

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

**Form S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Onconova Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other
jurisdiction of
incorporation or
organization)

2834
(Primary Standard
Industrial
Classification Code
Number)

22-3627252
(I.R.S.
Employer
Identification
No.)

**375 Pheasant Run
Newtown, PA 18940
(267) 759-3680**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Ramesh Kumar, Ph.D.
President and Chief Executive Officer
Onconova Therapeutics, Inc.
375 Pheasant Run
Newtown, PA 18954
(267) 759-3680**

(Name, address, including zip code, and telephone number including area code, of agent for service)

Copy to:

Joanne R. Soslow
Morgan, Lewis & Bockius LLP
1701 Market Street
Philadelphia, PA
(215) 963-5000

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this registration statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act of 1933, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act of 1933, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company or an emerging growth company. See definitions of "large accelerated filer", "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of securities to be registered	Proposed maximum aggregate offering price(1)	Amount of registration fee
Common Stock, par value \$0.01 per share (2)	\$ 15,000,000	\$ 1,867.50
Total	\$ 15,000,000	\$ 1,867.50

(1) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(o) of the Securities Act of 1933 (the "Act"). Includes the offering price of any additional securities that the underwriter has the option to purchase.

(2) Pursuant to Rule 416 under the Act, the shares being registered herein include such indeterminate number of shares as may be issued with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant files a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the Securities and Exchange Commission declares our registration statement effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated December 29, 2017

PRELIMINARY PROSPECTUS



Onconova Therapeutics, Inc.

Shares of Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on the NASDAQ Capital Market under the symbol "ONTX." On December 20, 2017, the last reported sale price of our common stock on the NASDAQ Capital Market was \$1.50 per share.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 10 of this prospectus and in the documents incorporated by reference into this prospectus.

	Per Share	Total
Public offering price	\$ _____	\$ 15,000,000
Underwriting discounts and commissions	\$ _____	\$ _____
Proceeds, before expenses, to us	\$ _____	\$ _____

We have granted the underwriter an option for a period of _____ days to purchase up to an additional _____ shares of our common stock to cover over-allotments, if any.

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

Delivery of the shares is expected to be made on or about _____, 20____.

The date of this prospectus is _____, 20____.

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ABOUT THIS PROSPECTUS

Unless the context otherwise requires, references in this prospectus to “Onconova,” “Onconova Therapeutics,” “Company,” “we,” “us” and “our” refer to Onconova Therapeutics, Inc. and its consolidated subsidiaries. This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission, which we refer to as the SEC or the Commission, utilizing a registration process. It is important for you to read and consider all of the information contained in this prospectus and any applicable prospectus before making a decision whether to invest in the common stock. You should also read and consider the information contained in the exhibits filed with our registration statement, of which this prospectus is a part, as described in “Where You Can Find More Information” in this prospectus.

You should rely only on the information contained in this prospectus and any applicable prospectus supplement, including the information incorporated by reference. We have not authorized anyone to provide you with different information. We are not offering to sell or soliciting offers to buy, and will not sell, any securities in any jurisdiction where it is unlawful. You should assume that the information contained in this prospectus or any prospectus supplement, as well as information contained in a document that we have previously filed or in the future will file with the SEC is accurate only as of the date of this prospectus, the applicable prospectus supplement or the document containing that information, as the case may be.

PROSPECTUS SUMMARY

The following summary highlights certain information contained elsewhere in this prospectus and the documents incorporated by reference herein. This summary does not contain all the information you will need in making your investment decision. You should carefully read this entire prospectus and the documents incorporated by reference herein. You should pay special attention to the “Risk Factors” section of this prospectus and the financial statements and other information incorporated by reference in this prospectus.

Our Business

Overview

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

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

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

Rigosertib

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

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continue to seek additional funding.

Rigosertib IV for higher-risk MDS

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

During 2014 and 2015, we held meetings with the U.S. Food and Drug Administration (“FDA”) European Medicines Agency (“EMA”) and several European national regulatory authorities to discuss and seek guidance on a path for approval of rigosertib IV in higher-risk MDS patients whose disease had failed HMA therapy. After discussions with the FDA and EMA, we refined our patient eligibility criteria by defining what we believe to be a more homogenous patient population. After regulatory feedback, input from key opinion leaders in the U.S. and Europe and based on learnings from the ONTIME study, we designed a new randomized controlled Phase 3 trial, referred to as INSPIRE. The INSPIRE trial is enrolling higher-risk MDS patients under 82 years of age who have progressed on, relapsed, or failed to respond to, previous treatment with HMAs within nine months or nine cycles over the course of one year after initiation of HMA therapy, and had their last dose of HMA within six months prior to enrollment in the trial. The primary endpoint of this study is overall survival of all randomized patients in the intent-to-treat (“ITT”) population and the International Prognostic Scoring System- Revised (IPSS-R) Very High Risk subgroup. This randomized trial of approximately 225 patients is expected to be conducted at more than 170 sites globally. The first patient in the INSPIRE trial was enrolled at the MD Anderson Cancer Center in December 2015, the first patient in Europe was enrolled in March, 2016, and the first patient in Japan was enrolled in July, 2016.

