

Onconova Therapeutics, Inc.  
Form POS AM  
April 25, 2016  
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As filed with the Securities and Exchange Commission on April 25, 2016

Registration No. 333-207533

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

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POST-EFFECTIVE AMENDMENT NO. 2

TO

**FORM S-1**

**REGISTRATION STATEMENT**  
**UNDER**  
**THE SECURITIES ACT OF 1933**

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**Onconova Therapeutics, Inc.**

(Exact name of registrant as specified in its charter)

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Delaware  
(State or other jurisdiction of

2834  
(Primary Standard Industrial

22-3627252  
(I.R.S. Employer

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incorporation or organization)

Classification Code Number)

Identification No.)

**Onconova Therapeutics, Inc.**

**375 Pheasant Run**

**Newtown, PA 18940**

**(267)-759-3680**

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

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

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

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**Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.**

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.X

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

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

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

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

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

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

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**EXPLANATORY NOTE**

This Post-Effective Amendment No. 2 (this Post-Effective Amendment ) to the Registration Statement on Form S-1 (File No. 333-207533) (the Registration Statement ) is being filed pursuant to the undertaking of the Registration Statement to update and supplement information contained in the Registration Statement, as originally filed and declared effective by the Securities and Exchange Commission (the SEC ) on November 3, 2015, to update the prospectus with the information contained in Company s Annual Report on Form 10-K for the year ended December 31, 2015 as filed with the SEC on March 28, 2016 and to make certain other updates contained herein.

The information included in this filing updates the Registration Statement and the prospectus contained therein. No additional securities are being registered under this Post-Effective Amendment. All applicable registration fees were paid at the time of the original filing of the Registration Statement.

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**The information in this prospectus is not complete and may be changed. Neither we nor the selling stockholder may sell these securities until the Securities and Exchange Commission declares our registration statement effective. This prospectus is not an offer to sell these securities and neither we nor the selling stockholder are soliciting an offer to buy these securities in any state where the offer or sale is not permitted.**

**Subject to completion, dated April 25, 2016**

PROSPECTUS

**Onconova Therapeutics, Inc.**

**5,200,000 shares of Common Stock**

This prospectus relates to the offer and sale of up to 5,200,000 shares of common stock, par value \$0.01, of Onconova Therapeutics, Inc., a Delaware corporation, by Lincoln Park Capital Fund, LLC, or Lincoln Park or the selling stockholder.

The shares of common stock being offered by the selling stockholder have been or may be issued pursuant to the purchase agreement dated October 8, 2015 that we entered into with Lincoln Park. See [The Lincoln Park Transaction](#) for a description of that agreement and [Selling Stockholder](#) for additional information regarding Lincoln Park. The prices at which Lincoln Park may sell the shares will be determined by the prevailing market price for the shares or in negotiated transactions.

We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholder.

The selling stockholder may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. See [Plan of Distribution](#) for more information about how the selling stockholder may sell the shares of common stock being registered pursuant to this prospectus. The selling stockholder is an [underwriter](#) within the meaning of Section 2(a)(11) of the Securities Act of 1933, as amended.

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We will pay the expenses incurred in registering the shares, including legal and accounting fees. See Plan of Distribution .

Our common stock is currently quoted on the Nasdaq Capital Market under the symbol ONTX . On April 21, 2016, the last reported sale price of our common stock on the Nasdaq Capital Market was \$0.50.

**Investing in our common stock involves substantial risks. See Risk Factors beginning on page 11.**

**We are an emerging growth company as defined by the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.**

**We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read the entire prospectus and any amendments or supplements carefully before you make your investment decision.**

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

The date of this prospectus is , 2016.

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**WHERE YOU CAN FIND MORE INFORMATION**

We file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission, or SEC. You may read and copy any documents we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, our filings with the SEC are available to the public through the SEC's Internet site at <http://www.sec.gov>. Information about us is also available on our website at <http://www.onconova.com>. This URL and the SEC's URL above are intended to be inactive textual references only. The information on the SEC's website and our website is not part of, and is not incorporated into, this prospectus.

We have filed a registration statement covering our shares of common stock subject to this offering, of which this prospectus forms a part. This prospectus, however, does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information concerning us and the securities we may offer and sell, you should read the entire registration statement and the exhibits to the registration statement. The registration statement has been filed electronically and may be obtained in any manner listed above. Any statements contained in this prospectus concerning the provisions of any document are not necessarily complete, and, in each instance, reference is made to the copy of such document filed as an exhibit to the registration statement or otherwise filed with the SEC. Each such statement is qualified in its entirety by such reference.

**INCORPORATION OF INFORMATION BY REFERENCE**

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

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, which we filed with the SEC on March 28, 2016;
- Our current reports on Form 8-K filed with the SEC on January 6, 2016, February 4, 2016, February 17, 2016 and March 9, 2016;
- The description of our common stock contained in our registration statement on Form 8-A filed on July 23, 2013 (Registration no. 001-36020) with the SEC, including any amendment or report filed for the purpose of updating such description;
- All documents filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, after the date of the initial filing of the registration



statement of which this prospectus is a part and prior to the effectiveness of such registration statement; and

- All documents filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and before we stop offering the securities under this prospectus.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon his or her written or oral request, a copy of any or all documents referred to above which have been or may be incorporated by reference into this prospectus but not delivered with this prospectus excluding exhibits to those documents unless they are specifically incorporated by reference into those documents. You can request those documents from us, at no cost, by writing or telephoning us at: Onconova Therapeutics, Inc., 375 Pheasant Run, Newtown, Pennsylvania, 18940, (267) 759-3036, Attention: Benjamin Hoffman.

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.

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**ABOUT THIS PROSPECTUS**

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

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

**PROSPECTUS SUMMARY**

*The items in the following summary are described in more detail later in this prospectus. This summary provides an overview of selected information and does not contain all of the information you should consider. Before investing in our common stock, you should read the entire prospectus carefully, including the information set forth under the headings Risk Factors and the consolidated financial statements and related notes included or incorporated by reference in this prospectus.*

**Overview**

We are a clinical-stage biopharmaceutical company focused on discovering and developing novel small molecule drug candidates to treat cancer. Using our proprietary chemistry platform, we have created an extensive library of targeted anti-cancer agents designed to work against cellular pathways important to cancer cells. We believe that the drug candidates in our pipeline have the potential to be efficacious in a variety of cancers. We have one actively enrolling 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 both intravenous and oral formulations as a single agent, and the oral formulation is also being tested in combination with azacitidine, in clinical trials for patients with myelodysplastic syndromes, or MDS, and related cancers.

In December 2015, we enrolled the first patient in a randomized controlled Phase 3 clinical trial of rigosertib IV in a population of patients with higher-risk MDS after failure of hypomethylating agent, or HMA, therapy. The trial, which we refer to as INSPIRE, is expected to enroll approximately 225 patients at more than 100 sites globally. The primary endpoint of INSPIRE is overall survival, and an interim analysis is anticipated. We anticipate reporting topline data from the INSPIRE trial in 2018.

During 2015, we sold shares of common stock for net proceeds of \$7.5 million and at December 31, 2015, we had approximately \$19.8 million in cash and cash equivalents. In January 2016, we completed a sale of common stock and warrants for net proceeds of approximately \$1.6 million. During 2015 and into 2016, we have taken significant actions to conserve cash, including reduction in personnel and expenditures. While we will continue to take cash conservation actions where appropriate, our costs will increase in subsequent quarters as more INSPIRE sites open and more patients enroll in the INSPIRE trial. We believe that our cash and cash equivalents, together with anticipated contractual cost-sharing payments from Baxalta for a portion of the INSPIRE trial costs, will be sufficient to fund our ongoing trials and operations into the first quarter of 2017, although there is substantial doubt about our ability to continue as a going concern.

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*Rigosertib*

Rigosertib is a small molecule that inhibits cellular signaling by acting as a Ras mimetic. This is believed to be mediated by the binding of rigosertib to the Ras-binding domain, or RBD, found in many Ras effector proteins, including the Raf and PI3K kinases. This mechanism of action provides a new approach to block the interactions between Ras and its targets containing RBD sites. Rigosertib is being tested as a single agent and in combination with azacitidine, in clinical trials of patients with MDS and related cancers. We have enrolled more than 1,200 patients in rigosertib clinical trials. We are a party to a license and development agreement with Baxalta, which is scheduled to terminate August 30, 2016. Pursuant to that agreement, Baxalta was granted certain rights to commercialize rigosertib in Europe, which rights will revert to us upon termination. We are also 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, although we could consider licensing commercialization rights to other territories as we seek additional funding.

