

Onconova Therapeutics, Inc.
Form 424B4
February 09, 2018
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Filed Pursuant to Rule 424b4
Registration No. 333-222374

PROSPECTUS

Onconova Therapeutics, Inc.

5,707,500 Units (each Unit contains one Share of Common Stock and one Warrant to purchase 0.1 Share of Series A Convertible Preferred Stock)

2,942,500 Pre-Funded Units (each Pre-Funded Unit contains one Pre-Funded Warrant to purchase one Share of Common Stock and one Warrant to purchase 0.1 Share of Series A Preferred Stock)

(2,942,500 Shares of Common Stock Underlying the Pre-Funded Warrants) and

(865,000 Shares of Series A Convertible Preferred Stock Underlying the Warrants)

We are offering up to 5,707,500 Units (Units, each Unit consisting of one share of Common Stock, par value \$0.01 per share (Common Stock) and one warrant (the Warrant) to purchase a 0.1 share of our Series A Convertible Preferred Stock, par value \$0.01 per share (Series A Preferred Stock). Each Warrant contained in a Unit has an exercise price of \$1.01 per 0.1 share of Preferred Stock. The Warrants contained in the Units will be exercisable immediately and will expire on the later of (i) the one-year anniversary of the date (the Charter Amendment Date) on which we publicly announce through the filing of a Current Report on Form 8-K that the amendment to our certificate of incorporation to sufficiently increase our authorized shares of Common Stock to cover the conversion of all outstanding shares of Series A Preferred Stock into Common Stock has been filed with the Secretary of State of the State of Delaware and (ii) the earlier of (A) the one-month anniversary of the date on which

we publicly release our top-line results of the INSPIRE Pivotal phase 3 that compare the overall survival (OS) of patients in the rigosertib group vs the Physician's Choice group, in all patients and in a subgroup of patients with IPSS-R very high risk and (B) December 31, 2019.

We are also offering the shares of Series A Preferred Stock that are issuable from time to time upon exercise of the Warrants contained in the Units. We do not currently have a sufficient number of authorized shares of Common Stock to cover the shares issuable upon the conversion of Series A Preferred Stock. As a result, before any shares of Series A Preferred Stock can become convertible, we need to receive stockholder approval of an amendment (the Charter Amendment) to our Tenth Amended and Restated Certificate of Incorporation, as amended, to sufficiently increase our authorized shares of Common Stock to cover the conversion of all outstanding shares of Series A Preferred Stock into Common Stock. We intend to seek such approval at a special meeting of stockholders or our 2018 annual meeting of stockholders. We cannot assure you that we will be able to obtain requisite stockholder approval of the Charter Amendment. The Series A Preferred Stock is not convertible until the next business day after the Charter Amendment Date starting at which time each 0.1 share of the Series A Preferred Stock will be convertible into one share of Common Stock. In the event our stockholders do not approve the Charter Amendment, the Series A Preferred Stock will not be convertible into Common Stock and the value of the Warrants and the Series A Preferred Stock may be negatively affected.

We are also offering to each purchaser whose purchase of Units in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding Common Stock immediately following the consummation of this offering, 2,942,500 pre-funded units (Pre-Funded Units, each Pre-Funded Unit consisting of one Pre-Funded Warrant (Pre-Funded Warrant) to purchase one share of Common Stock and one Warrant to purchase a 0.1 share of Series A Preferred Stock) in lieu of Units that would otherwise result in the purchaser's beneficial ownership exceeding 4.99% of our outstanding Common Stock (or at the election of the purchaser, 9.99%). Each Pre-Funded Warrant contained in a Pre-Funded Unit will be exercisable into one share of Common Stock. The purchase price of each Pre-Funded Unit will equal the price per Unit being sold to the public in this offering minus \$0.01, and the exercise price of each Pre-Funded Warrant included in the Pre-Funded Unit will be \$0.01 per share of Common Stock. This offering also relates to the shares of Common Stock issuable upon exercise of any Pre-Funded Warrants contained in the Pre-Funded Units sold in this offering. Each Warrant contained in a Pre-Funded Unit has an exercise price of \$1.01 per 0.1 share of Series A Preferred Stock. The Warrants contained in the Pre-Funded Units will be exercisable immediately and will expire on the later of (i) the one-year anniversary of the Charter Amendment Date and (ii) the earlier of (A) the one-month anniversary of the date on which we publicly release our top-line results of the INSPIRE Pivotal phase 3 that compare the overall survival (OS) of patients in the rigosertib group vs the Physician's Choice group, in all patients and in a subgroup of patients with IPSS-R very high risk and (B) December 31, 2019. We are also offering the shares of Series A Preferred Stock that are issuable from time to time upon exercise of the Warrants contained in the Pre-Funded Units.

Our Common Stock is listed on the Nasdaq Capital Market under the symbol ONTX. On February 7, 2018, the last reported sale price of Common Stock on the Nasdaq Capital Market was \$1.02 per share. We do not intend to apply for listing of the Pre-Funded Warrants, Warrants or Series A Preferred Stock on any securities exchange or other nationally recognized trading system. There is no established public trading market for the Pre-Funded Warrants, Warrants or Series A Preferred Stock, and we do not expect a market to develop.

The Units and the Pre-Funded Units will not be issued or certificated. The shares of Common Stock or Pre-Funded Warrants, as the case may be, and the Warrants can only be purchased together in this offering but the securities contained in the Units or Pre-Funded Units will be issued separately.

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One of our directors indicated interest in purchasing less than 1% of the Units sold in this offering at the public offering price and on the same terms as the other purchasers in this offering.

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

Investing in our securities involves risks. See Risk Factors beginning on page 11 of this prospectus and in the documents incorporated by reference into this prospectus.

	Per Unit	Per Pre-Funded Unit	Total
Public offering price	\$ 1.01	\$ 1.00	\$ 8,707,075
Underwriting discounts and commissions (1)	\$ 0.0707	\$ 0.0707	\$ 611,555
Proceeds, before expenses, to us (2)	\$ 0.9393	\$ 0.9393	\$ 8,095,520

(1) In addition, we have agreed to pay the underwriter a management fee in the amount of 1.0% of the aggregate offering price and to reimburse the underwriter for certain expenses. See Underwriting for additional information.

(2) Excludes potential proceeds from the exercise of the Warrants or the Pre-Funded Warrants being offered pursuant to this prospectus.

We have granted the underwriter the option to purchase up to 1,297,500 additional shares of Common Stock at a purchase price of \$1.00 per share and/or Warrants to purchase up to an aggregate of 129,750 shares of Series A Preferred Stock at a purchase price of \$0.01 per Warrant with an exercise price of \$1.01 per 0.1 share of Series A Preferred Stock, less the underwriting discounts and commissions. The underwriter may exercise its option at any time and from time to time within 30 days from the date of this prospectus. If the underwriter exercises the option in full, the total underwriting discounts and commissions payable by us will be \$703,288, and the total proceeds to us, before expenses, will be \$9,314,262.

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.

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The underwriter expects to deliver the securities to purchasers on or about February 12, 2018.

Sole Book-Running Manager

H.C. Wainwright & Co.

The date of this prospectus is February 8, 2018.

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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 our securities. 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. Neither we nor the underwriter have 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.

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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).

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

Rigosertib

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

Rigosertib IV for higher-risk MDS

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

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is on-going.

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

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

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

As called for in the INSPIRE Charter, the DMC has previously conducted two periodic safety

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reviews, and after each review, the trial continued per plan.

On January 17, 2018, we announced that we are moving forward with our Phase 3 INSPIRE pivotal trial following the interim analysis, consistent with the recommendation of the DMC. The DMC recommended continuation of the trial with a one-time expansion in enrollment, using a pre-planned sample size re-estimation, consistent with the statistical analysis plan. We remain blinded to the interim analysis results.

The statistical analysis plan for the INSPIRE trial featured an adaptive trial design, permitting several options following the interim analysis, which included continuation of the trial as planned, discontinuation of the trial for futility, trial expansion using pre-planned sample size re-estimation, and trial continuation for only the pre-defined treatment subgroup of patients classified as VHR based on the IPSS-R.

The expanded INSPIRE study will continue to enroll eligible patients based on the current trial design of the overall ITT population and will increase enrollment by adding 135 patients to the original target to reach a total enrollment of 360 patients, with the aim of increasing the power of the trial. Due to the adaptive trial design and the DMC's assessment, the INSPIRE trial will continue to analyze both the ITT and the VHR population for the primary endpoint of overall survival. The design of the trial with the expanded study enrollment will be identical to the current study design and will include the analysis of the overall survival endpoint in the ITT and the pre-specified VHR subgroup.

As of January 17, 2018, the INSPIRE study was active at approximately 175 trial sites in 22 countries across four continents, and has enrolled more than 170 patients. In Japan, patients have been enrolled to this study by Symbio Pharmaceuticals, our collaboration partner for Japan and Korea. We believe that this trial is the most advanced study for a new therapeutic agent in this indication, and there are no FDA approved therapies specifically for MDS patients after failure of front-line HMAs.

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:

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Response per IWG 2006

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

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

Safety/Tolerability of the Combination:

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

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

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

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

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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.

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Rigosertib oral for lower-risk MDS

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

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

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

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

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

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

Other Programs

The vast majority of our 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,

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such as c-MYC, leading to tumor cell death. We have been conducting a Phase 1 multi-site dose-escalation trial of briciclib in patients with advanced solid tumors refractory to current therapies. Safety and efficacy assessments are complete in six of the seven dose-escalation cohorts of patients in this trial. As of December 2015, the Investigational New Drug (IND) for briciclib is on full clinical hold following a drug product lot testing failure. We will be required to undertake appropriate remedial actions prior to re-initiating the clinical trial and completing the final dose-escalation cohort.

