

PROSPECTUS SUPPLEMENT
(To prospectus dated May 18, 2020)

ONCONOVA THERAPEUTICS, INC.

Up to \$25,000,000
Common Stock



We have entered into an Equity Distribution Agreement, or the Equity Distribution Agreement, with Piper Sandler & Co., or Piper Sandler, relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the Equity Distribution Agreement, we may offer and sell shares of our common stock, \$0.01 par value per share, having an aggregate offering price of up to \$25,000,000 from time to time through Piper Sandler acting as our agent.

Our common stock is listed on The Nasdaq Capital Market under the symbol "ONTX." On August 19, 2021, the last reported sale price of our common stock on The Nasdaq Capital Market was \$4.47 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made in sales deemed to be an "at the market offerings" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Piper Sandler will act as a sales agent on a best efforts basis and will use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between the Agent and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Piper Sandler will be entitled to compensation at a fixed commission rate of 3.0% of the gross sales price per share sold. See "Plan of Distribution" for additional information regarding compensation to be paid to Piper Sandler. In connection with the sale of the common stock on our behalf, Piper Sandler will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Piper Sandler will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Piper Sandler with respect to certain liabilities, including liabilities under the Securities Act and the Exchange Act of 1934, as amended, or the Exchange Act.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "Risk Factors" beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

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

Piper Sandler

The date of this prospectus supplement is August 20, 2021

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of a “shelf” registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, and is in two parts. The first part is this prospectus supplement, which describes the specific terms of offering of shares of our common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, 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 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.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We have not, and Piper Sandler has not, authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in this prospectus supplement, the accompanying prospectus or any free writing prospectus, or incorporated by reference herein or therein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our shares of common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. 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 “Information Incorporated by Reference” in this prospectus supplement and in the accompanying prospectus.

We and Piper Sandler are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the shares of our common stock 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 shares of our common stock 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.

When we refer to “Onconova,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Onconova Therapeutics, Inc., unless otherwise specified. When we refer to “you,” we mean the holders of common stock of the Company.

Our logo, “Onconova” and other trademarks or service marks of Onconova Therapeutics, Inc. appearing in this prospectus supplement are the property of Onconova Therapeutics, Inc. This prospectus supplement also includes trademarks, trade names and service marks that are the property of other organizations. Solely for convenience, our trademarks and trade names referred to in this prospectus supplement may appear

without the ® and ™ symbol, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and trade names.

MARKET, INDUSTRY AND OTHER DATA

This prospectus supplement, including the information incorporated by reference herein, contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs, including data regarding the estimated size of those markets. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

PROSPECTUS SUPPLEMENT SUMMARY

This summary provides a general overview of selected information and does not contain all of the information you should consider before buying our common stock. Therefore, you should read the entire prospectus supplement, accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the information incorporated by reference herein and therein, before deciding to invest in our common stock. Investors should carefully consider the information set forth under “Risk Factors” beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

Onconova Therapeutics, Inc.**Overview**

We are a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer. We have 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: 1. ON 123300, multi-kinase inhibitor in solid tumors; and 2. rigosertib alone or in combination with PD-1 inhibitors for treatment of solid tumors. We are currently evaluating potential compounds for in-licensing opportunities.

Our net losses were \$8.9 million and \$12.5 million for the six months ended June 30, 2021 and 2020, respectively. As of June 30, 2021, we had an accumulated deficit of \$437.4 million. We expect to incur significant expenses and operating losses for the foreseeable future as we continue the development of, and seek regulatory approval for, our product candidates, even if milestones under our license and collaboration agreements may be met. As of June 30, 2021, we had \$43.7 million in cash and cash equivalents.

Office Location

Our principal offices are located at 12 Penns Trail, Newtown, PA 18940, and our telephone number is (267) 759-3680. Our website address is <https://www.onconova.com/>. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement or the accompanying prospectus.

