book value of \$0.090 per share of our common stock to our existing stockholders and an immediate dilution in pro forma net tangible book value of \$0.809 per share of our common stock to purchasers in this offering.

The following table illustrates this calculation on a per share basis:

Offering price per share in this offering	\$ 1.00
Net tangible book deficit per share as of September 30, 2020	\$0.066
Increase in pro forma tangible book value per share attributable to shares sold in our registered direct offering closed on January 11, 2021	<u>\$0.035</u>
Pro forma net tangible book value per share as of September 30, 2020	\$0.101
Increase in pro forma net tangible book value per share attributable to purchasers in this offering	<u>\$0.090</u>
Pro forma as adjusted net tangible book value per share immediately after this offering	<u>\$0.191</u>
Dilution per share to purchasers in this offering	<u><u>\$0.809</u></u>

If the underwriters exercise their option in full to purchase additional shares of our common stock in this offering at the public offering price of \$1.00 per share, the pro forma as adjusted net tangible book value per share after the offering would be \$0.204 per share, the increase in the pro forma net tangible book value per share to existing stockholders would be \$0.103 per share and the dilution to purchasers in this offering would be \$0.796 per share.

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 at September 30, 2020.

Except as otherwise indicated herein, all information in this prospectus supplement, including the number of shares that will be outstanding after this offering, does not assume or give effect to the exercise of the underwriters' option to purchase additional shares in this offering.

To the extent that options or warrants are exercised, other equity awards vest, new equity awards are issued under our 2018 Equity Compensation Plan or pursuant to inducement awards, or we issue additional shares of common stock in the future, there may be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

UNDERWRITING

Guggenheim Securities, LLC is acting as representative of each of the underwriters named below. Guggenheim Securities, LLC is acting as the sole book-running manager and Maxim Group LLC and Noble Capital Markets, Inc. are acting as co-managers. Subject to the terms and conditions set forth in the underwriting agreement between us and the underwriters, each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Guggenheim Securities, LLC	22,500,000
Maxim Group LLC	1,250,000
Noble Capital Markets, Inc.	1,250,000
Total	<u>25,000,000</u>

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares of common stock sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts; Expenses

The underwriters have advised us that they propose initially to offer the shares to the public at the public offering price set forth on the cover of this prospectus supplement and to dealers at that price less a concession not in excess of \$0.036 per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discounts and commissions and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock from us, as applicable.

	Per Share	Total	
		No Exercise	Full Exercise
Public offering price	\$1.00	\$25,000,000	\$28,750,000
Underwriting discounts and commissions to be paid by us	\$0.06	\$ 1,500,000	\$ 1,725,000
Proceeds, before expenses, to us	\$0.94	\$23,500,000	\$27,025,000

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$340,000, which includes certain expenses incurred by the underwriters in connection with this offering that will be reimbursed by us. We have agreed to reimburse the underwriters for certain expenses incurred by them in connection with this offering (including certain fees and expenses of counsel for the underwriters and fees and expenses related to filings with and review by FINRA, in an aggregate amount not to exceed \$100,000).

Option to Purchase Additional Shares

We have granted the underwriters an option to purchase up to an additional 3,750,000 shares of common stock at the public offering price, less the underwriting discounts and commissions, within 30 days

from the date of this prospectus supplement. If the underwriters exercise this option, each underwriter will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

Right of First Refusal

We have granted Guggenheim Securities, LLC a right of first refusal for a period of 12 months from the date of closing of this offering to act as lead left bookrunner in connection with any public offering of our equity securities, other than a variable rate transaction or an at-the-market offering.

No Sales of Similar Securities

In connection with this offering, we have agreed with the underwriters that, subject to certain customary exceptions, without the prior written consent of Guggenheim Securities, LLC on behalf of the underwriters, we will not, for a period ending 90 days after the date of this prospectus supplement, or the Lock-Up Period, (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, or submit to, or file with, the SEC a registration statement under the Securities Act relating to, any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock, or publicly disclose the intention to undertake any of the foregoing, or (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or any such other securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, without the prior written consent of Guggenheim Securities, LLC.