*Myelodysplastic Syndromes*

MDS is a group of blood disorders that affect bone marrow function. MDS typically affects older patients. In MDS, the bone marrow cells become dysplastic, or defective. Therefore blood cells do not develop normally, such that too few healthy blood cells are released into the blood stream, leading to low blood cell counts, or cytopenias. Thus, many patients with MDS require frequent blood transfusions. In most cases, the disease worsens and the patient develops progressive bone marrow failure. In advanced stages of the disease, immature blood cells, or blasts, leave the bone marrow and enter the blood stream, leading to AML, which occurs in approximately one-third of patients with MDS.

Based on Surveillance Epidemiology and End Results (SEER) data from the National Cancer Institute, a marketing analytics firm has estimated the 2016 incidence of MDS will be approximately 17,390 cases and the prevalence of MDS at approximately 61,690 cases in the United States. We believe that the actual incidence numbers may be higher, due to underdiagnosing and underreporting of new cases of MDS to centralized cancer registries, and that the incidence of MDS in the United States is likely to increase, due to an aging population, improved disease awareness and diagnostic precision, and an increase in the number of cases of secondary, often chemotherapy-induced, MDS.

MDS is typically diagnosed using routine blood tests or by observing combination of certain symptoms, such as shortness of breath, weakness, easy bruising or bleeding, or fever with frequent infections. A diagnosis of MDS is confirmed by evaluating a bone marrow biopsy/aspirate showing dysplastic changes, and, in more advanced cases, the presence of excess blasts, meaning that blasts account for more than 5% of the total number of nucleated cells in the bone marrow. Several classification systems have been developed to gauge the severity of disease and help determine prognosis and treatment strategy. Two standard classification systems can be used, the French-American-British morphological classification system, or the FAB system, as modified by the World Health Organization, or WHO, and the recently revised International Prognostic Scoring System, or IPSS-R, to estimate anticipated survival for patients with MDS based on marrow function and marrow cytogenetics. IPSS-R ranks the severity of chromosome abnormalities, number of cytopenias, and percentage of bone marrow blasts observed at diagnosis to calculate a five-level risk score: Very Low, Low, Intermediate, High and Very High. MDS patients are generally classified using IPSS-R in order to assess the risk of dying or having their disease progress to AML.

*Treating Myelodysplastic Syndromes*

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We believe that most higher-risk and some lower-risk MDS patients in the United States are treated with azacitidine or decitabine, the two approved HMAs for treatment of MDS. A provider of information services and technology for the healthcare industry estimates that in the year ended June 2012, approximately 12,500 MDS patients in the United States received treatment with HMAs.

A significant number of higher-risk MDS patients fail or cannot tolerate treatment with azacitidine or decitabine, which represent the current standard of care for higher-risk MDS patients, and almost all patients who initially respond to therapy eventually progress. Median survival time of MDS patients who have failed HMAs is less than six months. Accordingly, we believe that a new therapy that would extend survival in these patients would represent a major contribution in the treatment of MDS.

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Allogeneic peripheral blood stem cell or bone marrow transplantation is a potentially curative therapy for MDS. However, since most patients with MDS are elderly and therefore ineligible for transplantation due to the arduous nature of the procedure, this option is generally considered only for the small proportion of younger MDS patients.

HMAs are believed to inhibit the methylation of DNA. Methylation is a biochemical process involving the addition of a methyl group to DNA and plays an important role in gene expression during cell division and differentiation. Hypomethylation may also restore normal function to genes that are critical for differentiation and proliferation. By contrast, rigosertib works by blocking multiple oncogenic pathways through a Ras mimetic mechanism. Because rigosertib has a mechanism of action that is different from HMAs, it may be active in patients who have failed treatment with those drugs. Furthermore, rigosertib's distinct mechanism of action has been shown to combine well with approved HMAs and preclinical studies testing the combination of rigosertib with azacitidine have demonstrated synergy between the two agents. Based on these studies and our current understanding of the mechanism of action of rigosertib, we believe that rigosertib has the potential to be developed in combination with azacitidine for front-line or second line MDS patients and for patients with AML who are not candidates for standard induction chemotherapy; or second-line AML who have failed induction chemotherapy.

Lower-risk MDS patients are those categorized as Very Low, Low or Intermediate risk by the IPSS-R scoring system, with transfusion-dependent anemia. The subset of del(5q) cytogenetic abnormality patients are generally treated with lenalidomide (Revlimid®). For all other lower-risk MDS patients, supportive care employing blood products, such as red blood cell and platelet transfusions, and erythroid stimulating agents, is the mainstay of therapy. Frequent transfusions introduce many risks, including iron overload, blood borne infections and immune-related reactions. We believe that a therapeutic agent that could lower or eliminate the need for transfusions over an extended period of time would fulfill a significant unmet medical need for this patient population.

*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. The ONTIME trial did not meet its primary endpoint 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.

During 2014 and 2015, we held meetings with the U.S. Food and Drug Administration, or FDA, European Medicines Agency, or 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 have refined the patient eligibility criteria in the new trial by defining 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, with overall survival as a primary endpoint. The INSPIRE trial is enrolling higher-risk MDS patients under 80 years of age who have progressed on, or failed to respond to, previous treatment with HMAs within the first nine months 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, and an interim analysis is anticipated. This randomized trial of approximately 225 patients is expected to be conducted at more than 100 sites globally. In August 2015, we submitted an updated investigational new drug application, or IND, to the FDA, and in August 2015 we submitted Clinical Trial Applications, or CTAs, with the United Kingdom, German and Austrian regulatory authorities for IV rigosertib as a treatment for higher-risk MDS after failure of HMA therapy. The first CTA has been cleared by the Medicines and Healthcare products Regulatory Agency. The first patient in the INSPIRE trial was enrolled at the MD Anderson Cancer Center in December 2015 and, as of March 22, 2016, fourteen clinical sites are open and recruiting patients. The first patient in Europe was enrolled on March 18, 2016.

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### *Safety and Tolerability of rigosertib IV in MDS and other hematologic malignancies*

Rigosertib IV monotherapy has been evaluated in several Phase 1, 2 and 3 studies in MDS and other hematologic malignancies. Three of the Phase 1 and 2 studies are completed and clinical study reports (CSRs) are available. The three other studies have not yet completed; thus data are subject to change. The most frequent reason for study discontinuation (48.0%) was progressive disease (PD) based on 2006 International Working Group (IWG) criteria (44.9%) or symptomatic deterioration (3.1%). The occurrence of adverse events (AEs) led to withdrawal of 21.2% of patients. Withdrawal was at patient's request in 15.4% of the cases. A total of 109 patients (24.4%) died due to TEAEs.

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Only four of the TEAEs leading to death were considered related to rigosertib: acute renal failure, renal failure, septic shock, and sepsis. Using the Medical Dictionary for Regulatory Activities (MedDRA) terminology, the most frequently reported drug-related TEAEs were in system organ class (SOC) categories of gastrointestinal (GI) disorders (28.2%) and general disorders and administration site conditions (21.0%). Individual TEAEs reported by at least 5% of patients across SOC categories included, by decreasing order of frequency, nausea (14.8%), fatigue (13.9%), diarrhoea (11.2%), constipation (8.5%), and decreased appetite (5.8%). The most frequently reported <sup>3</sup> Grade 3 drug-related TEAEs were in the SOC categories of blood and lymphatic system disorders (8.3%) and Investigations (6.5%). Individual TEAEs reported by at least 1% of patients across SOC categories were anemia (4.0%); neutrophil count decreased (3.1%); platelet count decreased (2.9% each); neutropenia and thrombocytopenia (2.2% each); hyponatraemia (2.0%); white blood cell count decreased (1.8%); febrile neutropenia (1.6%); and fatigue (1.6%). Among the 11.0% of patients whose serious adverse events (SAEs) were considered drug-related, the two most frequent events were febrile neutropenia and delirium (1.1% of patients each). Other drug-related SAEs included hyponatraemia, confusional state, dyspnoea, dizziness, and mental status changes (0.7% each); anaemia, fatigue, dehydration, haematuria, and pollakiuria (0.4% each); and autoimmune haemolytic anaemia, thrombocytopenia, diabetes insipidus, abdominal distension, gastrointestinal haemorrhage, retroperitoneal fibrosis, asthenia, malaise, pyrexia, cholecystitis, bacteraemia, bronchitis, cystitis escherichia, lung infection, pneumonia, sepsis, septic shock, sinusitis fungal, urinary tract infection, hypoglycaemia, muscular weakness, convulsion, headache, dysuria, nephrolithiasis, renal failure, renal failure acute, pulmonary alveolar haemorrhage, and respiratory distress (0.2% each). Three patients (0.7%), all enrolled in a Phase 1 dose-escalating study, experienced dose-limiting toxicities (DLTs), defined as drug-related TEAEs that occurred during the first cycle of rigosertib administration. DLTs included pneumonia, dysuria, and dyspnoea (1 patient, 0.2%, each).