Recilisib

Recilisib is a product candidate being developed in collaboration with the U.S. Department of Defense for acute radiation syndromes. We have completed four Phase 1 trials to evaluate the safety and pharmacokinetics of recilisib in healthy human adult subjects using both subcutaneous and oral formulations. We have also conducted animal studies and clinical trials of recilisib under the FDA's Animal Rule, which permits marketing approval for new medical countermeasures for which conventional human efficacy studies are not feasible or ethical, by relying on evidence from adequate and well-controlled studies in appropriate animal models to support efficacy in humans when the results of those studies establish that the drug is reasonably likely to produce a human clinical benefit. Human safety data, however, is still required. Ongoing studies of recilisib, focusing on animal models and biomarker development to assess the efficacy of recilisib are being conducted by third parties with government funding. We anticipate that any future development of recilisib beyond these ongoing studies would be conducted solely with government funding or by collaboration. Use of government funds to finance the research and development in whole or in part means any future effort to commercialize recilisib will be subject to federal laws and regulations on U.S. government rights in intellectual property. Additionally, we are subject to laws and regulations governing any research contracts, grants, or cooperative agreements under which government funding was provided.

Preclinical Product Candidates

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

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

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

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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.

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THE OFFERING

Units offered by us in this offering	5,707,500 Units, each consisting of one share of Common Stock and one Warrant to purchase a 0.1 share of Series A Preferred Stock.
Pre-Funded Units offered by us in this offering	We are also offering 2,942,500 Pre-Funded Units to each purchaser whose purchase of Units in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding Common Stock immediately following the consummation of this offering, (each Pre-Funded Unit consisting of one Pre-Funded Warrant to purchase one share of Common Stock and one Warrant to purchase 0.1 share of Series A Preferred Stock) in lieu of Units that would otherwise result in the purchaser's beneficial ownership exceeding 4.99% of our outstanding Common Stock (or at the election of the purchaser, 9.99%). Each Pre-Funded Warrant contained in a Pre-Funded Unit will be exercisable for one share of Common Stock. The purchase price of each Pre-Funded Unit will equal the price per Unit being sold to the public in this offering minus \$0.01, and the exercise price of each Pre-Funded Warrant included in the Pre-Funded Unit will be \$0.01 per share of Common Stock. This offering also relates to the shares of Common Stock issuable upon exercise of any Pre-Funded Warrants contained in the Pre-Funded Units sold in this offering. For each Pre-Funded Unit we sell, the number of Units we are offering will be decreased on a one-for-one basis. Because we will issue a Warrant as part of each Unit or Pre-Funded Unit, the number of Warrants sold in this offering will not change as a result of a change in the mix of the Units and Pre-Funded Units sold.
Warrants offered by us in this offering	Warrants to purchase an aggregate of 865,000 share of Series A Preferred Stock. Each Unit and each Pre-Funded Unit includes a Warrant to purchase a 0.1 share of Series A Preferred Stock. Each Warrant contained in a Unit has an exercise price of \$1.01 per share of Series A Preferred Stock, will be immediately separable from the Common Stock or Pre-Funded Warrant, as the case may be, will be exercisable immediately and will expire on the later of (i) the one-year anniversary of the Charter Amendment Date and (ii) the earlier of (A) the one-month anniversary of the date on which we publicly release our top-line results of the INSPIRE Pivotal phase 3 that compare the overall survival (OS) of patients in the rigosertib group vs the Physician's Choice group, in all patients and in a subgroup of patients with IPSS-R very high risk and (B) December 31, 2019.
Series A Preferred Stock	865,000 shares of Series A Preferred Stock issuable upon the exercise of the Warrants. The Series A Preferred Stock is not convertible until the next business day after the Charter Amendment Date, starting at which time each 0.1 share of the Series A Preferred Stock is convertible into one share of Common Stock. Notwithstanding the foregoing, we shall

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not effect any conversion of the Series A Preferred Stock, to the extent that, after giving effect to an attempted conversion, the holder of shares of Series A Preferred Stock (together with such holder's affiliates, and any persons acting as a group together with such holder or any of such holder's affiliates) would beneficially own a number of shares of Common Stock in excess of 4.99% of the shares of Common Stock then outstanding after giving effect to such exercise. In the event our stockholders do not approve the Charter Amendment, the Series A Preferred Stock will not be convertible into Common Stock and the value of the Warrants and the Series A Preferred Stock may be negatively affected. For additional information, see the subsection entitled "Description of Securities We Are Offering - Series A Convertible Preferred Stock" in this prospectus.

Insider Participation	One of our directors indicated interest in purchasing less than 1% of the Units to be sold in this offering at the public offering price and on the same terms as the other purchasers in this offering.
Offering Price	\$1.01 per Unit \$1.00 per Pre-Funded Unit
Option to purchase additional securities	The underwriter has the option to purchase up to 1,297,500 additional shares of Common Stock at a purchase price of \$1.00 per share and/or Warrants to purchase up to an aggregate of 129,750 shares of Series A Preferred Stock at a purchase price of \$0.01 per Warrant with an exercise price of \$1.01 per 0.1 share of Series A Preferred Stock, less the underwriting discounts and commissions. The underwriter may exercise its option at any time and from time to time within 30 days from the date of this prospectus.
Common stock to be outstanding after this offering	19,421,163 shares of Common Stock (assuming no sale of any Pre-Funded Units), or 20,718,663 shares of Common Stock if the underwriter exercises its option to purchase additional Units in full (assuming no sale of any Pre-Funded Units).
Use of proceeds	The net proceeds to us from this offering will be approximately \$7.5 million, or \$8.7 million if the underwriter's option to purchase additional Units is exercised in full), at the public offering price of \$1.01 per Unit, and after deducting estimated underwriting discounts and commissions and estimated offering expenses 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

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funding working capital needs. See Use of Proceeds on page 19.

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 securities.

Listing

Common Stock is listed on the Nasdaq Capital Market under the symbol ONTX. We do not intend to apply for listing of the Pre-Funded Warrants, Warrants or Series A Preferred Stock on any securities exchange or other nationally recognized trading system. There is no established public trading market for the Pre-Funded Warrants, Warrants or Series A Preferred Stock, and we do not expect a market to develop.

The number of shares of Common Stock outstanding after the offering is based on 10,771,163 shares outstanding as of December 31, 2017, and excludes as of such date:

- 894,996 shares of Common Stock issuable upon the exercise of stock options outstanding at December 31, 2017 with a weighted average exercise price of approximately \$40.41 per share;
- 3,294,771 shares of Common Stock issuable upon the exercise of outstanding warrants at December 31, 2017 with a weighted average exercise price of approximately \$5.10 per share;
- 57,632 shares of Common Stock reserved for future issuance under our 2013 Equity Compensation Plan at December 31, 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 Common Stock over the term of the purchase agreement, should we elect to sell shares to Lincoln Park.

As of February 7, 2018, the total number of our outstanding shares of Common Stock was 10,771,163.

Unless otherwise indicated, all information contained in this prospectus assumes no exercises by the underwriter of its option to purchase additional Units.

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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 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 our securities 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.

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

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

You will experience immediate and substantial dilution in the net tangible book value per share of Common Stock included in the Units or issuable upon exercise of the Pre-Funded Warrants in this offering.

Since the effective price per share of Common Stock included in the Units or issuable upon exercise of the Pre-Funded Warrants being offered is substantially higher than the net tangible book

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deficit per share of Common Stock outstanding prior to this offering, you will suffer immediate and substantial dilution in the net tangible book value of Common Stock included in the Units or issuable upon the exercise of the Pre-Funded Warrants issued in this offering. See the section titled "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase Units 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 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 stockholders. The price per share at which we sell or issue additional shares of Common Stock or other securities convertible into or exchangeable for Common Stock future transactions may be higher or lower than such price.

There is no public market for the Warrants, the Pre-Funded Warrants or the Series A Preferred Stock underlying the Warrants.

There is no established public trading market for the Warrants, the Pre-Funded Warrants or the Series A Preferred Stock underlying the Warrants, and we do not expect a market to develop. In addition, we do not intend to apply to list the Warrants, the Pre-Funded Warrants or the Series A Preferred Stock on any national securities exchange or other nationally recognized trading system, including The Nasdaq Capital Market. Without an active market, the liquidity of the Warrants, the Pre-Funded Warrants or the Series A Preferred Stock will be limited.

The Warrants and the Pre-Funded Warrants in this offering are speculative in nature.

Neither the Warrants nor the Pre-Funded Warrants in this offering confer any rights of Common Stock or Series A Preferred Stock ownership on its holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of Common Stock or Series A Preferred Stock at a fixed price, as the case maybe, and, with respect to the Warrants, during a fixed period of time. Specifically, commencing on the date of issuance, holders of the Warrants may exercise their right to acquire Series A Preferred Stock and pay an exercise price of \$1.01 per 0.1 share of Series A Preferred Stock, subject to certain adjustments, prior to the expiration of the Warrants on the later of (i) the one-year anniversary of the Charter Amendment Date and (ii) the earlier of (A) the one-month anniversary of the date on which we publicly release our top-line results of the INSPIRE Pivotal phase 3 that compare the overall survival (OS) of patients in the rigosertib group vs the Physician's Choice group, in all patients and in a subgroup of patients with IPSS-R very high risk and (B) December 31, 2019.