The foregoing restrictions shall not apply to the following:

- a) effecting the transactions contemplated hereby,
- b) the issuance of shares of common stock or securities convertible into or exercisable for shares of common stock pursuant to the conversion or exchange of convertible or exchangeable securities or the exercise of warrants or options (including net exercise) outstanding on the date of the underwriting agreement and described in the prospectus;
- c) grants of stock options, stock awards, restricted stock, or other equity awards and the issuance of shares of common stock or securities convertible into or exercisable or exchangeable for shares of common stock (whether upon the exercise of stock options or otherwise) to the Company's employees, officers, directors, advisors, or consultants pursuant to the terms of an equity compensation plan in effect as of the Closing Date and described in the Prospectus;
- d) the filing of any registration statement on Form S-8 relating to securities granted or to be granted pursuant to any plan in effect on the date of the underwriting agreement and described in the prospectus or any assumed benefit plan pursuant to an acquisition or similar strategic transaction; and
- e) shares of our common stock or other securities issued in connection with a transaction with a third party that includes a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets of the equity of another entity, provided that (x) the aggregate number of shares of our common stock that we may sell or issue or agree to sell or issue shall not exceed 5% of the total number of shares of common stock issued and outstanding as of the date of the underwriting agreement and (y) each recipient of shares of our common stock or securities convertible into or exercisable for shares of our common stock shall execute a lock-up agreement.

In connection with this offering, certain of our stockholders and our directors and executive officers have agreed with the underwriters that, subject to certain customary exceptions, without the prior written consent of Guggenheim Securities, LLC on behalf of the underwriters, they will not, for the Lock-Up Period, directly or indirectly, (a) offer, pledge, sell, contract to sell, solicit offers to purchase, grant any call option or purchase any put option with respect to, lend, or otherwise transfer or dispose of, directly or indirectly, any

shares of common stock or any securities convertible into or exercisable or exchangeable for common stock (including without limitation, common stock or such other securities which may be deemed to be beneficially owned by the undersigned in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) (collectively with the common stock, the “Relevant Securities”), (b) enter into any hedging, swap or other agreement or transaction that transfers, in whole or in part, any of the economic consequences of ownership of the Relevant Securities, whether any such transaction described in clause (a) or (b) above is to be settled by delivery of Relevant Securities, in cash or otherwise, (c) make any demand for, or exercise any right with respect to, the registration of any Relevant Securities, or (d) publicly disclose the intention to do any of the foregoing. The underwriters may, in their sole discretion, permit the sale of Relevant Securities during the restricted period in whole or in part and at any time, with or without notice.

The foregoing restrictions shall not apply to:

- a) the transfer of Relevant Securities (i) as a bona fide gift or gifts, (ii) by will, other testamentary document or intestate succession, (iii) to a family member, (iv) to a trust for the direct or indirect benefit of the lock-up party and/or one or more family members, (v) pursuant to a domestic order, divorce settlement, divorce decree, separation agreement or pursuant to an order of a court of competent jurisdiction enforcing such agreement, (vi) to a charitable trust, or (vii) to a corporation, limited liability company or partnership wholly owned by the lock-up party and/or one or more family members; provided, however, that no public disclosure or filing by any party (donor, donee, transferor or transferee) under the Exchange Act, or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on Form 5 made after the expiration of the Lock-up Period); provided, further, that (x) any such transfer shall not involve a disposition for value and (y) each resulting transferee or donee of Relevant Securities executes and delivers to the underwriters an agreement satisfactory to the underwriters in which such transferee agrees to be bound by the terms of the lock-up agreement for the remainder of the Lock-up Period;
- b) the transfer of Relevant Securities (i) as forfeitures to satisfy tax withholding obligations of the lock-up party in connection with the vesting or exercise of equity awards by the lock-up party existing as of the date of this prospectus supplement and described or incorporated by reference in this prospectus supplement, (ii) pursuant to a net exercise or cashless exercise (to satisfy exercise price or related withholding obligations) by the lock-up party of outstanding equity awards existing as of the date of this prospectus supplement and described or incorporated by reference in this prospectus supplement, provided that any shares of our common stock acquired upon the net exercise or cashless exercise of equity awards described in this clause (b) shall be subject to the restrictions set forth in the lock-up agreement; provided, further, that no public disclosure or filing by any party (donor, donee, transferor or transferee) under the Exchange Act, or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on Form 5 made after the expiration of the Lock-up Period);
- c) distributions of Relevant Securities to limited partners, members or stockholders of the lock-up party; provided, however, that no public disclosure or filing by any party (donor, donee, transferor or transferee) under the Exchange Act, or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on Form 5 made after the expiration of the Lock-up Period); provided, further, that (x) any such transfer shall not involve a disposition for value and (y) each resulting transferee or donee of Relevant Securities executes and delivers to the underwriters an agreement satisfactory to the underwriters in which such transferee agrees to be bound by the terms of the lock-up agreement for the remainder of the Lock-up Period;
- d) transactions relating to Relevant Securities acquired in open market transactions after the closing of this offering; provided, however, that no public disclosure or filing by any party (donor, donee, transferor or transferee) under the Exchange Act, or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution (other than a filing on Form 5 made after the expiration of the Lock-up Period); and