THE OFFERING

Common Stock Offered by Us	Shares of our common stock having an aggregate offering price of up to \$25,000,000.
Common Stock Outstanding After This Offering	Up to 21,373,881 shares, assuming the sale of up to 5,592,841 shares of our common stock a price of \$4.47 per share, which was the closing price of our common stock on The Nasdaq Capital Market on August 19, 2021. The actual number of shares issued will vary depending on the sales price under this offering.
Plan of Distribution	“At the market offering” that may be made from time to time through our sales agent, Piper Sandler. See “Plan of Distribution” on page S-10.
Use of Proceeds	We intend to use the net proceeds from this offering, if any, for general corporate purposes, which may include, among other things, working capital, funding our clinical programs and other research and development activities, and capital expenditures. See “Use of Proceeds” on page S-8.
Risk Factors	You should read the “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to purchase shares of our common stock.
Symbol on The Nasdaq Capital Market	“ONTX”

The number of shares of common stock to be outstanding after this offering is based on 15,781,040 shares of common stock outstanding as of June 30, 2021 and excludes in each case as of June 30, 2021:

- 60,431 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of approximately \$124.00 per share;
- 519,725 shares of Common Stock issuable upon the exercise of outstanding or issuable warrants having a weighted average exercise price of approximately \$42.23 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);
- 5,205 shares of common stock reserved for issuance pursuant to future awards under our 2018 Omnibus Incentive Compensation Plan, as amended (the “2018 Plan”).

In addition, unless we specifically state otherwise, all information in this prospectus assumes no exercise of outstanding stock options subsequent to June 30, 2021.

On July 30, 2021, stockholders approved the Onconova Therapeutics, Inc. 2021 Incentive Compensation Plan (the “2021 Plan”). The 2021 Plan is a successor to the 2018 Plan, as amended and restated. The 2021 Plan increased the shares of common stock available for issuance by an additional 1,300,000 shares.

RISK FACTORS

You should consider carefully the risks described below and discussed under the section captioned “Risk Factors” contained in our [annual report on Form 10-K for the year ended December 31, 2020](#) and [Quarterly Report on Form 10-Q for the six months ended June 30, 2021](#), as updated by our subsequent filings under the Exchange Act, each of which is incorporated by reference in this prospectus supplement in their entirety, together with other information in this prospectus supplement, and the information and documents incorporated by reference in this prospectus supplement, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Relating to this Offering

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering. We intend to use the net proceeds, if any, from this offering for general corporate purposes, which may include, among other things, working capital, funding our clinical programs and other research and development activities, and capital expenditures. We may also use a portion of the net proceeds to license intellectual property or to make acquisitions or investments, although we have no commitments or agreements to enter into such licenses, acquisitions or investments. See “Use of Proceeds.” Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock.

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

The price per share of our common stock being offered may be higher than the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 5,592,841 shares are sold at a price of \$4.47 per share, the last reported sale price of our common stock on The Nasdaq Capital Market on August 19, 2021, for aggregate proceeds of \$25.0 million in this offering, and after deducting commissions and estimated aggregate offering expenses payable by us, you will suffer immediate and substantial dilution of \$1.80 per share, representing the difference between the as adjusted net tangible book value per share of our common stock as of June 30, 2021 after giving effect to this offering and the assumed offering price of \$4.47 per share. See the section entitled “Dilution” below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, in the future we expect to offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