Moreover, following this offering, the market value of the Warrants and the Pre-Funded Warrants, if any, is uncertain and there can be no assurance that the market value of the Warrants or the Pre-Funded Warrants will equal or exceed their imputed offering price. Neither the Warrants nor the Pre-Funded Warrants will be listed or quoted for trading on any market or exchange.

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If we do not obtain shareholder approval to increase the number of our authorized shares of common stock in an amount sufficient to issue shares to those who purchase warrants in this offering, the warrants included in this offering may not have any value and you could lose part or all of your investment.

We do not currently have a sufficient number of authorized shares of Common Stock to cover the shares issuable upon conversion of the Series A Preferred stock being offered by this prospectus. As a result, before the Series A Preferred Stock can become convertible, we need to receive stockholder approval of the Charter Amendment (which is an amendment to our Tenth Amended and Restated Certificate of Incorporation, as amended, to sufficiently increase our authorized shares of Common Stock to cover the conversion of all outstanding shares of Series A Preferred Stock into Common Stock). We intend to seek such approval at a special meeting of stockholders or our 2018 annual meeting of stockholders. We cannot assure you that we will be able to obtain requisite stockholder approval of the Charter Amendment. In the event our stockholders do not approve the Charter Amendment, the Series A Preferred Stock will not be convertible into Common Stock and the value of the Warrants and the Series A Preferred Stock may be negatively affected.

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

Sales of a substantial number of shares of Common Stock or securities convertible or exchangeable into Common Stock in the public markets could depress the market price of 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 Common Stock would have on the market price of Common Stock.

Upon completion of this offering, based on our shares outstanding as of December 31, 2017, we will have 19,421,163 shares of Common Stock outstanding based on the issuance and sale of 5,707,500 Units and 2,942,500 Pre-Funded Units in this offering. Of these shares, only 1,554,207 shares are subject to a contractual lock-up with the underwriter for this offering for a period of 90 days following this offering. These shares can be sold, subject to any applicable volume limitations under federal securities laws, after the earlier of the expiration of, or release from, the 135-day lock-up period. The balance of our outstanding shares of Common Stock, including any shares of Common Stock included in the Units, issuable upon the exercise of the Pre-Funded Warrants, or issuable upon the conversion of the Series A Preferred Stock underlying the Warrants purchased in this offering other than shares acquired by our current stockholders who are also subject to the contractual lock-up, may be resold into the public market immediately without restriction, unless owned or purchased by our affiliates. Moreover, some of the holders of Common Stock have the right, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

As of December 31, 2017, there were approximately 894,996 shares subject to outstanding options or that are otherwise issuable under our 2013 Equity Compensation Plan, all of which shares we have registered under the Securities Act of 1933, as amended, or the Securities Act, on a registration statement on Form S-8. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described above, to the extent applicable.

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

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

If we issue substantially all of our available authorized shares of Common Stock in this offering, we will not be able to issue additional shares for future capital raising transactions or strategic transactions unless we obtain stockholders' approval to amend our certificate of incorporation to increase the number of authorized shares of Common Stock.

We have 25,000,000 authorized shares of Common Stock. As of January 26, 2018, we had 10,711,163 shares of Common Stock outstanding, 3,294,771 shares of Common Stock issuable upon the exercise of outstanding warrants, and 894,996 shares of Common Stock issuable upon the exercise of outstanding options. As a result, as of January 26, 2018, we had approximately 9,950,000 authorized shares of Common Stock available for issuance. If we issue substantially all of our available authorized shares of Common Stock in this offering, we will not be able to issue additional shares for future capital raising transactions or strategic transactions unless we obtain stockholders' approval to amend our certificate of incorporation to increase the number of authorized shares of Common Stock. This may cause a delay in our future capital raising, collaboration, partnership or other strategic transactions, and may have a material adverse effect on our business and financial condition.

We may issue additional series of preferred stock that rank senior or equally to the Series A Preferred Stock as to dividend payments and liquidation preference.

Neither our certificate of incorporation nor the Certificate of Designation for the Series A Preferred Stock prohibits us from issuing additional series of preferred stock that would rank senior or equally to the Series A Preferred Stock as to dividend payments and liquidation preference. Our certificate of incorporation provides that we have the authority to issue up to 5,000,000 shares of preferred stock. The issuances of other series of preferred stock could have the effect of reducing the amounts available to the Series A Preferred Stock in the event of our liquidation, winding-up or dissolution. It may also reduce cash dividend payments on the Series A Preferred Stock if we do not have sufficient funds to pay dividends on all Series A Preferred Stock outstanding and outstanding parity preferred stock.

The Series A Preferred Stock will rank junior to all our liabilities to third party creditors in the event of a bankruptcy, liquidation or winding up of our assets.

In the event of bankruptcy, liquidation or winding up, our assets will be available to pay obligations on the Series A Preferred Stock only after all our liabilities have been paid. The Series A Preferred Stock will effectively rank junior to all existing and future liabilities held by third party creditors. The terms of the Series A Preferred Stock do not restrict our ability to raise additional capital in the future through the issuance of debt. In the event of bankruptcy, liquidation or winding up, there may not be sufficient assets remaining, after paying our liabilities, to pay amounts due on any or all of the Series A Preferred Stock then outstanding.

Future issuances of preferred stock may adversely affect the market price for Common Stock.

Additional issuances and sales of preferred stock, or the perception that such issuances and sales could occur, may cause prevailing market prices for Common Stock to decline and may adversely affect our ability to raise additional capital in the financial markets at times and prices favorable to us.

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

We are required to meet certain qualitative and financial tests to maintain the listing of our securities on The Nasdaq Capital Market. As previously disclosed, as of March 31, 2017, June 30, 2017 and September 30, 2017, our total stockholders' equity was \$(2.7) million, \$0.4 million and \$(6.1) million, respectively. As a result, we did not comply with the Nasdaq's \$2.5 million minimum stockholders' equity requirement, nor the alternative compliance standards under Nasdaq Listing Rule 5550(b) for the continued listing of our securities on The Nasdaq Capital Market. In addition, as previously disclosed, the Nasdaq Staff notified us of the noncompliance and, after granting certain grace period and reviewing our proposed plan to regain compliance, the Nasdaq Staff had determined to seek to delist our securities from Nasdaq unless we requested a hearing before a Nasdaq Hearings Panel (the Panel). Accordingly, we requested and had a hearing on January 18, 2018 before the Panel, which has the authority to grant us an additional extension of time to regain compliance.

On February 2, 2018, we received a letter from the Panel stating that the Panel has granted the Company an extension to April 13, 2018 to regain compliance with the continuing listing requirements of the Nasdaq Capital Market, which may be accomplished by demonstrating minimum stockholders' equity of \$2.5 million or having the market value of listed securities of at least \$35 million for ten consecutive trading days, as defined in Nasdaq Listing Rule 5550(b).

We will not regain compliance after applying the net proceeds of this offering and we are looking at other alternatives including licensing and other capital raising arrangements. There is no assurance that we will regain compliance on or before April 13, 2018, and even if we do, that we will be able to maintain compliance. If we are unable to regain compliance by April 13, 2018 or maintain compliance and our securities are delisted, it could be more difficult to buy or sell our securities and to obtain accurate quotations, and the price of our securities could suffer a material decline. Delisting could also impair our ability to raise capital.

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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 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 securities on a national securities exchange;
- the potential for third party disputes and litigation;

- the performance of third parties, including contract research organizations (CROs) and third-party manufacturers; and
- 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

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warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all.

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

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USE OF PROCEEDS

The net proceeds to us from this offering will be approximately \$7.5 million, based on, the sale of 5,707,500 Units at the public offering price of \$1.01 per Unit and the sale of 2,942,500 Pre-Funded Units at the public offering price of \$1.00 per Pre-Funded Unit, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of Warrants issued pursuant to this offering. If the underwriter exercises its option to purchase the additional Units in full, we estimate that the net proceeds will be approximately \$8.7 million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of Warrants issued pursuant to this offering.

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 securities.

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.

These estimates exclude the proceeds, if any, from the exercise of the Warrants in this offering. If all of the Warrants sold in this offering were to be exercised in cash at an exercise price of \$1.01 per 0.1 share of Series A Preferred Stock, we would receive additional net proceeds of approximately \$8.7 million. However, the Warrants contain a cashless exercise provision that permit exercise of the Warrants on a cashless basis (i) at any time where there is no effective registration statement under the Securities Act of 1933, as amended, covering the issuance of the underlying shares of Series A Preferred Stock or (ii) on the expiration date of the Warrant. We cannot predict when or if the Warrants will be exercised or whether they will be exercised for cash. It is possible that the Warrants may be exercised solely on a cashless basis.

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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 5,707,500 Units at the public offering purchase price of \$1.01 per Unit and 2,942,500 Pre-Funded Warrants at the public offering price of \$1.00 per Pre-Funded Unit, after deducting estimated underwriting discounts and commissions and estimate offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the Warrants issued pursuant to this offering.