*Rigosertib oral in combination with azacitidine for MDS and AML*

We have completed enrollment in the Phase 2 portion of an open label Phase 1/2 clinical trial testing rigosertib oral in combination with the approved dose of injectable azacitidine for patients with higher-risk MDS and AML. This study is based on our published preclinical data demonstrating synergistic activity of this combination. We presented Phase 1 results from this trial at the American Society of Hematology (ASH) Annual Meeting in December 2014 and at the MDS Symposium in April 2015. These results showed encouraging activity in MDS and AML patients in terms of bone marrow and hematological responses. Patients in the Phase 1 portion were treated at the full standard dose of azacitidine, and the drug combination was well tolerated in repetitive cycles.

The Phase 2 portion of the trial was designed to assess whether treatment with rigosertib, in combination with the approved dose of injectable azacitidine, reduces the number of bone marrow blasts, improves peripheral blood counts and can resensitize the marrow blast cells to azacitidine for patients who were previously exposed to azacitidine. Patient enrollment in the Phase 2 portion of this trial was completed in the fourth quarter of 2015 and interim data were summarized by way of an oral presentation at the ASH Annual Meeting in December 2015.

The Phase 2 combination trial included both front-line MDS patients (that is, patients not previously treated with HMAs) and MDS patients whose disease had failed prior HMA therapy (second-line patients). The oral presentation at ASH presented results from a total of 37 MDS patients treated with the recommended Phase 2 dose of oral rigosertib (560 mg AM/280 mg PM) plus the full standard dose of injectable azacitidine. The combination of oral rigosertib and azacitidine was well tolerated, with a median duration of treatment of four months (range 1 to 27 months).

At the time of the ASH 2015 presentation, 30 MDS patients were evaluable for efficacy assessment per 2006 IWG, criteria. Twenty-three of 30 patients (77%) responded to the combination therapy, including six patients who had complete remissions. Hematologic improvement was observed in 13 of 26 patients that were evaluable for this part of the analysis. Notably, 16 of 19 (84%) HMA-naïve patients had a response to the combination therapy and 7 of 11 (64%) patients whose disease had previously failed HMAs responded. As of December 2015, the median duration of these responses had not yet been reached. Additional data collection continues for the patients remaining on study and may impact the final results of the trial.



*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 peripheral blood, whereas 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.

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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 have shown encouraging signs of efficacy of single agent oral rigosertib in transfusion-dependent, lower-risk MDS patients. 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 toxicity 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. Enrollment in this expansion cohort has been completed. We are collaborating with a methylation genomics company and academic collaborators to refine this genomic methylation test.

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

Oral rigosertib as a monotherapy has been evaluated in four Phase 1 and 2 studies in MDS and other hematologic malignancies. One study is completed and a CSR is available. The three other studies have not yet completed; thus final data are subject to change. The main reasons for study discontinuation were Investigator's decision (22.6%) and PD per the 2006 IWG criteria (19.4%). The occurrence of AEs led to withdrawal of 20.0% of patients. Patients requested withdrawal in 16.1% of the cases. Ten patients (6.1%) died due to TEAEs, none of which was considered related to rigosertib. The majority of patients (76.2%) experienced TEAEs that were considered drug-related. The most frequently reported drug-related TEAEs were in the SOC category of renal and urinary disorders (56.1% of patients); and 22.6% of patients experienced drug-related gastrointestinal disorders. Individual TEAEs reported by at least 5% of patients across SOC categories included, by decreasing order of frequency, pollakiuria (31.1%), dysuria (26.8%), haematuria (20.7%), urinary tract pain (17.7%), micturition urgency (17.7%), urinary tract infection (12.8%), diarrhoea (9.8%), fatigue (7.9%), decreased appetite (6.7%), nausea (9.8%), and cystitis (6.1%). Drug-related TEAEs were <sup>3</sup> Grade 3 in 20.1% of the patients. The most frequently reported <sup>3</sup> Grade 3 drug-related TEAEs were blood and lymphatic system disorders (6.7%), infections and infestations (4.9%), and investigations (4.9%). Individual drug-related TEAEs <sup>3</sup> Grade 3 reported by at least 1% of patients included neutropenia (3.7%), cystitis (3.0%); neutrophil count decreased and haematuria (2.4% each); thrombocytopenia and dysuria (1.8%); leukopenia, urinary tract infection, platelet count decreased, hyponatraemia, urinary tract pain, and dyspnoea (1.2% each). Among the 13 (7.9%) patients whose SAEs were considered drug-related, the events were mostly urinary. Drug-related SAEs included cystitis (3.0%), haematuria (1.2%); and anaemia, angina pectoris, adverse drug reaction, urinary tract infection, hyperglycaemia, dysuria, dyspnoea, and lung disorder (0.6% each). During Phase 1 studies, nine patients (5.5%) experienced 14 DLTs, which were defined as drug-related TEAEs that occurred during the first cycle of rigosertib administration. These included neutropenia, pain, cystitis, limb injury, alanine aminotransferase increased, aspartate aminotransferase increased, blood creatinine increased, hypoalbuminaemia, hypocalcaemia, hyponatraemia, haematuria, dyspnoea, and haematoma.

Oral rigosertib in combination with azacitidine is under evaluation in a Phase 2 trial for patients with MDS. As of December 2015, 37 MDS patients were evaluable for safety analysis. The occurrence of TEAEs led to study withdrawal in 19% of patients. 3 patients (8%) of patients died due to TEAEs, none of which was considered drug-related. The majority of patients, 84%, experienced TEAEs which were considered drug-related. The most frequently reported related events (at least 3 patients) were Dysuria (32%), Nausea and Haematuria (22% each), Pollakiuria (16%), Neutropenia (14%), Decreased appetite, Diarrhoea, and Thrombocytopenia (11% each). TEAEs of <sup>3</sup> Grade 3 severity were observed in 84% of the patients and were considered drug-related in 38% of the patients.

*Other Programs*

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

### *Briciclib*

Briciclib, another of our product candidates, 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

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process termed cap-dependent translation, which requires the function of eukaryotic initiation factor 4E protein, or eIF4E. In vitro evidence indicates briciclib binds to eIF4E, blocking cap-dependent translation of cyclin D1 and other cancer proteins, such as c-MYC, leading to tumor cell death. We have been conducting a Phase 1 multisite 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, however, the briciclib IND 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 Efficacy 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 studies in appropriate animal models to support efficacy in humans. 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.

*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.

**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](http://www.onconova.com). The information on, or that can be accessed through, our website is not part of this prospectus.

**Implications of Being an Emerging Growth Company**

As a company with less than \$1.0 billion in revenue during our last fiscal year, we qualify as an emerging growth company as defined in the Jumpstart our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting requirements and is relieved of certain other significant requirements that are otherwise generally applicable to public companies. As an emerging growth company,

- we may present only two years of audited financial statements and only two years of related Management's Discussion & Analysis of Financial Condition and Results of Operations;
- we are exempt from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002;
- we are permitted to provide less extensive disclosure about our executive compensation arrangements;
- we are not required to give our stockholders non-binding advisory votes on executive compensation or golden parachute arrangements; and
- we have elected to use an extended transition period for complying with new or revised accounting standards.