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

In an attempt to optimize enrollment, we have taken proactive measures to increase enrollment

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

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

Safety and Tolerability of rigosertib in MDS and other hematologic malignancies

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

Rigosertib oral in combination with azacitidine for higher-risk MDS

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

Response per IWG 2006

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

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

Safety/Tolerability of the Combination:

Oral rigosertib (560 mg qAM, 280 mg qPM) was administered on Day 1-21 of a 28-day cycle. Azacitidine 75 mg/m²/day SC or IV was administered for 7 days starting on Day 8. The combination of oral rigosertib and azacitidine was well tolerated. The most common TEAEs in $\geq 10\%$ of patients were

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nausea (41%), fatigue (39%), diarrhea (37%), constipation (37%) and dysuria (28%). The most common serious AEs were pneumonia (11%) and febrile neutropenia (7%). The most common AEs leading to discontinuation were AML (4%) and pneumonia (4%).

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

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

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

In June 2017, at the Congress of the European Hematology Association Meeting, we updated the data from the Phase 1/2 trial and highlighted results in AML patients included in this study. Response data was presented on eight evaluable patients with AML who were tested with the rigosertib and azacitidine combination. For the eight evaluable patients with AML, the combination was well tolerated and the safety profile was similar to single-agent azacitidine, based on safety information in the azacitidine FDA approved label. Based on the presented results of the combination studies, the authors concluded that continued study in AML was warranted. We will not commence further development of rigosertib oral in combination with azacitidine for AML without additional financing.

Rigosertib oral for lower-risk MDS

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

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

Data presented from the 09-05 trial also suggested the potential of a genomic methylation assessment of bone marrow cells to prospectively identify lower-risk MDS patients likely to respond to oral

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rigosertib. We therefore expanded the 09-05 trial by adding an additional cohort of 20 patients to advance the development of this genomic methylation test. To date, a biomarker which would predict response has not been identified. Further testing and development of oral rigosertib for lower-risk MDS will be required. We will not commence further development of rigosertib oral for lower-risk MDS without additional financing.

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

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

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

Other Programs

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

Briciclib

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

Recilisib

Recilisib is a product candidate being developed in collaboration with the U.S. Department of Defense for acute radiation syndromes. We have completed four Phase 1 trials to evaluate the safety and pharmacokinetics of recilisib in healthy human adult subjects using both subcutaneous and oral formulations. We have also conducted animal studies and clinical trials of recilisib under the FDA's Animal Rule, which permits marketing approval for new medical countermeasures for which conventional human efficacy studies are not feasible or ethical, by relying on evidence from adequate and well-controlled studies in appropriate animal models to support efficacy in humans when the results of those studies establish that the drug is reasonably likely to produce a human clinical benefit. Human safety data, however, is still required. Ongoing studies of recilisib, focusing on animal models and biomarker

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development to assess the efficacy of recilisib are being conducted by third parties with government funding. We anticipate that any future development of recilisib beyond these ongoing studies would be conducted solely with government funding or by collaboration. Use of government funds to finance the research and development in whole or in part means any future effort to commercialize recilisib will be subject to federal laws and regulations on U.S. government rights in intellectual property. Additionally, we are subject to laws and regulations governing any research contracts, grants, or cooperative agreements under which government funding was provided.

Preclinical Product Candidates

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

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

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

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CORPORATE INFORMATION

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

THE OFFERING

Common stock offered by us	Shares
Offering Price	\$ per Share
Common stock to be outstanding after this offering	shares, or shares if the underwriter exercises its option to purchase additional shares of our common stock in full.
Use of proceeds	We intend to use the net proceeds from this offering 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 working capital needs. See “Use of Proceeds” on page 15.
Risk factors	You should read the “Risk Factors” section of this prospectus and in the documents incorporated by reference into this prospectus for a discussion of factors to consider before deciding to invest in our common stock.
NASDAQ Capital Market symbol	“ONTX.”

The number of shares of our common stock outstanding after the offering is based on 9,851,164 shares outstanding as of September 30, 2017, and excludes as of such date:

- 907,373 shares of common stock issuable upon the exercise of stock options outstanding at September 30, 2017 with a weighted average exercise price of approximately \$41.09 per share;
- 3,294,771 shares of common stock issuable upon the exercise of outstanding warrants at September 30, 2017 with a weighted average exercise price of approximately \$5.10 per share;
- 42,355 shares of common stock reserved for future issuance under our 2013 Equity Compensation Plan at September 30, 2017; and
- any additional shares of common stock that we may issue to Lincoln Park Capital Fund, LLC (“Lincoln Park”), pursuant to a purchase agreement we entered into on October 8, 2015, which provides that, upon the terms and subject to the conditions and limitation set forth therein, Lincoln Park is committed to purchase up to an aggregate of an additional \$15 million of shares of our common stock over the term of the purchase agreement, should we elect to sell shares to Lincoln Park.

As of December 20, 2017, the total number of our outstanding shares of common stock was 10,771,163.

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Unless otherwise indicated, all information contained in this prospectus assumes no exercises by the underwriter of its over-allotment.

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, including those set forth below and those described in the “Risk Factors” section of our Annual Report on Form 10-K, as filed with the SEC on March 29, 2017, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, as filed with the SEC on November 9, 2017, which is 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 you should also carefully consider any other information we include or incorporate by reference in this prospectus.

Any of the risks we describe below or in the information incorporated herein by reference in this prospectus 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.