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

	September 30, 2017 (unaudited)	
	Actual	as Adjusted
Cash and cash equivalents	\$ 7,600,000	\$ 15,142,000
Long-term liabilities	14,880,000	14,880,000
Stockholders' equity*:		
Preferred stock, \$0.01 par value, 5,000,000 authorized, none issued and outstanding on actual and as adjusted basis		
Common stock, \$0.01 par value, 25,000,000 authorized, 9,851,164 shares issued and outstanding on an actual basis, 18,501,164 shares issued and outstanding on an as adjusted basis	99,000	186,000
Additional paid-in capital	349,103,000	356,558,000
Accumulated other comprehensive loss	(1,000)	(1,000)
Accumulated deficit	(356,109,000)	(356,109,000)
Total Onconova Therapeutics, Inc. stockholders' equity	(6,908,000)	634,000
Non-controlling interest	830,000	830,000
Total stockholders' equity	(6,078,000)	1,464,000

*

The above table is based on 9,851,164 shares of 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;

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- 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 Common Stock over the term of the purchase agreement, should we elect to sell shares to Lincoln Park.

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If you invest in Common Stock in this offering, your interest will be diluted to the extent of the difference between the effective public offering price per share of Common Stock included in the Units or issuable upon the exercise of the Pre-Funded Warrants and the as adjusted net tangible book value per share of 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 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 Common Stock outstanding as of September 30, 2017. After giving effect to our sale in this offering of 5,707,500 Units at the public offering price of \$1.01 per Unit and of 2,942,500 Pre-Funded Units at the public offering price of \$1.00 per Pre-Funded Unit, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the Warrants issued in this offering, our net tangible book value as of September 30, 2017 would have been \$1.5 million, or \$0.08 per share. This represents an immediate increase of net tangible book value of \$0.70 per share to our existing stockholders and an immediate dilution of \$0.93 per share to investors purchasing Units in this offering. The following table illustrates this per share dilution.

Public offering price per Unit		\$	1.01
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 Units in this offering		0.70	
As adjusted net tangible book value per share as of September 30, 2017 after giving effect to this offering			0.08
Dilution per share to investors purchasing Units in this offering	\$		0.93

If the underwriter exercises its option to purchase additional Units in full, the as adjusted net tangible book value per share after this offering would be \$0.13 per share, the increase in net tangible book value per share to existing stockholders would

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be \$0.75 per share and the dilution to new investors purchasing Units in this offering would be \$0.88 per share.

The above discussion and table are based on 9,851,164 shares of 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 Common Stock over the term of the purchase agreement, should we elect to sell shares to Lincoln Park.

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.

Table of Contents**EXECUTIVE COMPENSATION****Overview of Executive Compensation**

The compensation committee of our board of directors is responsible for overseeing the compensation of all of our executive officers. In this capacity, our compensation committee annually reviews and approves the compensation of our chief executive officer and other executive officers, including such goals and objectives relevant to the executive officers' compensation that the committee, in its discretion, determines are appropriate, evaluates their performance in light of those goals and objectives, and sets their compensation based on this evaluation.

2017 Summary Compensation Table

The following table sets forth information for the fiscal years ended December 31, 2017 and 2016 concerning compensation of our principal executive officer and the two most highly compensated executive officers during 2017. We refer to these three executive officers as our named executive officers.

Name and Principal Position	Year	Salary (\$)	Bonus \$(1)	Option Awards \$(2)	All Other Compensation \$(3)	Total (\$)
Ramesh Kumar, Ph.D. President and Chief Executive Officer	2017	538,150		81,890	23,581	643,621
	2016	413,172	254,028	177,729	19,707	864,636
Steven M. Fruchtmann, M.D. Chief Medical Officer and Senior Vice President, Research and Development	2017	436,154		49,105	19,315	504,574
	2016	421,784	142,800	119,283	7,179	691,046
Manoj Maniar, Ph.D. Senior Vice President, Product Development	2017	388,977		36,108	14,410	439,495
	2016	371,453	126,186	89,703	11,930	599,272

(1) Represents discretionary annual bonus amounts paid.

(2) The entries in the option awards column reflect the grant date fair value of the awards, as calculated for financial statement reporting purposes in accordance with Accounting Standards Codification (ASC) No. 718, *Compensation - Stock Compensation*. The option values were calculated using the Black-Scholes option pricing model. These amounts do not represent the actual value realized by the named executive officers. See Note 10 of the Notes to Consolidated Financial Statements for the fiscal year ended December 31, 2016 for a discussion of the relevant

assumptions used to determine the valuation of our stock options for accounting purposes.

(3) Includes amounts paid for insurance premiums on behalf of the named executive officer and matching funds paid pursuant to our 401(k) Plan.

Employment Agreements

We have entered into employment agreements with each of our named executive officers, and the compensation of our named executive officers is determined, in large part, by the terms of those employment agreements. Following are descriptions of the material terms of each named executive

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officer's employment agreement.

Ramesh Kumar, Ph.D.

We entered into an employment agreement with Dr. Kumar on July 1, 2015, which supersedes any prior employment agreements. The employment agreement continues indefinitely, unless terminated in accordance with the terms of the agreement.

The employment agreement provided for an initial base salary of \$543,375, subject to adjustment upon annual review by our board of directors, and an annual bonus of up to 55% of such base salary, payable upon our achievement of revenue or profit objectives, specific business plan goals or other performance milestones mutually agreed to by Dr. Kumar and our board of directors, provided that Dr. Kumar remain employed by us throughout the performance year. The bonus may be paid in the form of cash, stock options, shares of Common Stock, or a combination thereof, at our compensation committee's discretion. Dr. Kumar may also be entitled to additional compensation in recognition of extraordinary contributions, at the sole discretion of our compensation committee. On February 12, 2016, we entered into a letter agreement with Dr. Kumar pursuant to which Dr. Kumar agreed to a voluntary reduction in his base salary from \$543,375 to \$407,531, effective as of January 1, 2016. For purposes of severance and other benefits calculated based upon base salary, however, Dr. Kumar's base salary was deemed to remain at \$543,375. On December 9, 2016, our board of directors approved the termination of the voluntary salary reduction effective January 1, 2017. Pursuant to this approval, on March 27, 2017, we entered into a letter agreement with Dr. Kumar under which the voluntary salary reduction was terminated effective January 1, 2017.

Dr. Kumar is entitled to participate in all of our employee benefit plans and programs that are made generally available from time to time to our executive officers and is entitled to vacation benefits. Pursuant to his employment agreement, Dr. Kumar is entitled to term life insurance coverage in a face amount that is not less than his base salary, a reasonable transportation allowance if we relocate our research facility more than 40 miles from its present location, and up to \$10,000 annually for educational programs related to the performance of his duties. If Dr. Kumar dies during his employment, we will be entitled to a \$1 million death benefit under a key man life insurance policy. Dr. Kumar's employment agreement contains non-solicitation, non-competition, confidentiality and inventions assignment provisions that, among other things, prevent him from competing with us during the term of his employment and for a specified time thereafter.

If Dr. Kumar's employment is terminated due to his death, disability, by us for cause or by Dr. Kumar without good reason during the term of his employment agreement, we will pay to Dr. Kumar or his spouse or estate the balance of his accrued and unpaid salary, unreimbursed expenses, and unused accrued vacation time through the termination date.

If Dr. Kumar's employment is terminated by us without cause or by Dr. Kumar for good reason, other than during a change in control protection period, Dr. Kumar will be entitled to receive severance equal to his current base salary and target bonus for the fiscal year during which his employment ceases. If the termination is during a change in control protection period, Dr. Kumar will be entitled to receive severance equal to two times the sum of his current base salary and target bonus for the fiscal year during which his employment ceases, less any severance previously paid. A change in control protection period commences three months prior to and ends twelve months following a change in control. The Company will also reimburse Dr. Kumar for a portion of his medical insurance costs and all of Dr. Kumar's incentive stock options that are unvested as of the date of such termination would fully vest as of the date of termination.

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Steven Fruchtman, M.D.

We entered into an employment agreement with Dr. Fruchtman on July 1, 2015, which supersedes any prior employment agreements. The employment agreement continues indefinitely, unless terminated in accordance with the terms of the agreement.

The employment agreement provides for an initial base salary of \$420,000, subject to adjustment upon annual review, and subject to the compensation committee's sole discretion, an annual bonus, based on the performance of Dr. Fruchtman and the Company, of up to 40% of such base salary. The bonus may be paid in the form of cash, stock options, shares of Common Stock, or a combination thereof, at our compensation committee's discretion.

Dr. Fruchtman is entitled to participate in all of our employee benefit plans and programs that are made generally available from time to time to our executive officers and is entitled to vacation benefits. Dr. Fruchtman's employment agreement contains non-solicitation, non-competition, confidentiality and inventions assignment provisions that, among other things, prevent him from competing with us during the term of his employment and for a specified time thereafter. The Company will reimburse Dr. Fruchtman for reasonable expenses including certain commuting costs to the Company's offices.

If Dr. Fruchtman's employment is terminated due to his death, disability, by us for cause or by Dr. Fruchtman without good reason during the term of his employment agreement, we will pay to Dr. Fruchtman or his spouse or estate the balance of his accrued and unpaid salary, unreimbursed expenses, and unused accrued vacation time through the termination date.

If Dr. Fruchtman's employment is terminated by us without cause or by Dr. Fruchtman for good reason, other than during a change in control protection period, Dr. Fruchtman will be entitled to receive severance equal to the sum of his current base salary and target bonus for the fiscal year during which his employment ceases. If the termination is during a change in control protection period, Dr. Fruchtman will be entitled to receive severance equal to the sum of his current base salary and target bonus for the fiscal year during which his employment ceases. A change in control protection period is the twelve months following a change in control. The Company will also reimburse Dr. Fruchtman for a portion of his medical insurance costs and all of Dr. Fruchtman's incentive stock options that are unvested as of the date of such termination would fully vest as of the date of termination.

Manoj Maniar, Ph.D.