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We may take advantage of these provisions until the last day of our fiscal year following the fifth anniversary of the date of the first sale of our common equity securities pursuant to an effective registration statement under the Securities Act of 1933, as amended, or the Securities Act. However, if certain events occur prior to the end of such five-year period, including if we become a large accelerated filer, our annual gross revenues exceed \$1.0 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period.

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**THE OFFERING**

On October 8, 2015, we entered into the Purchase Agreement, pursuant to which Lincoln Park purchased 846,755 shares of our common stock for a total purchase price of \$1,500,000 as an Initial Purchase and has agreed to purchase from us up to an aggregate of \$15,000,000 of our common stock (subject to certain limitations) from time to time over a 36-month period. Also on October 8, 2015, we entered into a Registration Rights Agreement, or the Registration Rights Agreement, with Lincoln Park, pursuant to which we have filed with the SEC the registration statement that includes this prospectus to register for resale under the Securities Act of 1933, as amended, or the Securities Act, the shares that have been or may be issued to Lincoln Park under the Purchase Agreement.

Other than (i) 846,755 shares of our common stock that we have already issued to Lincoln Park in the Initial Purchase and (ii) 200,000 shares of our common stock that we have already issued to Lincoln Park pursuant to the terms of the Purchase Agreement as consideration for its commitment to purchase additional shares of our common stock under the Purchase Agreement, we do not have the right to commence any further sales to Lincoln Park under the Purchase Agreement until the SEC has declared effective the registration statement of which this prospectus forms a part. Thereafter, we may, from time to time and at our sole discretion, direct Lincoln Park to purchase shares of our common stock in amounts up to 100,000 shares (which amounts may be increased under certain circumstances) on any single business day up to \$1,000,000 per purchase, plus an additional accelerated amount under certain circumstances. There are no trading volume requirements or restrictions under the Purchase Agreement, and we will control the timing and amount of any sales of our common stock to Lincoln Park. The purchase price of the shares that may be sold to Lincoln Park under the Purchase Agreement will be based on the market price of our common stock preceding the time of sale as computed under the Purchase Agreement without any fixed discount. The purchase price per share will be equitably adjusted for any reorganization, recapitalization, non-cash dividend, stock split, or other similar transaction occurring during the business days used to compute such price. We may at any time in our sole discretion terminate the Purchase Agreement without fee, penalty or cost upon one business day notice. There are no restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement or Registration Rights Agreement other than a prohibition on entering into an Equity Line of Credit. Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement.

As of April 21, 2016, there were 27,401,035 shares of our common stock outstanding, of which 18,401,910 shares were held by non-affiliates. Although the Purchase Agreement provides that we may sell up to \$16,500,000 of our common stock to Lincoln Park, only 5,200,000 shares of our common stock are being offered under this prospectus, which represents 846,755 already purchased by Lincoln Park for proceeds of \$1,500,000, 200,000 shares that we issued to Lincoln Park as a commitment fee for making the commitment under the Purchase Agreement and an additional 4,153,245 shares which may be issued to Lincoln Park in the future under the Purchase Agreement. Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement. If all of the 5,200,000 shares offered by Lincoln Park under this prospectus were issued and outstanding as of the date hereof, such shares would represent 19.0% of the total number of shares of our common stock outstanding and 28.3% of the total number of outstanding shares held by non-affiliates, in each case as of the date hereof. If we elect to issue and sell more than the 5,200,000 shares offered under this prospectus to Lincoln Park, which we have the right, but not the obligation, to do, we must first register for resale under the Securities Act any such additional shares, which could cause additional substantial dilution to our stockholders. The number of shares ultimately offered for resale by Lincoln Park is dependent upon the number of shares we sell to Lincoln Park under the Purchase Agreement.

Under the rules of the NASDAQ Capital Market, in no event may we issue more than 19.99% of our shares outstanding (which is approximately 4,735,925 shares based on 23,691,472 shares outstanding immediately prior to the signing of the Purchase Agreement) under the Purchase Agreement unless we obtain stockholder approval or an exception pursuant to the rules of the NASDAQ Capital Market is obtained to issue more than 19.99%. This limitation shall not apply if, at any time the Exchange Cap is reached and at all times thereafter, the average price paid for all shares issued and sold under the Purchase Agreement is equal to or greater than \$1.56, which was the closing consolidated bid price of our Common Stock on October 7, 2015 including an increment for the commitment shares we issued to Lincoln Park. We are not required or permitted to issue any shares of Common Stock under the Purchase Agreement if such issuance would breach our obligations under the rules or regulations of the NASDAQ Capital Market.

Issuances of our common stock in this offering will not affect the rights or privileges of our existing stockholders, except that the economic and voting interests of each of our existing stockholders will be diluted as a



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result of any such issuance. Although the number of shares of common stock that our existing stockholders own will not decrease, the shares owned by our existing stockholders will represent a smaller percentage of our total outstanding shares after any such issuance to Lincoln Park.

**SECURITIES OFFERED**

|                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                    |
|--------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Common stock to be offered by the selling stockholder                                                                          | 5,200,000 shares consisting of:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>• 846,755 shares issued to Lincoln Park in the Initial Purchase;</li> <li>• 200,000 commitment shares issued to Lincoln Park; and</li> <li>• 4,153,245 shares we may sell to Lincoln Park from time to time after the effective date of the Registration Statement under the Purchase Agreement.</li> </ul> |
| Common stock outstanding as of April 21, 2016                                                                                  | 27,401,035 shares                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                    |
| Common stock to be outstanding after giving effect to the issuance of 4,153,245 additional shares under the Purchase Agreement | 31,554,280 shares                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                    |
| Use of Proceeds                                                                                                                | We will receive no proceeds from the sale of shares of common stock by Lincoln Park in this offering. However, we may receive up to \$16,500,000 under the Purchase Agreement with Lincoln Park. Any proceeds that we receive from sales to Lincoln Park under the Purchase Agreement will be used to fund the development of our clinical and preclinical programs, for other research and development activities and for general corporate purposes, which may include capital expenditures and funding our working capital needs. See Use of Proceeds. |                                                                                                                                                                                                                                                                                                                                                    |
| Risk factors                                                                                                                   | This investment involves a high degree of risk. See Risk Factors for a discussion of factors you should consider carefully before making an investment decision.                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                    |
| Symbol on Nasdaq Capital Market                                                                                                | ONTX                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                    |

The number of shares of common stock outstanding after this offering is based on 27,401,035 shares of our common stock outstanding as of April 21, 2016 and excludes:

- 5,671,213 shares of common stock issuable upon the exercise of stock options outstanding under our 2013 Equity Compensation Plan at a weighted average exercise price of \$7.26 per share; and

- 1,859,089 additional shares of common stock reserved for future issuance under our 2013 Equity Compensation Plan.

To the extent that outstanding options 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.

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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 most recent Annual Report on Form 10-K, as revised or supplemented by our Quarterly Reports on Form 10-Q filed with the SEC since the filing of our most recent Annual Report on Form 10-K, each of which is incorporated by reference into this prospectus, and you should also carefully consider any other information we include or incorporate by reference in this prospectus.

Any of the risks we describe below or in the information incorporated herein by reference in this prospectus could cause our business, financial condition or operating results to suffer. The market price of our common stock could decline if one or more of these risks and uncertainties develop into actual events. You could lose all or part of your investment.

***The sale or issuance of our common stock to Lincoln Park may cause dilution and the sale of the shares of common stock acquired by Lincoln Park, or the perception that such sales may occur, could cause the price of our common stock to fall***

On October 8, 2015, we entered into the Purchase Agreement with Lincoln Park, pursuant to which Lincoln Park has committed to purchase up to \$16,500,000 of our common stock. Concurrently with the execution of the Purchase Agreement, Lincoln Park purchased 846,755 shares of our common stock for total proceeds of \$1,500,000 and we issued 200,000 shares of our common stock to Lincoln Park as a fee for its commitment to purchase shares of our common stock under the Purchase Agreement. The purchase shares that may be sold pursuant to the Purchase Agreement may be sold by us to Lincoln Park at our discretion from time to time over a 36-month period which commenced November 3, 2015. The purchase price for the shares that we may sell to Lincoln Park under the Purchase Agreement will fluctuate based on the price of our common stock. Depending on market liquidity at the time, sales of such shares may cause the trading price of our common stock to fall.