Risks Associated with this Offering

Our management will have broad discretion over the use of any net proceeds from this offering, you may not agree with how we use the proceeds, and the proceeds may not be invested successfully.

Our management will have broad discretion as to the use of any net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you will be relying on the judgment of our management with regard to the use of any proceeds from the sale of shares of common stock in this offering, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for you.

You will experience immediate dilution.

Since the price per share of our common stock being offered is higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ per share in the net tangible book value of the common stock as of September 30, 2017. See the section entitled “Dilution” in this prospectus for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors.

Our shareholders may experience significant dilution as a result of future equity offerings or issuances and exercise of outstanding options and warrants.

In order to raise additional capital or pursue strategic transactions, we may in the future offer, issue or sell additional shares of common stock or other securities convertible into or exchangeable for shares of our common stock. We cannot assure you that we will be able to sell shares or other securities in any other transaction at a price per share or that have an exercise price or conversion price per shares that is equal to or greater than the price for the securities purchased by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing shareholders. The price per

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share at which we sell or issue additional shares of common stock or other securities convertible into or exchangeable for our common stock future transactions may be higher or lower than such price.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

We do not intend to pay any cash dividends on our common stock in the foreseeable future and, therefore, any return on your investment in our common stock must come from increases in the fair market value and trading price of our common stock.

We do not intend to pay any cash dividends on our common stock in the foreseeable future and, therefore, any return on your investment in our common stock must come from increases in the fair market value and trading price of our common stock.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

- our need for additional financing for our INSPIRE trial and other operations, and our ability to obtain sufficient funds on acceptable terms when needed, and our plans and future needs to scale back operations if adequate financing is not obtained;
- our ability to continue as a going concern;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the success and timing of our preclinical studies and clinical trials, including site initiation and patient enrollment, and regulatory approval of protocols for future clinical trials;
- our ability to enter into, maintain and perform collaboration agreements with other pharmaceutical companies, for funding and commercialization of our clinical product candidates or preclinical compounds, and our ability to achieve certain milestones under those agreements;

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- the difficulties in obtaining and maintaining regulatory approval of our product candidates, and the labeling under any approval we may obtain;
- our plans and ability to develop, manufacture and commercialize our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any of our product candidates;
- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;
- the successful development of our commercialization capabilities, including sales and marketing capabilities;
- recently enacted and future legislation and regulation regarding the healthcare system;
- the success of competing therapies and products that are or become available;
- our ability to maintain the listing of our common stock on a national securities exchange;
- the potential for third party disputes and litigation;
- the performance of third parties, including contract research organizations (“CROs”) and third-party manufacturers; and
- our expectations regarding CRO transition.

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

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

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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.

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately \$ million from the sale of the shares of common stock offered by us in this offering, after deducting underwriting discounts and commissions and estimated offering costs payable by us.

We intend to use the net proceeds from this offering 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.

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 the clinical development of our product candidates. 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 shares of our common stock.

As of the date of this prospectus, we cannot specify with certainty all of the particular uses of the proceeds from this offering. Accordingly, we will retain broad discretion over the use of such proceeds. Pending the use of the net proceeds from this offering as described above, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

CAPITALIZATION

The following table presents our cash, cash equivalents and capitalization, as of September 30, 2017:

- on an actual basis; and
- on an as adjusted basis to give further effect to the sale of _____ shares of common stock in this offering at a price of \$ _____ per share, after deducting underwriting discounts and commissions and estimate offering expenses payable by us.

You should read this information in conjunction with our consolidated financial statements and notes thereto incorporated by reference into this prospectus.

	<u>September 30, 2017</u>
	<u>(unaudited)</u>
Cash and cash equivalents	\$ 7,600,000
Total liabilities	14,880,000
Stockholders' equity*:	
Preferred stock, \$0.01 par value, 5,000,000 authorized at September 30, 2017 and December 31, 2016, none issued and outstanding at September 30, 2017	—
Common stock, \$0.01 par value, 25,000,000 authorized at September 30, 2017, 9,851,164 shares issued and outstanding at September 30, 2017	99,000
Additional paid-in capital	349,103,000
Accumulated other comprehensive loss	(1,000)
Accumulated deficit	(356,109,000)
Total Onconova Therapeutics, Inc. stockholders' deficit	(6,908,000)
Non-controlling interest	830,000
Total stockholders' (deficit) equity	(6,078,000)

* The above table is based on 9,851,164 shares of our common stock outstanding as of September 30, 2017 and exclude:

- 907,373 shares of common stock issuable upon the exercise of stock options outstanding at September 30, 2017 with a weighted average exercise price of approximately \$41.09 per share;
- 3,294,771 shares of common stock issuable upon the exercise of outstanding warrants at September 30, 2017 with a weighted average exercise price of approximately \$5.10 per share;

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- 42,355 shares of common stock reserved for future issuance under our 2013 Equity Compensation Plan at September 30, 2017; and
- any additional shares of common stock that we may issue to Lincoln Park, pursuant to a purchase agreement we entered into on October 8, 2015, which provides that, upon the terms and subject to the conditions and limitation set forth therein, Lincoln Park is committed to purchase up to an aggregate of an additional \$15 million of shares of our common stock over the term of the purchase agreement, should we elect to sell shares to Lincoln Park.

DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. As of September 30, 2017, our historical net tangible book value was \$6.08 million, or \$(0.62) per share, based on 9,851,164 shares of our common stock outstanding as of September 30, 2017. Our historical net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of our common stock outstanding as of September 30, 2017. After giving effect to our sale in this offering of _____ shares of common stock at the public offering price of \$ _____ per share, and after deducting placement agent fees and estimated offering expenses payable by us, our net tangible book value as of September 30, 2017 would have been \$ _____ million, or \$ _____ per share. This represents an immediate increase of net tangible book value of \$ _____ per share to our existing stockholders and an immediate dilution of \$ _____ per share to investors purchasing shares in this offering. The following table illustrates this per share dilution.

Public offering price per share		\$
Historical Net tangible book value per share at September 30, 2017	\$	(0.62)
Increase in net tangible book value per share attributable to investors purchasing our common stock in this offering		
As adjusted net tangible book value per share as of September 30, 2017 after giving effect to this offering		
Dilution per share to investors purchasing our common stock in this offering		\$

The above discussion and table are based on 9,851,164 shares of our common stock outstanding as of September 30, 2017 and exclude:

- 907,373 shares of common stock issuable upon the exercise of stock options outstanding at September 30, 2017 with a weighted average exercise price of approximately \$41.09 per share;
- 3,294,771 shares of common stock issuable upon the exercise of outstanding warrants at September 30, 2017 with a weighted average exercise price of approximately \$5.10 per share;
- 42,355 shares of common stock reserved for future issuance under our 2013 Equity Compensation Plan at September 30, 2017; and
- any additional shares of common stock that we may issue to Lincoln Park, pursuant to a purchase agreement we entered into on October 8, 2015, which provides that, upon the terms and subject to the conditions and limitation set forth therein, Lincoln Park is committed to purchase up to an aggregate of an additional \$15 million of shares of our common stock over the term of the purchase agreement, should we elect to sell shares to Lincoln Park.

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To the extent that outstanding options or warrants are exercised, you 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 additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

UNDERWRITING

is acting as the representative (the “Representative”) of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriters	Number of Shares
<hr/>	
Total	

Over-Allotment Option

We have granted the underwriters an option, exercisable for _____ days from the date of this prospectus, to purchase up to an aggregate of additional shares of common stock to cover over-allotments, if any, at the public offering price set forth on the cover page of this prospectus, less the underwriting discount. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. If the underwriters exercise this option, the underwriters will be obligated subject to certain conditions, to purchase the additional shares for which the option has been exercised.

Discount, Commissions and Expenses

The underwriters have advised us that they proposes to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of \$ _____ per share. After this offering, the public offering price, concession and reallowance to dealers may be changed by the underwriters. No such change shall change the amount proceeds to be received by us as set forth on the cover page of this prospectus. The shares of common stock are offered by the underwriters stated herein, subject to receipt and acceptance by them and subject to their right to reject any order in whole or in part. The underwriters have informed us that it does not intend to confirm sales to any accounts over which it exercises discretionary authority.

The following table shows the underwriting discount payable to the underwriters by us in connection with this offering. Such amounts are show assuming both no exercise and full exercise of the underwriters’ over-allotment option to purchase additional shares.

	Per Share	Total Without Exercise of Over Allotment Option	Total With Exercise of Over Allotment Option
Public Offering Price			
Underwriting discount (1)			
Proceeds, before expenses, to us			

(1) The underwriting discount shall be \$ _____ per share.

The expenses of the offering, not including the underwriting discount, payable by us are estimated to be \$ _____ .

Indemnification

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and liabilities arising from breaches of representations and warranties contained in the underwriting agreement, or to contribute to payments that the underwriters may be required to make in respect of those liabilities.

Lock-up Agreements

The Company has agreed, subject to certain exceptions, for a period of days after the date of the underwriting agreement, not to offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of, directly or indirectly any shares of common stock or any securities convertible into or exchangeable for our common stock either owned as of the date of the underwriting agreement or thereafter acquired without the prior written consent of the Representative.

The Company's officers, directors and certain shareholders have agreed, subject to limited exceptions, for a period of days after the date of the underwriting agreement, not to offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of, directly or indirectly any shares of common stock or any securities convertible into or exchangeable for our common stock either owned as of the date of the underwriting agreement or thereafter acquired, subject to certain exceptions, without the prior written consent of the Representative.

The Representative may, in its sole discretion and at any time or from time to time before the termination of the lock-up period, without notice, release all or any portion of the securities subject to lock-up agreements.

Stabilization, Short Positions and Penalty Bids

In connection with the offering, the underwriters may engage in stabilizing transactions, short sales and purchases to cover positions created by short sales, and penalty bids or purchases for the purpose of pegging, fixing or maintaining the price of the common stock, in accordance with Regulation M under the Exchange Act:

- Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.

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- A short position involves a sale by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase in the offering, which creates the syndicate short position. This short position may be either a covered short position or a naked short position. In a covered short position, the number of shares involved in the sales made by the underwriters in excess of the number of shares they are obligated to purchase is not greater than the number of shares that they may purchase by exercising its option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in its option to purchase additional shares. The underwriters may close out any short position by either exercising its option to purchase additional shares and/or purchasing shares in the open market. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through its option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
- Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions.
- Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of the common stock. As a result, the price of the common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on the NASDAQ Capital Market or otherwise and, if commenced, may be discontinued at any time.