We entered into an employment agreement with Dr. Maniar on July 1, 2015, which supersedes any prior employment agreements. The employment agreement continues indefinitely, unless terminated in accordance with the terms of the agreement.

The employment agreement provides for an initial base salary of \$371,135, subject to adjustment upon annual review by our board of directors, and subject to the compensation committee's sole discretion, an annual bonus, based on the performance of Dr. Maniar and the Company, of up to 40% of such base salary. The bonus may be paid in the form of cash, stock options, shares of Common Stock, or a combination thereof, at our compensation committee's discretion.

Dr. Maniar is entitled to participate in all of our employee benefit plans and programs that are made generally available from time to time to our executive officers and is entitled to vacation benefits. Dr. Maniar's employment agreement contains non-solicitation, non-competition, confidentiality and inventions assignment provisions that, among other things, prevent him from competing with us during the term of his employment and for a specified time thereafter.

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If Dr. Maniar's employment is terminated due to his death, disability, by us for cause or by Dr. Maniar without good reason during the term of his employment agreement, we will pay to Dr. Maniar or his spouse or estate the balance of his accrued and unpaid salary, unreimbursed expenses, and unused accrued vacation time through the termination date.

If Dr. Maniar's employment is terminated by us without cause or by Dr. Maniar for good reason, other than during a change in control protection period, Dr. Maniar will be entitled to receive severance equal to nine-twelfths of the sum of his current base salary and target bonus for the fiscal year during which his employment ceases. If the termination is during a change in control protection period, Dr. Maniar will be entitled to receive severance equal to the sum of his current base salary and target bonus for the fiscal year during which his employment ceases. A change in control protection period is the twelve months following a change in control. The Company will also reimburse Dr. Maniar for a portion of his medical insurance costs and all of Dr. Maniar's incentive stock options that are unvested as of the date of such termination would fully vest as of the date of termination.

Stock Option and Other Compensation Plans

We maintain our 2013 Equity Compensation Plan for the purpose of attracting key employees, directors and consultants, inducing them to remain with us and encouraging them to increase their efforts to make our business more successful. The plan provides for awards of stock options, stock appreciation rights, restricted stock, restricted stock Units, deferred shares and other equity-based awards.

The following table contains certain information regarding equity awards held by the named executive officers as of December 31, 2017:

Outstanding Equity Awards at 2017 Fiscal Year-End

Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date
Ramesh Kumar	9,376		57.60	3/16/2020
	5,251		61.30	12/9/2020
	1,033		61.30	12/4/2021
	18,754		132.80	12/18/2022
	10,500		150.00	7/25/2023
	13,500(1)		134.80	12/20/2023
	13,125(1)	4,375	39.80	12/17/2024
	5,833(1)	2,917	23.20	4/15/2025
	4,921(1)	3,829	14.80	9/24/2025
	14,644		6.50	1/25/2026
	18,333(2)	25,667	3.24	9/1/2026
	4,224(2)	8,449	2.65	12/15/2026
	13,452(2)	30,575	2.70	1/17/2027

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Steven Fruchtman	8,750(1)	3,250	43.70	1/11/2025
	2,333(1)	1,167	24.80	4/19/2025
	2,250(1)	1,750	14.80	9/24/2025
	12,410		6.50	1/25/2026
	10,416(2)	14,584	3.24	9/1/2026
	2,533(2)	5,066	2.65	12/15/2026

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	8,066(2)	18,335	2.70	1/17/2027
Manoj Maniar	5,625		57.60	3/16/2020
	2,625		61.30	12/9/2020
	378		61.30	12/4/2021
	3,000		132.80	12/18/2022
	500		150.00	7/25/2023
	4,000(1)		134.80	12/20/2023
	4,500(1)	1,500	39.80	12/17/2024
	2,666(1)	1,334	23.20	4/15/2025
	2,250(1)	1,750	14.80	9/24/2025
	10,340		6.50	1/25/2026
	7,083(2)	9,917	3.24	9/1/2026
	1,862(2)	3,725	2.65	12/15/2026
	5,931(2)	13,482	2.70	1/17/2027

(1) Shares vest in equal monthly installments over four years, 1/48th per month. The first shares vest one month after the date of grant.

(2) Shares vest in equal monthly installments over three years, 1/36th per month. The first shares vest one month after the date of grant.

Potential Payments Upon Termination of Employment or Change in Control

As discussed under the caption *Employment Agreements* above, we have agreements with our named executive officers pursuant to which they will receive severance payments upon certain termination events. The information below describes certain compensation that would be available under our existing plans and arrangements if (i) the named executive officer was terminated as of December 31, 2017 or (ii) if a Change in Control, as defined herein, occurred on December 31, 2017 and the named executive officer's employment had been subsequently terminated on the same date.

Acceleration of Equity Awards

Pursuant to the terms of each named executive officer's option agreements, in the event of a *Change in Control* that occurs during any time prior to such named executive officer's Termination of Service (as such terms are defined in our 2013 Equity Compensation Plan) with us, all stock options granted pursuant to such option agreement shall fully vest.

Termination Other than for Cause, Death or Disability; Resignation for Good Reason

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The payments and benefits to which each named executive officer would be entitled in the event the named executive officer's employment is terminated for any reason other than for cause, death, or disability, or if the named executive officer resigns for good reason, whether or not following a change in control is described above.

Equity Compensation Plan Information

The following table summarizes the total number of outstanding options and shares available for other future issuances of options under all of our equity compensation plans as of December 31, 2017. All of the outstanding awards listed below were granted under our 2013 Equity Compensation Plan. See "Stock Option and Other Compensation Plans" 2013 Equity Compensation Plan above for a summary of the 2013 Equity Compensation Plan.

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Plan Category	Number of Shares to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Shares Remaining Available for Future Issuance Under the Equity Compensation Plan (Excluding Shares in First Column)
Equity compensation plans approved by stockholders	894,996	\$ 40.41	57,632
Equity compensation plans not approved by stockholders			

In accordance with the terms of the 2013 Equity Compensation Plan, on January 1, 2018, the maximum aggregate number of shares of Common Stock that may be issued under the plan was automatically increased by 200,000 shares, such that immediately after such increase the number of shares remaining available for future issuance under the plan was 257,632.

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DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 25,000,000 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 January 26, 2018, 10,771,163 shares of 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 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 Common Stock are entitled to one vote for each share on all matters voted on by stockholders, including the election of directors. Holders of 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 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 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 Common Stock are, and any shares of Common Stock that we may issue in the future will be, fully paid and non-assessable.

We do not currently have a sufficient number of authorized shares of Common Stock to cover the shares issuable upon the conversion of Series A Preferred Stock. As a result, before any shares of Series A Preferred Stock can become convertible, we need to receive stockholder approval of the Charter Amendment to sufficiently increase our authorized shares of Common Stock to cover the conversion of all outstanding shares of Series A Preferred Stock into Common Stock. We intend to seek such approval at a special meeting of stockholders or our 2018 annual meeting of stockholders. If approved by our stockholders, we intend to file the Charter Amendment with the Secretary of State of Delaware as soon as practicable following the special meeting or the annual meeting, as the case may be, and the Charter Amendment will be effective upon such filing.

We cannot assure you that we will be able to obtain requisite stockholder approval of the Charter Amendment. If the Charter Amendment is not approved by our stockholders, our Tenth Amended and Restated Certificate of Incorporation, as amended, will continue as currently in effect. In the event our stockholders do not approve the Charter Amendment, the Series A Preferred Stock will not be convertible into Common Stock and the value of the Warrants and the Series A Preferred Stock may be negatively affected.

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.

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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 Common Stock and the voting and other rights of the holders of Common Stock.

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Following this offering, we will have designated 1,044,488 shares of our preferred stock as Series A Convertible Preferred Stock. See Description of Securities We Are Offering Series A Convertible Preferred Stock for a description of our Series A Convertible Preferred Stock.

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

Delaware Anti-Takeover Law

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

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

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, lease, exchange, mortgage, pledge, transfer or other disposition of 10% or more of the assets of the corporation to or with the interested stockholder;

- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

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

- the owner of 15% or more of the outstanding voting stock of the corporation;
- an affiliate or associate of the corporation who was the owner of 15% or more of the

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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.

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 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.

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Transfer Agent

The transfer agent and registrar for Common Stock is EQ Shareowner Services.

Listing

Our Common Stock is listed on the Nasdaq Capital Market under the symbol ONTX.

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DESCRIPTION OF SECURITIES WE ARE OFFERING

We are offering (i) 5,707,500 Units, each Unit consisting of one share of Common Stock and one Warrant to purchase a 0.1 share of Series A Preferred Stock, and (ii) 2,942,500 Pre-Funded Units, each Pre-Funded Unit consisting of one Pre-Funded Warrant to purchase one share of Common Stock and one Warrant to purchase a 0.1 share of Series A Preferred Stock. The share of Common Stock and accompanying Warrant included in each Unit will be issued separately, and the Pre-Funded Warrant to purchase one share of Common Stock and the accompanying Warrant included in each Pre-Funded Unit will be issued separately. Units or Pre-Funded Units will not be issued or certificated. We are also registering the shares of Common Stock included in the Units and the shares of Common Stock issuable from time to time upon exercise of the Pre-Funded Warrants included in Pre-Funded Units, the Warrants included in the Units and the Pre-Funded Units offered hereby, the Pre-Funded Warrants included in the Pre-Funded Units, and shares of Series A Preferred Stock issuable upon the exercise of the Warrants.