We generally have the right to control the timing and amount of any sales of our shares to Lincoln Park, except that, pursuant to the terms of our agreements with Lincoln Park. Additional sales of our common stock, if any, to Lincoln Park will depend upon market conditions and other factors to be determined by us. Lincoln Park may ultimately purchase all, some or none of the shares of our common stock that may be sold pursuant to the Purchase Agreement and, after it has acquired shares, Lincoln Park may sell all, some or none of those shares. Therefore, sales to Lincoln Park by us could result in substantial dilution to the interests of other holders of our common stock. Additionally, the sale of a substantial number of shares of our common stock to Lincoln Park, or the anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales.

***We may require additional financing to sustain our operations and without it we may not be able to continue operations.***

At December 31, 2015 we had an accumulated deficit of \$318.6 million. Since our inception, we have incurred net losses and generally negative cash flows from our operations. For the years ended December 31, 2015, and 2014, we reported net losses of \$24.0 million and \$63.8 million, respectively. We do not currently have sufficient financial resources to fund our operations or those of our subsidiaries. Therefore, we need additional funds to continue these operations.

We may direct Lincoln Park to purchase up to \$16,500,000 worth of shares of our common stock under our agreement over a 36-month period generally in amounts up to 100,000 shares of our common stock on any such business day, of which Lincoln Park purchased, upon entering into the Purchase Agreement, 846,755 shares of our common stock for total proceeds of \$1,500,000. Assuming a purchase price of \$0.50 per share (the closing sale price of the common stock on April 21, 2016) and the purchase by Lincoln Park of the full 4,153,245 purchase shares under the purchase agreement that are registered pursuant to this Registration Statement, additional proceeds to us would only be approximately \$2,118,154.

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The extent we rely on Lincoln Park as a source of funding will depend on a number of factors including, the prevailing market price of our common stock and the extent to which we are able to secure working capital from other sources. If obtaining sufficient funding from Lincoln Park were to prove unavailable or prohibitively dilutive, we will need to secure another source of funding in order to satisfy our working capital needs. Even if we sell all \$16,500,000 under the Purchase Agreement to Lincoln Park, we may still need additional capital to fully implement our business, operating and development plans. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could be a material adverse effect on our business, operating results, financial condition and prospects.

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**CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus includes forward-looking statements. We may, in some cases, use terms such as believes, estimates, anticipates, expects, plan, intends, may, could, might, will, should, approximately or other words that convey uncertainty of future events or outcomes to identify forward-looking statements. Forward-looking statements appear in a number of places throughout this report 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 report, 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 report. In addition, even if our results of operations, financial condition and liquidity, and events in the industry in which we operate are consistent with the forward-looking statements contained in this report, they may not be predictive of results or developments in future periods.

Actual results could differ materially from our forward-looking statements due to a number of factors, including risks related to:

- our need for additional financing for our 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 drug candidates or preclinical compounds, and our

ability to achieve certain milestones under those agreements;

- the difficulties in obtaining and maintaining regulatory approval of our product candidates, and the labeling under any approval we may obtain;
- our plans and ability to develop, manufacture and commercialize our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;

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

Any forward-looking statements that we make in this prospectus speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this prospectus or to reflect the occurrence of unanticipated events. 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 set forth in our most recent Annual Report on Form 10-K, as revised or supplemented by our Quarterly Reports on Form 10-Q filed with the SEC since the filing of our most recent Annual Report on Form 10-K, to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements in this report and you should not place undue reliance on any forward-looking statements.





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**THE LINCOLN PARK TRANSACTION**

**General**

On October 8, 2015, we entered into the Purchase Agreement and the Registration Rights Agreement with Lincoln Park. Pursuant to the terms of the Purchase Agreement, Lincoln Park made the Initial Purchase of 846,755 shares of our common stock for a total purchase price of \$1,500,000 and has agreed to purchase from us up to an aggregate of \$15,000,000 of our common stock (subject to certain limitations) from time to time over a 36-month period. Pursuant to the terms of the Registration Rights Agreement, we have filed with the SEC the registration statement that includes this prospectus to register for resale under the Securities Act the shares that have been or may be issued to Lincoln Park under the Purchase Agreement.

Concurrently with the execution of the Purchase Agreement on October 8, 2015, Lincoln Park purchased 846,755 shares of our common stock for total proceeds of \$1,500,000, the Initial Purchase, and we issued to Lincoln Park 200,000 shares of our common stock as a fee for its commitment to purchase shares of our common stock under the Purchase Agreement. We do not have the right to commence any further sales to Lincoln Park under the Purchase Agreement until the SEC has declared effective the registration statement of which this prospectus forms a part. Thereafter and upon satisfaction of the other conditions set forth in the Purchase Agreement, we may, from time to time and at our sole discretion, direct Lincoln Park to purchase shares of our common stock in amounts up to 100,000 shares on any single business day, which amounts may be increased but in no event greater than \$1,000,000 per such purchase. The purchase price per share is based on the market price of our common stock immediately preceding the time of sale as computed under the Purchase Agreement without any fixed discount. Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement.

**Purchase of Shares Under the Purchase Agreement**

Under the Purchase Agreement, on any business day selected by us, we may direct Lincoln Park to purchase up to 100,000 shares of our common stock on any such business day. On any day that the closing sale price of our common stock is not below \$1.50 the purchase amount may be increased, at our sole discretion, to up to 125,000 shares of our common stock, on any day that the closing sale price of our common stock is not below \$2.00 the purchase amount may be increased, at our sole discretion, to up to 150,000 shares of our common stock, on any day that the closing sale price of our common stock is not below \$2.50 the purchase amount may be increased, at our sole discretion, to up to 175,000 shares of our common stock, on any day that the closing sale price of our common stock is not below \$3.00 the purchase amount may be increased, at our sole discretion, to up to 200,000 shares of our common stock and on any day that the closing sale price of our common stock is not below \$3.50, the purchase amount may be increased, at our sole discretion, to up to 250,000 shares of our common stock. The amount of any single Regular Purchase may not exceed \$1,000,000 per purchase. The purchase price per share for each such Regular Purchase will be equal to the lower of:

- the lowest sale price for our common stock on the purchase date of such shares; or
- the arithmetic average of the three lowest closing sale prices for our common stock during the 10 consecutive business days ending on the business day immediately preceding the purchase date of such shares.

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In addition to Regular Purchases described above, we may also direct Lincoln Park, on any business day on which we have properly submitted a Regular Purchase notice and our Closing Price is not below \$0.50, to purchase an additional amount of our common stock, which we refer to as an Accelerated Purchase, not to exceed the lesser of:

- 30% of the aggregate shares of our common stock traded during normal trading hours on the purchase date;  
and
- three times the number of purchase shares purchased pursuant to the corresponding Regular Purchase.

The purchase price per share for each such Accelerated Purchase will be equal to the lower of:

- 97% of the volume weighted average price during (i) the entire trading day on the purchase date, if the volume of shares of our common stock traded on the purchase date has not exceeded a volume

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maximum calculated in accordance with the Purchase Agreement, or (ii) the portion of the trading day of the purchase date (calculated starting at the beginning of normal trading hours) until such time at which the volume of shares of our common stock traded has exceeded such volume maximum; or

- the closing sale price of our common stock on the accelerated purchase date.

In the case of both Regular Purchases and Accelerated Purchases, the purchase price per share will be equitably adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction occurring during the business days used to compute the purchase price.

Other than as set forth above, there are no trading volume requirements or restrictions under the Purchase Agreement, and we will control the timing and amount of any sales of our common stock to Lincoln Park.