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

Other Relationships

From time to time, the underwriters and their affiliates have provided, and may provide in the future, various advisory, investment and commercial banking and other services to us in the ordinary course of business, for which they have received and may continue to receive customary fees and commissions. However, except as disclosed in this prospectus, we have no present arrangements with the underwriters for any further services.

DESCRIPTION OF CAPITAL STOCK

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

Common Stock

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

Preferred Stock

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

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

Delaware Anti-Takeover Law

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

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an

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interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding specified shares; or

- at or subsequent to the date of the transaction, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66²/₃% of the outstanding voting stock which is not owned by the interested stockholder.
- Section 203 defines a “business combination” to include:
 - any merger or consolidation involving the corporation and the interested stockholder;
 - any sale, lease, exchange, mortgage, pledge, transfer or other disposition of 10% or more of the assets of the corporation to or with the interested stockholder;
 - subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
 - subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
 - the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.
- In general, Section 203 defines an “interested stockholder” as any person that is:
 - the owner of 15% or more of the outstanding voting stock of the corporation;
 - an affiliate or associate of the corporation who was the owner of 15% or more of the outstanding voting stock of the corporation at any time within three years immediately prior to the relevant date; or
 - the affiliates and associates of the above.

Under specific circumstances, Section 203 makes it more difficult for an “interested stockholder” to effect various business combinations with a corporation for a three-year period, although the stockholders may, by adopting an amendment to the corporation’s certificate of incorporation or bylaws, elect not to be governed by this section, effective 12 months after adoption.

Our certificate of incorporation and 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.

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Certificate of Incorporation and Bylaws

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

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

Transfer Agent

The transfer agent and registrar for our common stock is Wells Fargo Bank, N.A.

Listing

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

EXPERTS

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

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Morgan, Lewis & Bockius LLP, Philadelphia, Pennsylvania. The underwriter is being represented in connection with this offering by .

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy and information statements and other information with the SEC. Our SEC filings, including the registration statement, are available to the public from the SEC's website at www.sec.gov. To receive copies of public records not posted to the SEC's website at prescribed rates, you may complete an online form at www.sec.gov, send a fax to (202) 772-9337 or submit a written request to the SEC, Office of FOIA/PA Operations, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information.

We also make available free of charge on our website, www.onconova.com, all materials that we file electronically with the SEC, including our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, Section 16 reports and amendments to those reports as soon as reasonably practicable after such materials are electronically filed with, or furnished to, the SEC. Information contained on our website or any other website is not incorporated by reference into this prospectus and does not constitute a part of this prospectus.

INCORPORATION BY REFERENCE

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

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 that we filed with the SEC on March 29, 2017, including the information required by Part III, Items 10 through 14, of Form 10-K, which is incorporated by reference to our definitive proxy statement for our 2017 annual meeting of stockholders filed on April 12, 2017;
- Our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017, June 30, 2017 and September 30, 2017 that we filed with the SEC on May 15, 2017, August 14, 2017 and November 9, 2017, respectively;
- Our Current Reports on Form 8-K filed with the SEC on April 20, 2017, April 24, 2017, May 18, 2017, May 25, 2017, August 18, 2017, November 13, 2017 and November 17, 2017;
- The description of our common stock contained in our registration statement on Form 8-A filed on July 23, 2013 (Registration no. 001-36020) with the SEC, including any amendment or report filed for the purpose of updating such description; 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 terminate the offering 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 Hutchinson.

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.

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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.



PROSPECTUS

Shares of Common Stock

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PART II
Information Not Required In Prospectus

Item 13. Other Expenses of Issuance and Distribution.

The following is a statement of estimated expenses in connection with the issuance and distribution of the securities being registered, excluding dealer-manager fees. All expenses incurred with respect to the registration of the common stock will be borne by us. All amounts are estimates except the SEC registration fee and the FINRA filing fee.

	Amount to be Paid
SEC Registration Fee	\$ 1,867.50
FINRA Filing Fee	*
NASDAQ Fee	*
Printing Expenses	30,000
Legal Fees and Expenses	80,000
Accounting Fees and Expenses	30,000
Transfer Agent Fees and Expenses	20,000
Miscellaneous Expenses	25,000
Total	<u>\$ *</u>

* These fees will provided upon amendment.

Item 14. Indemnification of Directors and Officers.

We are incorporated under the laws of the State of Delaware. Section 145 of the Delaware General Corporation Law provides that a Delaware corporation may indemnify any persons who are, or are threatened to be made, parties to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of such corporation), by reason of the fact that such person was an officer, director, employee or agent of such corporation, or is or was serving at the request of such person as an officer, director, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation's best interests and, with respect to any criminal action or proceeding, had no reasonable cause to believe that his or her conduct was illegal. A Delaware corporation may indemnify any persons who are, or are threatened to be made, a party to any threatened, pending or completed action or suit by or in the right of the corporation by reason of the fact that such person was a director, officer, employee or agent of such corporation, or is or was serving at the request of such corporation as a director, officer, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees) actually and reasonably incurred by such

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person in connection with the defense or settlement of such action or suit provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation's best interests except that no indemnification is permitted without judicial approval if the officer or director is adjudged to be liable to the corporation. Where an officer or director is successful on the merits or otherwise in the defense of any action referred to above, the corporation must indemnify him or her against the expenses which such officer or director has actually and reasonably incurred. Our certificate of incorporation and bylaws provide for the indemnification of our directors and officers to the fullest extent permitted under the Delaware General Corporation Law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duties as a director, except for liability for any:

- transaction from which the director derives an improper personal benefit;
- act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or redemption of shares; or
- breach of a director's duty of loyalty to the corporation or its stockholders.