Common Stock

The material terms and provisions of Common Stock and each other class of our securities which qualifies or limits Common Stock are described under the caption "Description of Capital Stock" in this prospectus.

Series A Convertible Preferred Stock

General

Our Board of Directors is authorized to issue up to 5,000,000 shares of preferred stock in one or more series without shareholder approval. Our Board of Directors may determine the designations, powers, preferences and the relative, participating, optional or other special rights, and any qualification, limitations and restrictions, of each series of preferred stock. Our Board of Directors has designated 1,044,488 shares of preferred stock as Series A Convertible Preferred Stock, which we refer to herein as the Series A Preferred Stock. As of February 2, 2018, there were no shares of preferred stock outstanding.

Rank

The Series A Preferred Stock ranks (1) on parity with Common Stock on an "as converted" basis, (2) senior to any series of our capital stock hereafter created specifically ranking by its terms junior to the Series A Preferred Stock, (3) on parity with any series of our capital stock hereafter created specifically ranking by its terms on parity with the Series A Preferred Stock, and (4) junior to any series of our capital stock hereafter created specifically ranking by its terms senior to the Series A Preferred Stock in each case, as to dividends or distributions of assets upon our liquidation, dissolution or winding up whether voluntary or involuntary.

Conversion

We do not currently have a sufficient number of authorized shares of Common Stock to cover the shares issuable upon the conversion of Series A Preferred Stock. As a result, before any shares of Series A Preferred Stock can become convertible, we need to receive stockholder approval of the Charter Amendment to sufficiently increase our authorized shares of Common Stock to cover the conversion of all outstanding shares of Series A Preferred Stock into Common Stock. We intend to seek such approval at a special meeting of stockholders or our 2018 annual meeting of stockholders. We cannot assure you that we will be able to

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obtain requisite stockholder approval of the Charter Amendment. Series A Preferred Stock is not convertible until the next business day after the Charter Amendment Date (which is the date on which we publicly announce through the filing of a Current Report on Form 8-K that the Charter Amendment has been filed with the Secretary of State of the State of Delaware), starting at which time each 0.1 share of the Series A Preferred Stock is convertible into one (1) share of Common Stock, provided that the holder will be prohibited from converting Series A Preferred Stock into shares of Common Stock if, as a result of such conversion, the holder would own more than 4.99% of the number of shares of Common Stock outstanding immediately after giving effect to the issuance of the shares of Common Stock issuable upon conversion of the Series A Preferred Stock, or, at the election of a holder, together with its affiliates, would own more than 9.99% of the number of shares of Common Stock outstanding immediately after giving effect to the issuance of the shares of Common Stock issuable upon conversion of the Series A Preferred Stock. The conversion rate of the Series A Preferred Stock is subject to proportionate adjustments for stock splits, reverse stock splits and similar events, but is not subject to adjustment based on price anti-dilution provisions. In the event our stockholders do not approve the Charter Amendment, the Series A Preferred Stock will not be convertible into Common Stock and the value of Series A Preferred Stock may be negatively affected.

Dividends

In addition to stock dividends or distributions for which proportionate adjustments will be made, holders of Series A Preferred Stock are entitled to receive dividends on shares of Series A Preferred Stock equal, on an as-if-converted-to-common-stock basis, to and in the same form as dividends actually paid on shares of the Common Stock when, as and if such dividends are paid on shares of the Common Stock. No other dividends are payable on shares of Series A Preferred Stock.

Voting Rights

Except as provided in the Certificate of Designation or as otherwise required by law, the holders of Series A Preferred Stock will have no voting rights. However, we may not, without the consent of holders of a majority of the outstanding shares of Series A Preferred Stock, alter or change adversely the powers, preferences or rights given to the Series A Preferred Stock, increase the number of authorized shares of Series A Preferred Stock, or enter into any agreement with respect to the foregoing.

Liquidation Rights

Upon any liquidation, dissolution or winding-up of the Company, whether voluntary or involuntary, the holders of Series A Preferred Stock are entitled to receive, pari passu with the holders of Common Stock, out of the assets available for distribution to stockholders an amount equal to such amount per share as would have been payable had all shares of Series A Preferred Stock been converted into Common Stock immediately before such liquidation, dissolution or winding up, without giving effect to any limitation on conversion as a result of the Beneficial Ownership Limitation, as described below.

Beneficial Ownership Limitation

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We may not effect any conversion of the Series A Preferred Stock, and a holder does not have the right to convert any portion of the Series A Preferred Stock to the extent that, after giving effect to the conversion set forth in a notice of conversion such holder would beneficially own in excess of the Beneficial Ownership Limitation, or such holder, together with such holder's affiliates, and any persons acting as a group together with such holder or affiliates, would beneficially own in excess of the Beneficial Ownership Limitation. The Beneficial Ownership Limitation is 4.99% of the number of shares of the Common Stock outstanding immediately after giving effect to the issuance of shares of

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Common Stock issuable upon conversion of Series A Preferred Stock held by the applicable holder. A holder may, with 61 days prior notice to us, elect to increase or decrease the Beneficial Ownership Limitation; provided, however, that in no event may either the holder Beneficial Ownership Limitation or the affiliate Beneficial Ownership Limitation be 9.99% or greater.

Exchange Listing

We do not plan on making an application to list the shares of Series A Preferred Stock on the Nasdaq Capital Market, any national securities exchange or other nationally recognized trading system. Our Common Stock issuable upon conversion of the Series A Preferred Stock is listed on the Nasdaq Capital Market.

Failure to Deliver Conversion Shares.

If we fail to timely deliver shares of Common Stock upon conversion of the Series A Preferred Stock (the Conversion Shares) within the time period specified in the Certificate of Designation (within three trading days after delivery of the notice of conversion, or any shorter standard settlement period in effect with respect to trading market on the date notice is delivered), and if the holder has not exercised its Buy-In rights as described below with respect to such shares, then we are obligated to pay to the holder, as liquidated damages, an amount equal to \$50 per trading day (increasing to \$100 per trading day after the third trading day and \$200 per trading day after the tenth trading day) for each \$5,000 of Conversion Shares for which the Series A Preferred Stock converted which are not timely delivered. If we make such liquidated damages payments, we are not also obligated to make Buy-In payments with respect to the same Conversion Shares.

Compensation for Buy-In on Failure to Timely Deliver Shares

If we fail to timely deliver the Conversion Shares to the holder, and if after the required delivery date the holder is required by its broker to purchase (in an open market transaction or otherwise) or the holder or its brokerage firm otherwise purchases, shares of Common Stock to deliver in satisfaction of a sale by the holder of the Conversion Shares which the holder anticipated receiving upon such conversion or exercise (a Buy-In), then we are obligated to (A) pay in cash to the holder the amount, if any, by which (x) the holder's total purchase price (including brokerage commissions, if any) for the shares of Common Stock so purchased, minus any amounts paid to the holder by us as liquidated damages for late delivery of such shares, exceeds (y) the amount obtained by multiplying (1) the number of Conversion Shares that we were required to deliver times (2) the price at which the sell order giving rise to such purchase obligation was executed, and (B) at the option of the holder, either reinstate the portion of the Series A Preferred Stock and equivalent number of Conversion Shares for which such conversion was not honored (in which case such conversion shall be deemed rescinded) or deliver to the holder the number of shares of Common Stock that would have been issued had we timely complied with its conversion and delivery obligations.

Subsequent Rights Offerings; Pro Rata Distributions

If we grant, issue or sell any Common Stock equivalents pro rata to the record holders of any class of shares of Common Stock (the Purchase Rights), then a holder of Series A Preferred Stock will be entitled to acquire, upon the terms applicable to such Purchase Rights, the aggregate

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Purchase Rights which the holder could have acquired if the holder had held the number of shares of Common Stock acquirable upon conversion of the Series A Preferred Stock (without regard to any limitations on conversion). If we declare or make any dividend or other distribution of its assets (or rights to acquire its assets) to holders of Common Stock, then a holder of Series A Preferred Stock is entitled to participate in

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such distribution to the same extent as if the holder had held the number of shares of Common Stock acquirable upon complete conversion of the Series A Preferred Stock (without regard to any limitations on conversion).

Fundamental Transaction

If, at any time while the Series A Preferred Stock is outstanding, (i) the Company, directly or indirectly, in one or more related transactions effects any merger or consolidation of the Company with or into another person, (ii) the Company, directly or indirectly, effects any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets in one or a series of related transactions, (iii) any, direct or indirect, purchase offer, tender offer or exchange offer (whether by the Company or another person) is completed pursuant to which holders of Common Stock are permitted to sell, tender or exchange their shares for other securities, cash or property and has been accepted by the holders of 50% or more of the outstanding Common Stock, (iv) the Company, directly or indirectly, in one or more related transactions effects any reclassification, reorganization or recapitalization of the Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property, or (v) the Company, directly or indirectly, in one or more related transactions consummates a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with another person whereby such other person acquires more than 50% of the outstanding shares of Common Stock (not including any shares of Common Stock held by the other person or other persons making or party to, or associated or affiliated with the other persons making or party to, such stock or share purchase agreement or other business combination) (each a Series A Preferred Stock Fundamental Transaction), then the Series A Preferred Stock automatically converts and the holder will receive, for each Conversion Share that would have been issuable upon such conversion immediately prior to the occurrence of such Series A Preferred Stock Fundamental Transaction (without regard to the Beneficial Ownership Limitation), the number of shares of Common Stock of the successor or acquiring corporation or of the Company, if it is the surviving corporation, and any additional consideration (the Series A Preferred Stock Alternate Consideration) receivable as a result of such Series A Preferred Stock Fundamental Transaction by a holder of the number of shares of Common Stock for which the Series A Preferred Stock is convertible immediately prior to such Series A Preferred Stock Fundamental Transaction (without regard to the Beneficial Ownership Limitation). For purposes of any such conversion, the determination of the conversion ratio will be appropriately adjusted to apply to such Series A Preferred Stock Alternate Consideration based on the amount of Alternate Consideration issuable in respect of one share of Common Stock in such Series A Preferred Stock Fundamental Transaction. If holders of Common Stock are given any choice as to the securities, cash or property to be received in a Series A Preferred Stock Fundamental Transaction, then the holder will be given the same choice as to the Series A Preferred Stock Alternate Consideration it receives upon automatic conversion of the Series A Preferred Stock following such Fundamental Transaction.