**Events of Default**

Events of default under the Purchase Agreement include the following:

- the effectiveness of the registration statement of which this prospectus forms a part lapses for any reason (including, without limitation, the issuance of a stop order), or any required prospectus supplement and accompanying prospectus are unavailable for the resale by Lincoln Park of our common stock offered hereby, and such lapse or unavailability continues for a period of 10 consecutive business days or for more than an aggregate of 30 business days in any 365-day period;
- suspension by our principal market of our common stock from trading for a period of three consecutive business days;
- the de-listing of our common stock from our principal market, provided our common stock is not immediately thereafter trading on the New York Stock Exchange, the NASDAQ Global Select Market, the NASDAQ Global Market, the NYSE Amex or the OTC Bulletin Board (or nationally recognized successor thereto);
- the transfer agent's failure for five business days to issue to Lincoln Park shares of our common stock which Lincoln Park is entitled to receive under the Purchase Agreement;

- any breach of the representations or warranties or covenants contained in the Purchase Agreement or any related agreement which has or which could have a material adverse effect on us subject to a cure period of five business days;
- if we issue more than 19.99% of the Company's aggregate outstanding Common Stock, determined as of the date of the Purchase Agreement, in violation of the Nasdaq Capital Market rules;
- any voluntary or involuntary participation or threatened participation in insolvency or bankruptcy proceedings by or against us; or
- if at any time we are not eligible to transfer our common stock electronically or a material adverse change in our business, financial condition, operations or prospects has occurred.

Lincoln Park does not have the right to terminate the Purchase Agreement upon any of the events of default set forth above. During an event of default, all of which are outside of Lincoln Park's control, we cannot initiate any Regular Purchases or Accelerated Purchases under the Purchase Agreement.

#### **Our Termination Rights**

We have the unconditional right, at any time, for any reason and without any payment or liability to us, to give notice to Lincoln Park to terminate the Purchase Agreement. In the event of bankruptcy proceedings by or against us, the Purchase Agreement will automatically terminate without action of any party.

Table of Contents**No Short-Selling or Hedging by Lincoln Park**

Lincoln Park has agreed that neither it nor any of its affiliates shall engage in any direct or indirect short-selling or hedging of our common stock during any time prior to the termination of the Purchase Agreement.

**Effect of Performance of the Purchase Agreement on Our Stockholders**

All 5,200,000 shares registered in this offering which may be sold by us to Lincoln Park under the Purchase Agreement are expected to be freely tradable. It is anticipated that shares registered in this offering will be sold over a period of up to 36-months which commenced on November 3, 2015. The sale by Lincoln Park of a significant amount of shares registered in this offering at any given time could cause the market price of our common stock to decline and to be highly volatile. Lincoln Park may ultimately purchase all, some or none of the remaining 4,153,245 shares of common stock registered in this offering not yet issued. If we sell these shares to Lincoln Park, Lincoln Park may sell all, some or none of such shares. Therefore, sales to Lincoln Park by us under the Purchase Agreement may result in substantial dilution to the interests of other holders of our common stock. In addition, if we sell a substantial number of shares to Lincoln Park under the Purchase Agreement, or if investors expect that we will do so, the actual sales of shares or the mere existence of our arrangement with Lincoln Park may make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect such sales. However, we have the right to control the timing and amount of any sales of our shares to Lincoln Park and the Purchase Agreement may be terminated by us at any time at our discretion without any cost to us.

Pursuant to the terms of the Purchase Agreement, we have the right, but not the obligation, to direct Lincoln Park to purchase up to \$16,500,000 of our common stock, inclusive of the 846,755 shares issued to Lincoln Park for the \$1,500,000 Initial Purchase and exclusive of the 200,000 shares issued to Lincoln Park as a commitment fee. Depending on the price per share at which we sell our common stock to Lincoln Park, we may be authorized to issue and sell to Lincoln Park under the Purchase Agreement more shares of our common stock than are offered under this prospectus. If we choose to do so, we must first register for resale under the Securities Act any such additional shares, which could cause additional substantial dilution to our stockholders. The number of shares ultimately offered for resale by Lincoln Park under this prospectus is dependent upon the number of shares we direct Lincoln Park to purchase under the Purchase Agreement.

The following table sets forth the amount of gross proceeds we would receive from Lincoln Park from our sale of shares to Lincoln Park under the Purchase Agreement at varying purchase prices:

| Assumed Average Purchase Price Per Share | Number of Registered Shares to be Issued if Full Purchase (1)(2) | Percentage of Outstanding Shares After Giving Effect to the Issuance to Lincoln Park (3) | Proceeds from the Sale of Shares to Lincoln Park Under the \$16.5M Purchase Agreement |
|------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| \$ 0.50(5)                               | 5,000,000(4)                                                     | 15.8%                                                                                    | \$ 2,500,000                                                                          |
| \$ 1.00                                  | 5,000,000(4)                                                     | 15.8%                                                                                    | \$ 5,000,000                                                                          |
| \$ 2.50                                  | 5,000,000                                                        | 15.8%                                                                                    | \$ 12,500,000                                                                         |
| \$ 4.00                                  | 4,125,000                                                        | 13.4%                                                                                    | \$ 16,500,000                                                                         |

(1) Although the Purchase Agreement provides that we may sell up to \$16,500,000 of our common stock to

Lincoln Park, we are only registering 5,200,000 shares under this prospectus, which may or may not cover all the shares we ultimately sell to Lincoln Park under the Purchase Agreement, depending on the purchase price per share. As a result, we have included in this column only those shares that we are registering in this offering.

- (2) The number of registered shares to be issued excludes the 200,000 commitment shares because no proceeds will be attributable to such commitment shares.
- (3) The denominator is based on 27,401,035 shares outstanding as of April 21, 2016 , which includes the 846,755 shares issued to Lincoln Park for the \$1,500,000 Initial Purchase and the 200,000 shares issued to Lincoln Park as commitment shares in connection with this offering and the number of shares set forth in the adjacent column which we would have sold to Lincoln Park at the applicable assumed average purchase price per share. The numerator does not include the 200,000 shares issued to Lincoln Park as commitment shares in connection with this

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offering, and is based on the number of shares registered in this offering to be issued under the Purchase Agreement. The number of shares in such column does not include shares that may be issued to Lincoln Park under the Purchase Agreement which are not registered in this offering.

(4) The number of registered shares to be issued assumes that we have received stockholder approval to issue shares above the limits imposed by the NASDAQ Capital Market.

(5) The closing sale price of our shares on April 21, 2016.



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**USE OF PROCEEDS**

This prospectus relates to shares of our common stock that may be offered and sold from time to time by Lincoln Park. We will receive no proceeds from the sale of shares of common stock by Lincoln Park in this offering. However, we may receive gross proceeds of up to \$16,500,000 under the Purchase Agreement. We estimate that the net proceeds to us from the sale of our common stock to Lincoln Park pursuant to the Purchase Agreement will be up to \$16,415,000 over an approximately 36-month period, assuming that we sell the full amount of our common stock that we have the right, but not the obligation, to sell to Lincoln Park under that agreement and other estimated fees and expenses. See "Plan of Distribution" elsewhere in this prospectus for more information.

We currently expect to use the net proceeds we receive under the Purchase Agreement 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.

Table of Contents**THE SELLING STOCKHOLDER**

This prospectus relates to the possible resale by the selling stockholder, Lincoln Park, of shares of common stock that have been or may be issued to Lincoln Park pursuant to the Purchase Agreement. We are filing the registration statement of which this prospectus forms a part pursuant to the provisions of the Registration Rights Agreement, which we entered into with Lincoln Park on October 8, 2015 concurrently with our execution of the Purchase Agreement, in which we agreed to provide certain registration rights with respect to sales by Lincoln Park of the shares of our common stock that have been or may be issued to Lincoln Park under the Purchase Agreement.

Lincoln Park, as the selling stockholder, may, from time to time, offer and sell pursuant to this prospectus any or all of the shares that we have sold or may sell to Lincoln Park under the Purchase Agreement. The selling stockholder may sell some, all or none of its shares. We do not know how long the selling stockholder will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholder regarding the sale of any of the shares.