The common stock offered hereby will be sold in “at the market offerings” and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and accordingly may experience different levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and number of shares sold in this offering. In addition, subject to the final determination by our board of directors or any restrictions we may place in any applicable placement notice, there is no minimum or maximum sales price for shares to be sold in this offering. Investors may experience a decline in the value of the shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, including the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “potential,” “positioned,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to: any projections of financial information; any statements about historical results that may suggest trends for our business; any statements of the plans, strategies and objectives of management for future operations; any statements of expectation or belief regarding future events, technology developments, our products, product sales, product candidates, partnerships, expenses, liquidity, cash flow, market growth rates or enforceability of our intellectual property rights and related litigation expenses; and any statements of assumptions underlying any of the foregoing. You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein completely and with the understanding that our actual results may differ materially from what we expect as expressed or implied by our forward-looking statements. In light of the significant risks and uncertainties to which our forward-looking statements are subject, you should not place undue reliance on or 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 discuss many of these risks in greater detail in the documents incorporated by reference herein, including under the heading “Risk Factors.” These forward-looking statements represent our estimates and assumptions only as of the dates of this prospectus supplement, the accompanying base prospectus and the documents incorporated by reference herein and therein, and any free writing prospectus, as applicable, regardless of the time of delivery of this prospectus supplement or any sale of our common stock and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this prospectus supplement. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$25,000,000 from time to time. The amount of proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold, and will be reduced by commissions and other expenses of this offering. There can be no assurance that we will be able to sell any shares under or fully utilize the Equity Distribution Agreement with Piper Sandler as a source of financing. We intend to use the net proceeds, if any, from this offering for general corporate purposes, which may include, among other things, working capital, funding our clinical programs and other research and development activities and capital expenditures.

The amounts and timing of our actual expenditures will depend on numerous factors, including our development and commercialization efforts with respect to our product candidates, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds, if any, from this offering in short-term, investment-grade, interest-bearing securities.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Our net tangible book value as of June 30, 2021 was approximately \$33.0 million, or \$2.09 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of June 30, 2021. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering.

After giving effect to the sale of our common stock in the aggregate amount of \$25.0 million in this offering at an assumed offering price of \$4.47, the last reported sale price of our common stock on The Nasdaq Capital Market on August 19, 2021, and after deducting commissions and estimated aggregate offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2021 would have been approximately \$57.1 million, or \$2.67 per share. This represents an immediate increase in net tangible book value of \$0.58 per share to existing stockholders and immediate dilution in net tangible book value of \$1.80 per share to new investors purchasing our common stock in this offering. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share	\$4.47
Net tangible book value per share as of June 30, 2021	\$2.09
Increase per share attributable to new investors	<u>\$0.58</u>
As adjusted net tangible book value per share after this offering	<u>\$2.67</u>
Dilution per share to new investors	<u>\$1.80</u>

The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$4.47 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$25.0 million is sold at that price, would cause our as adjusted net tangible book value per share after the offering to be \$2.80 per share and would increase the dilution in net tangible book value per share to new investors to \$2.67 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$4.47 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$25.0 million is sold at that price, would cause our as adjusted net tangible book value per share after the offering to be \$2.48 per share and would decrease the dilution in net tangible book value per share to new investors to \$0.99 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

To the extent that outstanding options to purchase common stock are exercised, investors purchasing our common stock in this offering will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that 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.

The number of shares of common stock to be outstanding after this offering is based on 15,781,040 shares of common stock outstanding as of June 30, 2021 and excludes in each case as of June 30, 2021:

- 60,431 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of approximately \$124.00 per share;
- 519,725 shares of Common Stock issuable upon the exercise of outstanding or issuable warrants having a weighted average exercise price of approximately \$42.23 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);
- 5,205 shares of common stock reserved for issuance pursuant to future awards under our 2018 Plan.

PLAN OF DISTRIBUTION

We have entered into the Equity Distribution Agreement with Piper Sandler, under which we may offer and sell up to \$25,000,000 of our shares of common stock from time to time through Piper Sandler acting as agent. Sales of our shares of common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell our shares of common stock under the Equity Distribution Agreement, we will notify Piper Sandler of the number of shares to be issued, the time period during which such sales are requested to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Piper Sandler, unless Piper Sandler declines to accept the terms of such notice, Piper Sandler has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Piper Sandler under the Equity Distribution Agreement to sell our shares of common stock are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Piper Sandler is generally anticipated to occur on the second full business day following the date on which the sale was made. Sales of our shares of common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Piper Sandler may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Piper Sandler a commission of 3.0% of the aggregate gross proceeds we receive from each sale of our shares of common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Piper Sandler for the fees and disbursements of its counsel, payable upon execution of the Equity Distribution Agreement, in an amount not to exceed (a) \$50,000 in connection with the establishment of this at-the-market offering program and (b) thereafter, \$3,000 for each quarter in which we submit a placement notice to Piper Sandler for services in connection with the transactions contemplated hereunder. In accordance with Financial Industry Regulatory Authority, Inc. Rule 5110 these reimbursed fees and expenses are deemed sales compensation in connection with this offering. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Piper Sandler under the terms of the Equity Distribution Agreement, will be approximately \$130,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Piper Sandler will provide written confirmation to us before the open on The Nasdaq Capital Market on the day following each day on which our shares of common stock are sold under the Equity Distribution Agreement. Each confirmation will include the number of shares sold on that day, the volume-weighted average price of the shares sold and the proceeds to us of such shares.