The Warrants

The following is a summary of all material terms and provisions of the Warrants that are being offered hereby, the form of which has been filed as an exhibit to the registration statement of which this prospectus is a part. Prospective investors should carefully review the terms and provisions of the form of Warrant for a complete description of the terms and conditions of the Warrants.

Duration and Exercise Price

Each Warrant offered hereby will have an exercise price equal to \$1.01 per 0.1 share of Series A Preferred Stock. The Warrants will be immediately exercisable and may be exercised until the later of

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(i) the one-year anniversary of the Charter Amendment Date and (ii) the earlier of (A) the one-month anniversary of the date on which we publicly release our top-line results of the INSPIRE Pivotal phase 3 that compare the overall survival (OS) of patients in the rigosertib group vs the Physician's Choice group, in all patients and in a subgroup of patients with IPSS-R very high risk and (B) December 31, 2019, at which time they will be automatically exercised on a cashless basis. The exercise price and number of shares of Series A Preferred Stock issuable upon exercise is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting Series A Preferred Stock and the exercise price. The Warrants will be issued separately from the Common Stock or Pre-Funded Warrants sold as part of the Units or Pre-Funded Units, respectively, and may be transferred separately immediately thereafter. Warrants will be issued in certificated form only.

Exercisability

The Warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of Series A Preferred Stock purchased upon such exercise (except in the case of a cashless exercise as discussed below).

Cashless Exercise

If, at the time a holder exercises its Warrants, a registration statement registering the issuance of the shares of Series A Preferred Stock underlying the Warrants under the Securities Act is not then effective or available for the issuance of such shares, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of Series A Preferred Stock determined according to a formula set forth in the Warrant. The Warrants will be automatically exercised on a cashless basis on the expiration date.

Fundamental Transactions

In the event of any fundamental transaction, as described in the Warrants and generally including any merger with or into another entity, sale of all or substantially all of our assets, tender offer or exchange offer, or reclassification of Common Stock, then upon any subsequent exercise of a Warrant, the holder will have the right to receive as alternative consideration, for each share of Common Stock that the holder would have received upon such holder's exercise of the Warrant into shares of Series A Preferred Stock and the conversion of such shares of Series A Preferred Stock to shares of Common Stock (without giving effect to any limitation on conversion as a result of the Series A Preferred Stock Beneficial Ownership Limitation) immediately prior to the occurrence of such fundamental transaction, the number of shares of common stock of the successor or acquiring corporation or of our company, if it is the surviving corporation, and any additional consideration receivable upon or as a result of such transaction by a holder of the number of shares of Common Stock for which the holder would have received upon such holder's exercise of the Warrant into shares of Series A Preferred Stock and the conversion of such shares of Series A Preferred Stock to shares of Common Stock (without giving effect to any limitation on conversion as a result of the Series A Preferred Stock Beneficial Ownership Limitation) immediately prior to the occurrence of such fundamental transaction.

Transferability

Subject to applicable laws and a standard legend with regard to restriction on transfer only in compliance with a public offering or an available exemption therefrom, the Warrant may be transferred at the option of the holder upon surrender of the Warrant to us together with the appropriate instruments of transfer.

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No Listing

There is no established trading market for the Warrants, and we do not expect an active trading market to develop. We do not intend to apply to list the Warrants on any securities exchange or other trading market. Without a trading market, the liquidity of the Warrants will be extremely limited.

Right as a Stockholder

Except as otherwise provided in the Warrants or by virtue of the holder's ownership of shares of Series A Preferred Stock, such holder of Warrants does not have the rights or privileges of a holder of a Series A Preferred Stock, including any voting rights, until such holder exercises such holder's Warrants.

Waivers and Amendments

No term of the Warrants may be amended or waived without the written consent of the holder of such warrant.

Pre-Funded Warrants

The following is a summary of all material terms and provisions of the Pre-Funded Warrants that are being offered hereby, the form of which has been filed as an exhibit to the registration statement of which this prospectus is a part. Prospective investors should carefully review the terms and provisions of the form of Pre-Funded Warrant for a complete description of the terms and conditions of the Pre-Funded Warrants.

Pre-funded warrants provide any purchaser in this offering with the ability to purchase Pre-Funded Units (each Pre-Funded Unit consisting of one Pre-Funded Warrant to purchase one share of Common Stock and one Warrant to purchase a 0.1 share of Series A Preferred Stock) in lieu of Units that would otherwise result in the purchaser's beneficial ownership exceeding 4.99% of our outstanding Common Stock (or, at the election of the purchaser, 9.99%). This is accomplished through purchasing Pre-Funded Warrants at a price equal to the purchase price for Units, less \$0.01, which \$0.01 is the exercise price for the Pre-Funded Warrants. Each Pre-Funded Warrant is exercisable into one share of Common Stock as offered hereunder. Thus, the purchaser is paying essentially the purchase price for a Unit at closing of the offering but is not deemed to beneficially own the shares of Common Stock included in the Units until the purchaser exercises the Pre-Funded Warrant. Once purchased, the purchase price of the Pre-Funded Warrants is not refundable. While the Pre-Funded Warrants permit waiver of provisions by us and the holder of the Pre-Funded Warrants, this would not affect the pre-funding as that is the purchase price of the instrument which is paid at the time of closing and becomes part of our proceeds received from this offering. In addition, the Pre-Funded Warrants are perpetual and do not have an expiration date.

Duration and Exercise Price

Each Pre-Funded Warrant will have an outstanding exercise price per share equal to \$0.01. The Pre-Funded Warrants will be immediately exercisable and may be exercised at any time until the Pre-Funded Warrants are exercised in full. The exercise price and number of shares of Common Stock issuable upon exercise is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting Common Stock and the exercise price. The Pre-Funded Warrants will be issued separately from the accompanying Warrants included in the Pre-Funded Units, and may be transferred separately immediately thereafter.

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Exercisability

The Pre-Funded Warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of Common Stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of the Pre-Funded Warrant to the extent that the holder would own more than 4.99% of the outstanding Common Stock immediately after exercise, except that upon at least 61 days' prior notice from the holder to us, the holder may increase the amount of ownership of outstanding Common Stock after exercising the holder's Pre-Funded Warrants up to 9.99% of the number of shares of Common Stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the Pre-Funded Warrants. Purchasers of Pre-Funded Units in this offering may also elect prior to the issuance of the Pre-Funded Warrants to have the initial exercise limitation set at 9.99% of our outstanding Common Stock.

Cashless Exercise

If, at the time a holder exercises its Pre-Funded Warrants, there is no effective registration statement registering, or the prospectus contained therein is not available for an issuance of the shares of Common Stock underlying the Pre-Funded Warrants to the holder, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to exercise its Pre-Funded Warrants on a cashless basis and receive upon such exercise (either in whole or in part) the net number of shares of Common Stock determined according to a formula set forth in the Pre-Funded Warrant.

Fundamental Transactions

In the event of any fundamental transaction, as described in the Pre-Funded Warrants and generally including any merger with or into another entity, sale of all or substantially all of our assets, tender offer or exchange offer, or reclassification of Common Stock, then upon any subsequent exercise of a Pre-Funded Warrant, the holder will have the right to receive as alternative consideration, for each share of Common Stock that would have been issuable upon such exercise immediately prior to the occurrence of such fundamental transaction, the number of shares of Common Stock of the successor or acquiring corporation or of our company, if it is the surviving corporation, and any additional consideration receivable upon or as a result of such transaction by a holder of the number of shares of Common Stock for which the Pre-Funded Warrant is exercisable immediately prior to such event.

Transferability

Subject to applicable laws, a Pre-Funded Warrant may be transferred at the option of the holder upon surrender of the Pre-Funded Warrant to us together with the appropriate instruments of transfer.

Fractional Shares

No fractional shares of Common Stock will be issued upon the exercise of the Pre-Funded Warrants. Rather, the number of shares of Common Stock to be issued will be rounded up to the nearest whole number.

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Trading Market

There is no established trading market for the Pre-Funded Warrants on any securities exchange or nationally recognized trading system, and we do not expect an active trading market to develop. We do not intend to list the Pre-Funded Warrants on any securities exchange or other trading market. Without a trading market, the liquidity of the Pre-Funded Warrants will be extremely limited.

Right as a Stockholder

Except as otherwise provided in the Pre-Funded Warrants or by virtue of the holder's ownership of shares of Common Stock, such holder of Pre-Funded Warrants does not have the rights or privileges of a holder of Common Stock, including any voting rights, until such holder exercises such holder's Pre-Funded Warrants.

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UNDERWRITING

We have entered into an underwriting agreement dated February 8, 2018, with H.C. Wainwright & Co., LLC as the sole book-running manager of this offering. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriter and the underwriter has agreed to purchase from us, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus. The public offering price shown on the cover page of this prospectus was determined by negotiation between us and the underwriter at the time of pricing, and may be at a discount to the current market price.