The following table presents information regarding the selling stockholder and the shares that it may offer and sell from time to time under this prospectus. The table is prepared based on information supplied to us by the selling stockholder, and reflects its holdings prior to commencement of the offering. Neither Lincoln Park nor any of its affiliates has held a position or office, or had any other material relationship, with us or any of our predecessors or affiliates. As used in this prospectus, the term *selling stockholder* includes Lincoln Park and any donees, pledgees, transferees or other successors in interest selling shares received after the date of this prospectus from Lincoln Park as a gift, pledge or other non-sale related transfer. Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Exchange Act. The percentage of shares beneficially owned prior to the offering is based on 27,401,035 shares of our common stock actually outstanding as of April 21, 2016.

| <b>Selling Stockholder</b>         | <b>Shares<br/>Beneficially<br/>Owned Before<br/>this Offering</b> | <b>Percentage of<br/>Outstanding<br/>Shares<br/>Beneficially<br/>Owned Before<br/>this Offering</b> | <b>Shares to be Sold in<br/>this Offering</b> | <b>Percentage of<br/>Outstanding<br/>Shares<br/>Beneficially<br/>Owned After<br/>this Offering</b> |
|------------------------------------|-------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|-----------------------------------------------|----------------------------------------------------------------------------------------------------|
| Lincoln Park Capital Fund, LLC (1) | 1,046,755(2)                                                      | 3.8%(3)                                                                                             | 5,200,000(4)                                  | *                                                                                                  |

---

\* Less than 1%

(1) Josh Scheinfeld and Jonathan Cope, the Managing Members of Lincoln Park Capital, LLC, are deemed to be beneficial owners of all of the shares of common stock owned by Lincoln Park Capital Fund, LLC. Messrs. Cope and Scheinfeld have shared voting and investment power over the shares being offered under the prospectus filed with the SEC in connection with the transactions contemplated under the Purchase Agreement. Lincoln Park Capital, LLC is not a licensed broker dealer or an affiliate of a licensed broker dealer.

(2) Represents 846,755 shares of our common stock purchased by Lincoln Park upon entering into the Purchase Agreement for total proceeds of \$1,500,000 and 200,000 shares of our common stock issued to Lincoln Park on

October 8, 2015 as a fee for its commitment to purchase additional shares of our common stock under the Purchase Agreement which shares are covered by the registration statement that includes this prospectus. See the description under the heading "The Lincoln Park Transaction" for more information about the Purchase Agreement.

(3) Based on 27,401,035 outstanding shares of our common stock as of April 21, 2016, which includes 846,755 shares of our common stock purchased by Lincoln Park upon entering into the Purchase Agreement for total proceeds of \$1,500,000 and 200,000 shares of our common stock issued to Lincoln Park on October 8, 2015 as a fee for its commitment to purchase additional shares of our common stock under the Purchase Agreement. Although we may at our discretion elect to issue to Lincoln Park up to an additional amount of \$15,000,000 of our common stock under the Purchase Agreement, other than the shares described in the immediately preceding sentence, such shares are not beneficially owned by Lincoln Park and are not included in determining the percentage of shares beneficially owned before this offering.

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**DIVIDEND POLICY**

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our corporation and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future.

Table of Contents**MARKET PRICE OF COMMON STOCK**

Our common stock began trading on the NASDAQ Global Select Market on July 25, 2013 under the symbol ONTX. Prior to that time, there was no public market for our common stock. Shares sold in our initial public offering on July 24, 2013 were priced at \$15.00 per share. On February 5, 2016, we transferred the listing of our shares to the NASDAQ Capital Market. The following table sets forth for the periods indicated the high and low intra-day sale prices per share of our common stock as reported on the NASDAQ Global Market or NASDAQ Capital Market:

|                                             | <b>High</b> | <b>Low</b> |
|---------------------------------------------|-------------|------------|
| <b><i>Year Ending December 31, 2016</i></b> |             |            |
| First Quarter                               | \$ 1.03     | \$ 0.32    |
| Second Quarter (through April 21, 2016)     | 0.60        | 0.43       |
| <b><i>Year Ended December 31, 2015</i></b>  |             |            |
| First Quarter                               | \$ 4.43     | \$ 2.15    |
| Second Quarter                              | 3.02        | 2.26       |
| Third Quarter                               | 4.00        | 1.35       |
| Fourth Quarter                              | 1.89        | 0.92       |
| <b><i>Year Ended December 31, 2014</i></b>  |             |            |
| First Quarter                               | \$ 16.22    | \$ 6.05    |
| Second Quarter                              | 6.49        | 4.10       |
| Third Quarter                               | 5.78        | 4.24       |
| Fourth Quarter                              | 5.00        | 3.24       |

In February 2016, we transferred the listing of our common stock from the NASDAQ Global Select Market to the NASDAQ Capital Market and subsequently received a deficiency letter from NASDAQ notifying us that we had failed to meet the minimum bid price required for continued listing for 30 consecutive business days. In accordance with NASDAQ listing rules, we have been provided an initial period of 180 calendar days, or until August 8, 2016, to regain compliance. On April 21, 2016, the last reported sale price of our common stock on the NASDAQ Capital Market was \$0.50 per share. As of April 21, 2016, we had 167 holders of record of our common stock. The actual number of holders of common stock is greater than these numbers of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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**PLAN OF DISTRIBUTION**

The common stock offered by this prospectus is being offered by the selling stockholder, Lincoln Park. The common stock may be sold or distributed from time to time by the selling stockholder directly to one or more purchasers or through brokers, dealers, or underwriters who may act solely as agents at market prices prevailing at the time of sale, at prices related to the prevailing market prices, at negotiated prices, or at fixed prices, which may be changed. The sale of the common stock offered by this prospectus could be effected in one or more of the following methods:

- ordinary brokers transactions;
- transactions involving cross or block trades;
- through brokers, dealers, or underwriters who may act solely as agents
- at the market into an existing market for the common stock;
- in other ways not involving market makers or established business markets, including direct sales to purchasers or sales effected through agents;
- in privately negotiated transactions; or
- any combination of the foregoing.

In order to comply with the securities laws of certain states, if applicable, the shares may be sold only through registered or licensed brokers or dealers. In addition, in certain states, the shares may not be sold unless they have been registered or qualified for sale in the state or an exemption from the state's registration or qualification requirement is available and complied with.

Lincoln Park is an underwriter within the meaning of Section 2(a)(11) of the Securities Act.

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Lincoln Park has informed us that it intends to use an unaffiliated broker-dealer to effectuate all sales, if any, of the common stock that it may purchase from us pursuant to the Purchase Agreement. Such sales will be made at prices and at terms then prevailing or at prices related to the then current market price. Each such unaffiliated broker-dealer will be an underwriter within the meaning of Section 2(a)(11) of the Securities Act. Lincoln Park has informed us that each such broker-dealer will receive commissions from Lincoln Park that will not exceed customary brokerage commissions. In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus.

Brokers, dealers, underwriters or agents participating in the distribution of the shares as agents may receive compensation in the form of commissions, discounts, or concessions from the selling stockholder and/or purchasers of the common stock for whom the broker-dealers may act as agent. The compensation paid to a particular broker-dealer may be less than or in excess of customary commissions. Neither we nor Lincoln Park can presently estimate the amount of compensation that any agent will receive.

We know of no existing arrangements between Lincoln Park or any other stockholder, broker, dealer, underwriter or agent relating to the sale or distribution of the shares offered by this prospectus. At the time a particular offer of shares is made, a prospectus supplement, if required, will be distributed that will set forth the names of any agents, underwriters or dealers and any compensation from the selling stockholder, and any other required information.

We will pay the expenses incident to the registration, offering, and sale of the shares to Lincoln Park. We have agreed to indemnify Lincoln Park and certain other persons against certain liabilities in connection with the offering of shares of common stock offered hereby, including liabilities arising under the Securities Act or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities. Lincoln Park has agreed to indemnify us against liabilities under the Securities Act that may arise from certain written information furnished to us

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by Lincoln Park specifically for use in this prospectus or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities.

Lincoln Park has represented to us that at no time prior to the Purchase Agreement has Lincoln Park or its agents, representatives or affiliates engaged in or effected, in any manner whatsoever, directly or indirectly, any short sale (as such term is defined in Rule 200 of Regulation SHO of the Exchange Act) of our common stock or any hedging transaction, which establishes a net short position with respect to our common stock. Lincoln Park agreed that during the term of the Purchase Agreement, it, its agents, representatives or affiliates will not enter into or effect, directly or indirectly, any of the foregoing transactions.

We have advised Lincoln Park that it is required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes the selling stockholder, any affiliated purchasers, and any broker-dealer or other person who participates in the distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase any security which is the subject of the distribution until the entire distribution is complete. Regulation M also prohibits any bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of the securities offered by this prospectus.