In connection with the sale of our shares of common stock on our behalf, Piper Sandler will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of Piper Sandler will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Piper Sandler against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Piper Sandler may be required to make in respect of such liabilities.

The offering of our shares of common stock pursuant to the Equity Distribution Agreement will terminate upon the earlier of (i) the sale of all shares of common stock subject to the Equity Distribution Agreement and (ii) the termination of the Equity Distribution Agreement as permitted therein. We and Piper Sandler may each terminate the sales agreement at any time upon specified prior notice.

This summary of the material provisions of the Equity Distribution Agreement does not purport to be a complete statement of its terms and conditions. A copy of the Equity Distribution Agreement is filed as an exhibit to a current report on Form 8-K filed under the Exchange Act and incorporated by reference in this prospectus supplement.

Piper Sandler and its affiliates has provided, and may in the future provide, various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services

they have received, and may in the future receive, customary fees. In the course of its business, Piper Sandler may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Piper Sandler may at any time hold long or short positions in such securities.

A prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Piper Sandler, and Piper Sandler may distribute the prospectus supplement and the accompanying prospectus electronically.

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon by our counsel, Morgan, Lewis & Bockius LLP, Philadelphia, Pennsylvania. Piper Sandler is being represented in connection with this offering by White & Case LLP, New York, New York.

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, 2020](#) 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 forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement and the accompanying prospectus certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement and the accompanying prospectus, 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 and the accompanying prospectus 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.

We file reports, proxy statements and other information with the SEC under the Exchange Act. The SEC maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to “incorporate by reference” the information we file with them which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement and the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus modifies or replaces that statement. We incorporate by reference the documents listed below and any future information filed (rather than furnished) with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act between the date of this prospectus and the termination of this offering, provided, however, that we are not incorporating any information furnished under Item 2.02 or Item 7.01 of any current report on Form 8-K:

- our [Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 18, 2021](#), as [amended by Form 10-K/A filed with the SEC on April 30, 2021](#);
- the information specifically incorporated by reference into our [Annual Report on Form 10-K for the year ended December 31, 2020](#), from our Definitive [Proxy Statement on Schedule 14A, filed with the SEC on May 28, 2021](#);
- our Quarterly Reports on Form 10-Q for the [quarter ended March 31, 2021, filed with the SEC on May 17, 2021](#), and for [quarter ended June 30, 2021, filed with the SEC on August 16, 2021](#);
- our Current Report on Form 8-K and 8-K/A, as applicable, filed with the SEC on [January 8, January 15, February 12, February 16, February 19, February 24, March 4, March 4, April 1, May 3, May 14, May 20, June 22, June 25, July 16, July 30, August 4, and August 5, 2021](#); and
- the description of our Common Stock contained in our [Registration Statement on Form 8-A, filed with the SEC on July 23, 2013](#), including any amendments or reports filed for the purpose of updating such description.

These documents may also be accessed on our website at www.onconova.com. Except as otherwise specifically incorporated by reference in this prospectus supplement and the accompanying prospectus, information contained in, or accessible through, our website is not a part of this prospectus supplement and the accompanying prospectus.