- e) the transfer of Relevant Securities pursuant to a bona fide third-party tender offer for all of our outstanding shares, merger, consolidation or other similar transaction made to all holders of our securities involving a change of control of the Company (including, without limitation, the entering into of any lock-up, voting or similar agreement pursuant to which the lock-up party may agree to transfer, sell, tender or otherwise dispose of Relevant Securities in connection with such transaction, or vote any Relevant Securities in favor of any transaction), provided that in the event that such tender offer, merger, consolidation or other such transaction is not completed, such securities held by the lock-up party shall remain subject to the provisions of the lock-up agreement.

The Nasdaq Capital Market Listing

Our shares of common stock are listed on The Nasdaq Capital Market under the symbol “ONTX.”

Price Stabilization and Short Positions

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representative may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option described above. The underwriters may close out any covered short position by either exercising their option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. “Naked” short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of the offering.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on The Nasdaq Capital Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representative will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

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

market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates have in the past, and may in the future, engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they have received, and may in the future receive, customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers.

Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is EQ Shareowner Services. Its telephone number is (651) 453-2166.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area, or a Member State, no shares have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the competent authority in that Member State, all in accordance with the Prospectus Regulation, except that offers of shares may be made to the public in that Member State at any time under the following exemptions under the Prospectus Regulation:

- A. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters; or
- C. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares shall require the Company or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and the Company that it is a “qualified investor” within the meaning of Article 2(e) of the Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed

that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Member State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an “offer to the public” in relation to shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (“SIX”) or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority (“FINMA”), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (“CISA”). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Morgan, Lewis & Bockius LLP, Philadelphia, Pennsylvania. White & Case LLP, New York, New York, has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

EXPERTS

The consolidated financial statements of Onconova Therapeutics, Inc. appearing in Onconova Therapeutics, Inc.'s [Annual Report \(Form 10-K\) for the year ended December 31, 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

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus supplement forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus supplement regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov.

We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. Please note, however, that we have not incorporated any other information by reference from our website, other than the documents listed under the heading "Incorporation of Certain Information by Reference" on page [S-21](#) of this prospectus supplement. In addition, you may request copies of these filings at no cost by writing or telephoning us at the following address or telephone number:

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

INCORPORATION OF CERTAIN 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 another document that we have filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus supplement. Information in this prospectus supplement supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement and the accompanying prospectus. We incorporate by reference our documents listed below and any future filings made by us with the SEC (File No. 001-36020) under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of this prospectus supplement and until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed “filed” with the SEC, including any information furnished pursuant to Item 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

- 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 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](#);
- 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), [January 8, 2021](#) and [January 15, 2021](#); and
- [The description of our common stock contained in our registration statement on Form 8-A filed on July 23, 2013 \(Registration no. 001-36020\) with the SEC, including any amendment or report filed for the purpose of updating such description](#);

Information in such future filings updates and supplements the information provided in this prospectus supplement and the accompanying prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

To obtain copies of these filings, see “Where You Can Find More Information” on page [S-20](#) of this prospectus supplement.

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 Depositary, or a nominee of the Depositary (we will refer to any debt security represented by a global debt security as a book-entry debt security), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a certificated debt security), as described in the applicable prospectus supplement.

Certificated Debt Securities

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

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

Book-Entry Debt Securities

We may issue the debt securities of a series in the form of one or more book-entry debt securities that would be deposited with a depositary or its nominee identified in the prospectus supplement. We may issue book-entry debt securities in either temporary or permanent form. We will describe in the prospectus

supplement the terms of any depositary arrangement and the rights and limitations of owners of beneficial interests in any book-entry debt security.

DESCRIPTION OF WARRANTS

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

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

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

As of 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.

25,000,000 Shares



Common Stock

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager

Guggenheim Securities

Co-Managers

Maxim Group LLC

Noble Capital Markets

February 11, 2021