Our certificate of incorporation includes such a provision. Expenses incurred by any officer or director in defending any such action, suit or proceeding in advance of its final disposition shall be paid by us upon delivery to us of an undertaking, by or on behalf of such director or officer, to repay all amounts so advanced if it shall ultimately be determined that such director or officer is not entitled to be indemnified by us.

As permitted by the Delaware General Corporation Law, we have entered into indemnification agreements with our directors and executive officers. These agreements, among other things, require us to indemnify each director and officer to the fullest extent permitted by law and advance expenses to each indemnitee in connection with any proceeding in which indemnification is available.

At present, there is no pending litigation or proceeding involving any of our directors or executive officers as to which indemnification is required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

We have an insurance policy covering our officers and directors with respect to certain liabilities, including liabilities arising under the Securities Act.

Item 15. Recent Sales of Unregistered Securities.

On October 8, 2015, the Company entered into the Purchase Agreement with Lincoln Park, pursuant to which the Company has the right to sell to, and Lincoln Park is obligated to purchase from the Company, up to \$16.5 million in shares of the Company's common stock, subject to certain limitations, from time to time, over the 36-month period commencing on the date that this registration statement is declared effective by the SEC and a final prospectus in connection therewith is filed. On October 8, 2015, Lincoln Park purchased 846,755 shares of the Company's common stock for a total purchase price of

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\$1,500,000 as an initial purchase under the Purchase Agreement and the Company issued 200,000 shares of common stock pursuant to the terms of the Purchase Agreement as consideration for its commitment to purchase additional shares of common stock under the Purchase Agreement. The sale of such shares to Lincoln Park was not registered under the Securities Act because it was made in a transaction exempt from registration under Section 4(a)(2) of the Securities Act and/or Rule 506 promulgated thereunder.

On January 5, 2016, the Company entered into a Securities Purchase Agreement (the “Purchase Agreement”) with an institutional investor (the “Investor”) providing for the issuance and sale by the Company of 1,936,842 shares of the Company’s common stock at a purchase price of \$0.95 per share and warrants to purchase 968,421 shares of the Company’s common stock (the “Private Placement Warrants”) for aggregate gross proceeds of \$1,840,000. The shares of the Company’s common stock were offered pursuant to an effective shelf registration statement on Form S-3, declared effective by the SEC on November 20, 2014 (File No. 333-199219). The Private Placement Warrants were issued and sold without registration under the Securities Act in reliance on the exemptions provided by Section 4(a)(2) of the Securities Act and/or Regulation D promulgated thereunder and in reliance upon similar exemptions under applicable state laws. Each Private Placement Warrant shall be initially exercisable on the six (6) month anniversary of the issuance date at an exercise price equal to \$1.15 per share of common stock, subject to customary adjustments, and have a term of exercise of five (5) years from the initial exercise date. H.C. Wainwright & Co., LLC acted as the Company’s exclusive placement agent for the issuance and sale of the shares of common stock and Private Placement Warrants, and was paid a cash fee equal to 7.5% of the gross proceeds received by the Company from the sale of the securities in the transactions and was reimbursed by the Company for up to \$50,000 in expenses.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits

The exhibits to the registration statement are listed in the Exhibit Index to this registration statement and are incorporated herein by reference.

(b) Financial statement schedules

All schedules have been omitted because either they are not required, are not applicable or the information is otherwise set forth in the financial statements and related notes thereto.

Item 17. Undertakings.

The undersigned registrant hereby undertakes:

- (I) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933 (the “Act”);
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information in the registration statement.
- Notwithstanding

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the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement.

Provided, however, that Paragraphs (1)(i), (1)(ii) and (1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

If the registrant is subject to Rule 430C (§230.430C of this chapter), each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A (§230.430A of this chapter), shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424 (§230.424 of this chapter);

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- (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b) (1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

EXHIBIT INDEX

Exhibit Number	Exhibit Description
1.1†	Form of Underwriting Agreement
3.1	Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc. (Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 30, 2013).
3.2	Amended and Restated Bylaws of Onconova Therapeutics, Inc. (Incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed on July 30, 2013).
3.3	Certificate of Amendment to Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc. (Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on May 31, 2016).
4.1	Form of Certificate of Common Stock (Incorporated by reference to Exhibit 4.1 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013.)
4.2	Eighth Amended and Restated Stockholders' Agreement, effective as of July 27, 2012, by and among Onconova Therapeutics, Inc. and certain stockholders named therein (Incorporated by reference to Exhibit 4.2 to Pre-Effective Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on July 11, 2013).
4.3	Amendment No. 1 to Eighth Amended and Restated Stockholders' Agreement, effective as of July 9, 2013 (Incorporated by reference to Exhibit 4.2 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013).
4.4	Form of Warrant Certificate issued pursuant to Warrant Agreement, dated as of July 27, 2016, by and between Onconova Therapeutics, Inc. and Wells Fargo Bank, N.A., as Warrant Agent (Incorporated by reference to Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q filed on August 15, 2016)
4.5	Form of Pre-Funded Warrants issued as of July 27, 2016 (Incorporated by reference to Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q filed on August 15, 2016)
5.1	Opinion of Morgan, Lewis & Bockius LLP
10.1*	Development and License Agreement, effective as of September 19, 2012, by and between Onconova Therapeutics, Inc. and Baxter Healthcare SA (Incorporated by reference to Exhibit 10.1 to Pre-Effective Amendment No. 2 the Company's Registration Statement on Form S-1 filed on July 18, 2013).