A copy of the underwriting agreement has been filed as an exhibit to the registration statement of which this prospectus is a part. The shares we are offering are being offered by the underwriter subject to certain conditions specified in the underwriting agreement.

An associated person of the underwriter has agreed to purchase an aggregate of 300,000 shares of common stock and warrants to purchase up to an aggregate of 30,000 shares of Series A Preferred Stock in this offering for a total purchase price of \$303,000.

We have been advised by the underwriter that it proposes to offer the shares directly to the public at the public offering price set forth on the cover page of this prospectus. Any shares sold by the underwriter to securities dealers will be sold at the public offering price less a selling concession not in excess of \$0.04545 per share.

The underwriting agreement provides that the underwriter's obligation to purchase the securities we are offering is subject to conditions contained in the underwriting agreement. The underwriter is obligated to purchase and pay for all of the securities offered by this prospectus.

No action has been taken by us or the underwriter that would permit a public offering of our securities in any jurisdiction where action for that purpose is required. None of the securities included in this offering may be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sales of any of the securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons who receive this prospectus are advised to inform themselves about and to observe any restrictions relating to this offering of the securities and the distribution of this prospectus. This prospectus is neither an offer to sell nor a solicitation of any offer to buy the securities in any jurisdiction where that would not be permitted or legal.

The underwriter has advised us that it does not intend to confirm sales to any accounts over which it exercises discretionary authority.

Underwriting Discounts, Commissions and Expenses

We have agreed to pay an underwriter discount equal to 7% of the aggregate gross proceeds raised in this offering.

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The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriter's option to purchase additional securities.

	Per Unit	Per Pre-Funded Unit	Without Option Exercise	Total	With Full Option Exercise
Public offering price	1.01	1.00	8,807,075		10,017,550
Underwriting discounts and commissions	0.0707	0.0707	611,555		703,288
Proceeds, before expenses, to us	0.9393	0.9393	8,095,520		9,314,262

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We estimate the total expenses payable by us for this offering to be approximately \$1.2 million, which amount includes (i) underwriting discounts and commissions of \$0.6 million (\$0.7 million if the underwriter's option to purchase additional securities is exercised in full) based upon the public offering price per Unit of \$1.01, (ii) a management fee in the amount of \$87,000 which represents 1.0% of the aggregate offering price, (iii) \$50,000 non-accountable expense allowance payable to the underwriter, (iv) reimbursement of the accountable expenses of the underwriter equal to \$110,000 (none of which has been paid in advance), including the legal fees of the underwriter being paid by us, and (v) other estimated expenses of approximately \$335,000 which include legal, accounting, printing costs and various fees associated with the registration and listing of our shares.

Underwriter Warrants

We have agreed to issue to the underwriter warrants to purchase a number of shares of Series A Preferred Stock convertible into Common Stock equal to 5% of the aggregate number of the Units and Pre-Funded Units sold in this offering (warrants to purchase 432,500 shares of Series A Preferred Stock). The underwriter warrants will have substantially the same terms as the terms of the Warrants offered pursuant to this prospectus, except that the exercise price per share equal to 125% of the public offering price for the shares sold in this offering (\$1.2625 per 0.1 share of Series A Preferred Stock) and the exercise period of the underwriter warrants shall be subject to the limitation on exercise set forth in FINRA Rule 5110 (f)(2)(G)(i). Pursuant to FINRA Rule 5110(g), the underwriter warrants and any shares issued upon exercise of the underwriter warrants shall not be sold, transferred, assigned, pledged, or hypothecated, or be the subject of any hedging, short sale, derivative, put or call transaction that would result in the effective economic disposition of the securities by any person for a period of 180 days immediately following the date of effectiveness or commencement of sales of this offering, except the transfer of any security: (i) by operation of law or by reason of our reorganization; (ii) to any FINRA member firm participating in the offering and the officers or partners thereof, if all securities so transferred remain subject to the lock-up restriction set forth above for the remainder of the time period; (iii) if the aggregate amount of our securities held by the underwriter or related persons do not exceed 1% of the securities being offered; (iv) that is beneficially owned on a pro rata basis by all equity owners of an investment fund, provided that no participating member manages or otherwise directs investments by the fund and the participating members in the aggregate do not own more than 10% of the equity in the fund; or (v) the exercise or conversion of any security, if all securities remain subject to the lock-up restriction set forth above for the remainder of the time period.

Right of First Refusal

We have also granted the underwriter, for a period of 10 months from the closing date of this offering, a right of first refusal to act as sole book-running manager for each and every future public or private equity or debt offering by us or any of our successors or subsidiaries. We have also agreed to a tail fee equal to the cash and warrant compensation in this offering if any investor to which the underwriter introduced us with respect to this offering during the term of its engagement provides us with further capital in a public or private offering or capital raising transaction, with certain exceptions, during the 6-month period following termination of our engagement of the underwriter.

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Option to Purchase Additional Securities

We have granted the underwriter the option to purchase up to 1,297,500 additional shares of Common Stock at a purchase price of \$1.00 per share and/or Warrants to purchase up to an aggregate of 129,750 shares of Series A Preferred Stock at a purchase price of \$0.01 per Warrant with an exercise price of \$1.01 per 0.1 share of Series A Preferred Stock, less the underwriting discounts and commissions. The underwriter may exercise its option at any time and from time to time within 30 days from the date of this prospectus. If any additional Units are purchased pursuant to the option, the underwriter will offer these securities on the same terms as those on which the other Units are being offered hereby.

Listing

Common Stock is currently traded on the Nasdaq Capital Market under the symbol ONTX. On February 2, 2018, the last reported sale price of Common Stock was \$1.36 per share. We do not intend to apply for listing of the Pre-Funded Warrants, Warrants or Series A Preferred Stock on any securities exchange or other nationally recognized trading system. There is no established public trading market for the Pre-Funded Warrants, Warrants or Series A Preferred Stock, and we do not expect a market to develop

Lock-up Agreements

Our officers and directors and certain of our stockholders have agreed with the underwriter to be subject to a lock-up period of 135 days following the date of this prospectus. This means that, during the applicable lock-up period, such persons may not offer for sale, contract to sell, sell, distribute, grant any option, right or warrant to purchase, pledge, hypothecate or otherwise dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into, or exercisable or exchangeable for, shares of Common Stock. Certain limited transfers are permitted during the lock-up period if the transferee agrees to these lock-up restrictions. We have also agreed in the underwriting agreement, subject to certain exceptions, to similar lock-up restrictions on the issuance and sale of our securities for 90 days following the closing of this offering. The underwriter may, in its sole discretion and without notice, waive the terms of any of these lock-up agreements.

Insider Participation

One of our directors indicated interest in purchasing less than 1% of the Units to be sold in this offering at the public offering price and on the same terms as the other purchasers in this offering.

Stabilization, Short Positions and Penalty Bids

The underwriter may engage in syndicate covering transactions, stabilizing transactions and penalty bids or purchases for the purpose of pegging, fixing or maintaining the price of Common Stock:

- Syndicate covering transactions involve purchases of securities in the open market after the distribution has been completed in order to cover syndicate short positions. Such a naked short position would be closed out by buying securities in the open market. A naked short position is more likely to be created if the underwriter is concerned that there could be downward pressure

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on the price of the securities in the open market after pricing that could adversely affect investors who purchase in the offering.

- Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specific maximum.
- Penalty bids permit the underwriter to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These syndicate covering transactions, stabilizing transactions and penalty bids may have the effect of raising or maintaining the market prices of our securities or preventing or retarding a decline in the market prices of our securities. As a result, the price of Common Stock may be higher than the price that might otherwise exist in the open market. Neither we nor the underwriter make any representation or prediction as to the effect that the transactions described above may have on the price of Common Stock. These transactions may be effected on the Nasdaq Capital Market, in the over-the-counter market or on any other trading market and, if commenced, may be discontinued at any time.

In connection with this offering, the underwriter also may engage in passive market making transactions in Common Stock in accordance with Regulation M during a period before the commencement of offers or sales of shares of Common Stock in this offering and extending through the completion of the distribution. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for that security. However, if all independent bids are lowered below the passive market maker's bid that bid must then be lowered when specific purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

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

Indemnification

We have agreed to indemnify the underwriter against certain liabilities, including certain liabilities arising under the Securities Act, or to contribute to payments that the underwriter may be required to make for these liabilities.

Other Relationships

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The underwriter and its respective affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. The underwriter has received, or may in the future receive, customary fees and commissions for these transactions.

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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 Lowenstein Sandler LLP, New York, New York.

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.

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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, November 17, 2017, January 17, 2018, January 30, 2018, February 6, 2018 and February 8, 2018;
- The description of 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.

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

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

Table of Contents

Onconova Therapeutics, Inc.

5,707,500 Units (each Unit contains one Share of Common Stock and one Warrant to purchase 0.1 Share of Series A Convertible Preferred Stock)

2,942,500 Pre-Funded Units (each Pre-Funded Unit contains one Pre-Funded Warrant to purchase one Share of Common Stock and one Warrant to purchase 0.1 Share of Series A Preferred Stock)

(2,942,500 Shares of Common Stock Underlying the Pre-Funded Warrants) and

(865,000 Shares of Series A Convertible Preferred Stock Underlying the Warrants)

PROSPECTUS

Sole Book-Running Manager

H.C. Wainwright & Co.

February 8, 2018