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents by writing or telephoning us at the following address:

Onconova Therapeutics, Inc.
12 Penns Trail, Newtown, PA 18940
Attention: Suzanne Hutchinson
(267) 759-3680

PROSPECTUS

**Onconova Therapeutics, Inc.****\$150,000,000****Common Stock, Preferred Stock,
Debt Securities, Warrants and Units
and****113 Shares of Common Stock Offered by Selling Stockholders**

This prospectus covers our offer and sale from time to time of any combination of common stock, preferred stock, debt securities, warrants or units described in this prospectus in one or more offerings. This prospectus provides a general description of the securities we may offer and sell. Each time we offer and sell securities we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement will also describe the specific manner in which we will offer the securities and may also add, update or change information contained in this prospectus. The aggregate offering price of all securities sold by us under this prospectus may not exceed \$150,000,000.

In addition, the selling stockholders to be named in the applicable prospectus supplement may offer and sell up to an aggregate of 113 shares of our common stock from time to time, in amounts, at prices and on terms that will be determined at the time the shares of our common stock are offered. The prospectus supplement may also add, update or change information contained in this prospectus. We will not receive proceeds from the sale of shares of our common stock by the selling stockholders.

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

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

Our common stock is currently listed on the Nasdaq Capital Market under the symbol "ONTX." On April 23, 2020, the last reported sale price of our common stock on the Nasdaq Capital Market was \$0.3014 per share.

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

Investing in these securities involves risks, including those set forth in the "Risk Factors" section of the applicable prospectus supplement and any related free writing prospectus and in the documents incorporated by reference into this prospectus.

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

This prospectus is dated May 18, 2020.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC. This prospectus covers the primary offering by us of up to an aggregate offering price of \$150,000,000 of securities. In addition, under this prospectus, the selling stockholders, to be named in a prospectus supplement to this prospectus, may, from time to time, offer and sell up to an aggregate 113 shares of our common stock in one or more offerings. We may offer and sell any combination of the securities described in this prospectus and the selling stockholders may offer and sell shares of common stock in one or more offerings. This prospectus provides you with a general description of the securities we may offer and sell. Each time we offer and sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading “Where You Can Find More Information,” before investing in any of the securities offered.

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

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

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

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an Internet website at <http://www.sec.gov> that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. Our SEC filings are accessible through the Internet at that website. Our reports on Forms 10-K, 10-Q and 8-K, and amendments to those reports, are also available for download, free of charge, as soon as reasonably practicable after these reports are filed with the SEC, at our website at www.onconova.com. The content contained in, or that can be accessed through, our website is not a part of this prospectus.

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

INCORPORATION OF INFORMATION BY REFERENCE

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

- [Our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 that we filed with the SEC on March 27, 2020, including the information required by Part III, Items 10 through 14, of Form 10-K, which we incorporate by reference to our definitive proxy statement for our 2020 annual meeting of stockholders filed on April 23, 2020;](#)
- Our Current Reports on Form 8-K filed with the SEC on [January 3, 2020](#), [January 17, 2020](#) and [January 23, 2020](#);
- The description of our common stock contained in our [registration statement on Form 8-A filed on July 23, 2013 \(Registration no. 001-36020\)](#) with the SEC, including any amendment or report filed for the purpose of updating such description;
- All documents filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is a part and prior to the effectiveness of such registration statement; and
- All documents filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and before we stop offering the securities under this prospectus.

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

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

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain, and any prospectus supplement may contain, forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements, other than statements of historical facts, included or incorporated in this prospectus or any prospectus supplement regarding our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. We may, in some cases, use terms such as “believes,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should,” “approximately” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements appear in a number of places throughout this prospectus and the documents incorporated by reference herein, and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, protection of our intellectual property portfolio, the degree of clinical utility of our products, particularly in specific patient populations, our ability to develop commercial and manufacturing functions, expectations regarding clinical trial data, our results of operations, cash needs, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

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

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

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

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

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

You should also read carefully the factors described in the “Risk Factors” section of this prospectus and in documents incorporated by reference herein, to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus and in documents incorporated by reference herein will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all.