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- 10.2* [License Agreement, effective as of July 5, 2011, by and between Onconova Therapeutics, Inc. and Symbio Pharmaceuticals Limited \(Incorporated by reference to Exhibit 10.2 to Pre-Effective Amendment No. 2 the Company's Registration Statement on Form S-1 filed on July 18, 2013\).](#)
 - 10.3* [First Amendment to License Agreement, effective as of September 2, 2011, by and between Onconova Therapeutics, Inc. and Symbio Pharmaceuticals Limited \(Incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.4* [License Agreement, effective as of January 1, 1999, by and between Onconova Therapeutics, Inc. and Temple University—Of The Commonwealth System of Higher Education \(Incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.5* [Amendment to License Agreement, effective as of September 1, 2000, by and between Temple University—Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc. \(Incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.6* [Amendments to Exclusive License Agreement, effective as of March 21, 2013, by and between Temple University—Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc. \(Incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.7* [Definitive Agreement, effective as of May 12, 2010, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society \(Incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.8* [First Amendment to Definitive Agreement, effective as of June 23, 2011, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society \(Incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.9* [Second Amendment to Definitive Agreement, effective as of May 29, 2012, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society \(Incorporated by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.10* [Third Amendment to Definitive Agreement, effective as of January 5, 2013, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society \(Incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.11* [Termination of Agreement, effective as of February 5, 2013, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society \(Incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.12* [Limited Liability Company Agreement of GBO, LLC, dated as of December 12, 2012, by and between Onconova Therapeutics, Inc. and GVK Biosciences Private Limited \(Incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
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- 10.13 [Onconova Therapeutics, Inc. 2007 Equity Compensation Plan, and forms of agreement thereunder \(Incorporated by reference to Exhibit 10.13 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013\).](#)
 - 10.14 [Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Ramesh Kumar, Ph.D. \(Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 8, 2015\).](#)
 - 10.15 [Letter Agreement, effective as of January 1, 2016, by and between Onconova Therapeutics, Inc. and Ramesh Kumar, Ph.D. \(Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on February 17, 2016\).](#)
 - 10.16 [Amended and Restated Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Thomas McKearn, M.D., Ph.D. \(Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on July 8, 2015\).](#)
 - 10.17 [Amended and Restated Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Ajay Bansal. \(Incorporated by reference to Exhibit 10.4 to the Company's Current Report on Form 8-K filed on July 8, 2015\).](#)
 - 10.18 [Consulting Agreement, effective as of January 1, 2012, by and between Onconova Therapeutics, Inc. and E. Premkumar Reddy, Ph.D., including Consultant Agreement Renewal, dated February 27, 2013 \(Incorporated by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 filed on June 14, 2013\).](#)
 - 10.19 [Form of Indemnification Agreement entered into by and between Onconova Therapeutics, Inc. and each director and executive officer \(Incorporated by reference to Exhibit 10.24 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013\).](#)
 - 10.20 [Onconova Therapeutics, Inc. 2013 Equity Compensation Plan, and forms of agreement thereunder \(Incorporated by reference to Exhibit 10.25 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013\).](#)
 - 10.21 [Onconova Therapeutics, Inc. 2013 Performance Bonus Plan \(Incorporated by reference to Exhibit 10.26 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013\).](#)
 - 10.22 [Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Dr. Manoj Manair \(Incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed on July 8, 2015\).](#)
 - 10.23 [Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Mark Guerin \(Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on February 17, 2016\).](#)
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- 10.24 [Amended and Restated Employment Agreement between Onconova Therapeutics, Inc. and Steven Fruchtman, M.D. \(Incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed on August 13, 2015\).](#)
- 10.25 [Purchase Agreement between Onconova Therapeutics, Inc. and Lincoln Park Capital Fund, LLC, dated October 8, 2015 \(Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 8, 2015\).](#)
- 10.26 [Dealer-Manager Agreement dated July 7, 2016, between Onconova Therapeutics, Inc. and Maxim Group LLC \(\(Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 13, 2016\)](#)
- 10.27 [At Market Issuance Sales Agreement, dated December 5, 2016, between Onconova Therapeutics, Inc. and FBR Capital Markets & Co. \(Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 5, 2016\)](#)
- 10.28 [Letter Agreement, effective as of January 1, 2017, by and between Onconova Therapeutics, Inc. and Ramesh Kumar, Ph.D.](#)
- 21.1 [Subsidiaries of Onconova Therapeutics, Inc. \(Incorporated by reference to Exhibit 21.1 to the Company's Annual Report on Form 10-K filed on March 29, 2017\).](#)
- 23.1 [Consent of Ernst & Young, LLP.](#)
- 23.2 [Consent of Morgan, Lewis & Bockius LLP \(included in Exhibit 5.1\)](#)
- 24.1 [Power of Attorney \(included on the signature page of this Registration Statement\)](#)

† To be filed by amendment.

* Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Newtown, Pennsylvania on December 29, 2017.

Onconova Therapeutics, Inc.

By: /s/ RAMESH KUMAR, PH.D

Name: Ramesh Kumar, Ph.D

Title: *President and Chief Executive Officer*

Morgan Lewis

December 29, 2017

Onconova Therapeutics, Inc.
375 Pheasant Run
Newtown, PA 18940

Re: Onconova Therapeutics, Inc., Registration Statement on Form S-1

Ladies and Gentlemen:

We have acted as counsel to Onconova Therapeutics, Inc., a Delaware corporation (the “Company”), in connection with its filing of a Registration Statement on Form S-1 (the “Registration Statement”) under the Securities Act of 1933, as amended (the “Act”), with the Securities and Exchange Commission (the “Commission”) on the date hereof. The Registration Statement relates to the proposed offering and sale of up to \$25,000,000 of shares of common stock, par value \$0.01 per share, of the Company (the “Common Stock”), including shares that may be purchased by one or more underwriters pursuant to an option to purchase additional shares of Common Stock (the “Shares”). The number of Shares shall include all shares of Common Stock registered in connection with the offering contemplated by the Registration Statement, including any additional shares of Common Stock registered by the Company pursuant to Rule 462(b) under the Act.

In connection with this opinion letter, we have examined the Registration Statement and originals, or copies certified or otherwise identified to our satisfaction, of the Company’s Certificate of Incorporation and Bylaws and such other documents, records and instruments as we have deemed appropriate for purposes of the opinion set forth herein.

We have assumed the genuineness of all signatures, the legal capacity of all natural persons, the authenticity of the documents submitted to us as originals, the conformity with the originals of all documents submitted to us as certified, facsimile, or photostatic copies and the authenticity of the originals of all documents submitted to us as copies.

Based upon the foregoing, we are of the opinion that the Shares have been duly authorized by the Company and, when issued and sold by the Company and delivered by the Company against receipt of the purchase price thereof, at a price not less than the par value of the Common Stock and not less than a price per share at which the total number of Shares would exceed the total number of shares of Common Stock available under the Company’s Certificate of Incorporation, in the manner contemplated by the Registration Statement, will be validly issued, fully paid and non-assessable.

The opinions expressed herein are limited to Delaware General Corporation Law.

Morgan, Lewis & Bockius LLP
1701 Market Street
Philadelphia, PA 19103-2921
United States

📞 +1.215.963.5000
📠 +1.215.963.5001

We hereby consent to the use of this opinion as Exhibit 5.1 to the Registration Statement and any post-effective amendment to the Registration Statement, and to the reference to us under the caption "Legal Matters" in the prospectus included in the Registration Statement. In giving such consent, we do not hereby admit that we are acting within the category of persons whose consent is required under Section 7 of the Act or the rules or regulations of the Commission thereunder.

Very truly yours,

/s/ Morgan, Lewis & Bockius LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in the Registration Statement on Form S-1 and related Prospectus of Onconova Therapeutics, Inc. for the registration of up to \$15 million in shares of common stock and to the incorporation by reference therein of our report dated March 29, 2017, with respect to the consolidated financial statements of Onconova Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2016, filed with the Securities and Exchange Commission.

Philadelphia, Pennsylvania
December 29, 2017

POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that the undersigned officers and directors of Onconova Therapeutics, Inc., a Delaware corporation (the "Corporation"), hereby constitute and appoint each of Ramesh Kumar, Ph.D and Mark Guerin the true and lawful agents and attorneys-in-fact of the undersigned with full power and authority in said agents and attorneys-in-fact, and in any one or more of them, to sign for the undersigned and in their respective names as an officer/director of the Corporation, any and all amendments (including post-effective amendments) to this registration statement on Form S-3 (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act) and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, and with full power of substitution, hereby ratifying and confirming all that each of said attorneys-in-fact, or his substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities indicated on December 29, 2017.

Name	Title
<u>/s/ RAMESH KUMAR, PH.D.</u> Ramesh Kumar, Ph.D.	Director, President and Chief Executive Officer (Principal Executive Officer)
<u>/s/ MARK GUERIN</u> Mark Guerin	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)
<u>/s/ HENRY S. BIENEN, PH.D.</u> Henry S. Bienen, Ph.D.	Director
<u>/s/ JEROME E. GROOPMAN, M.D.</u> Jerome E. Groopman, M.D.	Director
<u>/s/ MICHAEL B. HOFFMAN</u> Michael B. Hoffman	Chairman, Board of Directors
<u>/s/ JAMES J. MARINO</u> James J. Marino	Director
<u>/s/ VIREN MEHTA, PHARM.D</u> Viren Mehta, Pharm.D	Director
<u>/s/ E. PREMKUMAR REDDY, PH.D</u> E. Premkumar Reddy, Ph.D	Director
<u>/s/ JACK E. STOVER</u> Jack E. Stover	Director