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

RISK FACTORS

Our business is influenced by many factors that are difficult to predict, and that involve uncertainties that may materially affect actual operating results, cash flows and financial condition. Before making an investment decision, you should carefully consider these risks set forth in the “Risk Factors” section of our [Annual Report on Form 10-K](#), as filed with the SEC on March 27, 2020, which are incorporated by reference into this prospectus, as well as any amendment or update to our risk factors reflected in subsequent filings with the SEC and any applicable prospectus supplement or any free writing prospectus. You should also carefully consider any other information we include or incorporate by reference in this prospectus. Any such risk could cause our business, financial condition or operating results to suffer. The market price of our common stock could decline if one or more of these risks and uncertainties develop into actual events. You could lose all or part of your investment.

ONCONOVA THERAPEUTICS, INC.

Overview

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

In December 2015, we enrolled the first patient into our INSPIRE trial, a randomized controlled Phase 3 clinical trial of intravenous rigosertib (“rigosertib IV”) in a population of patients with higher-risk MDS after failure of hypomethylating agent (“HMA”) therapy. The primary endpoint of INSPIRE is improvement in overall survival. An interim analysis of the trial was performed in January 2018. We completed enrollment of the required 360 randomized patients in March 2020. As of March 2020, more than 85% of the required death events have been reported. Based on survival events and trends to date, we anticipate reporting topline survival data in the second half of 2020, following at least 288 confirmed death events.

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

CORPORATE INFORMATION

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

USE OF PROCEEDS

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

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

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

DESCRIPTION OF SECURITIES

We may offer shares of our common stock and preferred stock, various series of debt securities, warrants or units to purchase any of such securities, with a total value of up to \$150,000,000, from time to time in one or more offerings under this prospectus at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities that we may offer. In connection with each offering, we will provide a prospectus supplement that will describe the specific amounts, prices and terms of the securities being offered, including, to the extent applicable:

- designation or classification;
- aggregate offering price;
- rates and times of payment of dividends;
- redemption, conversion or exchange terms;
- conversion or exchange prices or rates and any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- restrictive covenants;
- voting or other rights; and
- important federal income tax considerations.

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

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

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 250,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share. As of April 24, 2020, 167,416,070 shares of our common stock, and no shares of our preferred stock, were outstanding.

Common Stock

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

Preferred Stock

We may issue any class of preferred stock in any series. Our board of directors has the authority, subject to limitations prescribed under Delaware law, to issue preferred stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation,

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

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

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

Delaware Anti-Takeover Law

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

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding specified shares; or
- at or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 ²/₃% of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a “business combination” to include:

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

In general, Section 203 defines an “interested stockholder” as any person that is:

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

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

may, by adopting an amendment to the corporation’s certificate of incorporation or bylaws, elect not to be governed by this section, effective 12 months after adoption.

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

Certificate of Incorporation and Bylaws

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

- permit our board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (as of April 24, 2020, 1,044,488 shares have been designated as Series A Convertible Preferred Stock and 1,796,875 shares have been designated as Series B Convertible Preferred Stock);
- provide that all vacancies on our board of directors, including as a result of newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder’s notice;
- not provide for cumulative voting rights, thereby allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election; and
- provide that special meetings of our stockholders may be called only by the board of directors or by such person or persons requested by a majority of the board of directors to call such meetings.

Transfer Agent and Registrar

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

Listing

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

DESCRIPTION OF DEBT SECURITIES

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

We may offer under this prospectus up to \$150,000,000 aggregate principal amount of secured or unsecured debt securities, or if debt securities are issued at a discount, or in a foreign currency or composite currency, such principal amount as may be sold for an initial public offering price of up to \$150,000,000. The debt securities may be either senior debt securities, senior subordinated debt securities or subordinated

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

General

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

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

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

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

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

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

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

Payment of Interest and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, as 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.

ONCONOVA THERAPEUTICS, INC.

Up to \$25,000,000

Common Stock



PROSPECTUS SUPPLEMENT

Piper Sandler

August 20, 2021