This offering will terminate on the date that all shares offered by this prospectus have been sold by Lincoln Park.

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



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**DESCRIPTION OF CAPITAL STOCK**

Our authorized capital stock consists of 75,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share. As of April 21, 2016, 27,401,035 shares of our common stock, and no shares of our preferred stock, were outstanding.

**Common Stock**

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

**Preferred Stock**

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

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

*Delaware Anti-Takeover Law*

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

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

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

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

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

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

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

*Certificate of Incorporation and Bylaws*

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

- permit our board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that all vacancies on our board of directors, including as a result of newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;

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- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- not provide for cumulative voting rights, thereby allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election; and
- provide that special meetings of our stockholders may be called only by the board of directors or by such person or persons requested by a majority of the board of directors to call such meetings.

**Transfer Agent and Registrar**

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

**Listing**

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

**LEGAL MATTERS**

The validity of the shares of common stock offered hereby and certain other legal matters will be passed upon for us by Pepper Hamilton LLP, Princeton, New Jersey.

**EXPERTS**

The consolidated financial statements of Onconova Therapeutics, Inc. appearing in Onconova Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2015 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.

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**5,200,000 Shares**

**ONCONOVA THERAPEUTICS, INC.**

**Common Stock**

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**PROSPECTUS**

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**, 2016**

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**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 13. Other Expenses of Issuance and Distribution**

The following table sets forth the estimated costs and expenses payable by the registrant in connection with the sale of the securities being registered. All amounts are estimates.

|                              |    |           |
|------------------------------|----|-----------|
| SEC registration fee         | \$ | 780.23    |
| Legal fees and expenses      |    | 50,000.00 |
| Accounting fees and expenses |    | 25,000.00 |
| Miscellaneous expenses       |    | 9,219.77  |
| Total                        | \$ | 85,000.00 |

**Item 14. Indemnification of Directors and Officers**

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

A Delaware corporation may indemnify any persons who are, or are threatened to be made, a party to any threatened, pending or completed action or suit by or in the right of the corporation by reason of the fact that such person was a director, officer, employee or agent of such corporation, or is or was serving at the request of such corporation as a director, officer, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation's best interests except that no indemnification is permitted without judicial approval if the officer or director is adjudged to be liable to the corporation. Where an officer or director is successful on the merits or otherwise in the defense of any action referred to above, the corporation must indemnify him or her against the expenses which such officer or director has actually and reasonably incurred. Our certificate of incorporation and bylaws provide for the indemnification of our directors and officers to the fullest extent permitted under the Delaware General Corporation Law.

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



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

Our certificate of incorporation includes such a provision. Expenses incurred by any officer or director in defending any such action, suit or proceeding in advance of its final disposition shall be paid by us upon delivery to us of an

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undertaking, by or on behalf of such director or officer, to repay all amounts so advanced if it shall ultimately be determined that such director or officer is not entitled to be indemnified by us.

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

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

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

**Item 15. Recent Sales of Unregistered Securities**

On October 8, 2015, the Company entered into the Purchase Agreement with Lincoln Park, pursuant to which the Company has the right to sell to, and Lincoln Park is obligated to purchase from the Company, up to \$16.5 million in shares of the Company's common stock, subject to certain limitations, from time to time, over the 36-month period commencing on the date that this registration statement is declared effective by the SEC and a final prospectus in connection therewith is filed. On October 8, 2015, Lincoln Park purchased 846,755 shares of the Company's common stock for a total purchase price of \$1,500,000 as an initial purchase under the Purchase Agreement and the Company issued 200,000 shares of common stock pursuant to the terms of the Purchase Agreement as consideration for its commitment to purchase additional shares of common stock under the Purchase Agreement. The sale of such shares to Lincoln Park was not registered under the Securities Act because it was made in a transaction exempt from registration under Section 4(a)(2) of the Securities Act and/or Rule 506 promulgated thereunder.

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

**Item 16. Exhibits and Financial Statement Schedules**

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(a) Exhibits

| <b>Exhibit Number</b> | <b>Exhibit Description</b>                                                                                                                                                                                   |
|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 3.1                   | Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc. <i>(Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 25, 2013).</i> |
| 3.2                   | Amended and Restated Bylaws of Onconova Therapeutics, Inc. <i>(Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 25, 2013).</i>                             |

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| <b>Exhibit Number</b> | <b>Exhibit Description</b>                                                                                                                                                                                                                                                                                                           |
|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 4.1                   | Form of Certificate of Common Stock ( <i>Incorporated by reference to Exhibit 4.1 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013.</i> )                                                                                                                                    |
| 4.2                   | Eighth Amended and Restated Stockholders' Agreement, effective as of July 27, 2012, by and among Onconova Therapeutics, Inc. and certain stockholders named therein ( <i>Incorporated by reference to Exhibit 4.2 to Pre-Effective Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on July 11, 2013.</i> ) |
| 4.3                   | Amendment No. 1 to Eighth Amended and Restated Stockholders' Agreement, effective as of July 9, 2013 ( <i>Incorporated by reference to Exhibit 4.2 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013.</i> )                                                                   |
| 4.4                   | Form of Warrant ( <i>Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on January 6, 2016.</i> )                                                                                                                                                                                            |
| 5.1                   | Opinion of Pepper Hamilton LLP                                                                                                                                                                                                                                                                                                       |
| 10.1                  | * Development and License Agreement, effective as of September 19, 2012, by and between Onconova Therapeutics, Inc. and Baxter Healthcare SA ( <i>Incorporated by reference to Exhibit 10.1 to Pre-Effective Amendment No. 2 the Company's Registration Statement on Form S-1 filed on July 18, 2013.</i> )                          |
| 10.2                  | * License Agreement, effective as of July 5, 2011, by and between Onconova Therapeutics, Inc. and Symbio Pharmaceuticals Limited ( <i>Incorporated by reference to Exhibit 10.2 to Pre-Effective Amendment No. 2 the Company's Registration Statement on Form S-1 filed on July 18, 2013.</i> )                                      |
| 10.3                  | * First Amendment to License Agreement, effective as of September 2, 2011, by and between Onconova Therapeutics, Inc. and Symbio Pharmaceuticals Limited ( <i>Incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 filed on June 14, 2013.</i> )                                            |
| 10.4                  | * License Agreement, effective as of January 1, 1999, by and between Onconova Therapeutics, Inc. and Temple University Of The Commonwealth System of Higher Education ( <i>Incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 filed on June 14, 2013.</i> )                               |
| 10.5                  | * Amendment to License Agreement, effective as of September 1, 2000, by and between Temple University Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc. ( <i>Incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 filed on June 14, 2013.</i> )                |
| 10.6                  | * Amendments to Exclusive License Agreement, effective as of March 21, 2013, by and between Temple University Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc. ( <i>Incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 filed on June 14, 2013.</i> )        |
| 10.7                  | * Definitive Agreement, effective as of May 12, 2010, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 filed on June 14, 2013.</i> )                                                              |
| 10.8                  | * First Amendment to Definitive Agreement, effective as of June 23, 2011, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 filed on June 14, 2013.</i> )                                          |
| 10.9                  | * Second Amendment to Definitive Agreement, effective as of May 29, 2012, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1 filed on June 14, 2013.</i> )                                          |



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| <b>Exhibit Number</b> | <b>Exhibit Description</b>                                                                                                                                                                                                                                                                                                           |
|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10.10                 | * Third Amendment to Definitive Agreement, effective as of January 5, 2013, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ).                                       |
| 10.11                 | Termination of Agreement, effective as of February 5, 2013, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ).                                                       |
| 10.12                 | * Limited Liability Company Agreement of GBO, LLC, dated as of December 12, 2012, by and between Onconova Therapeutics, Inc. and GVK Biosciences Private Limited ( <i>Incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ).                                   |
| 10.13                 | + Onconova Therapeutics, Inc. 2007 Equity Compensation Plan, and forms of agreement thereunder ( <i>Incorporated by reference to Exhibit 10.13 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013</i> ).                                                                       |
| 10.14                 | + Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Ramesh Kumar, Ph.D. ( <i>Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 8, 2015</i> ).                                                                                     |
| 10.15                 | + Letter Agreement, effective as of January 1, 2016, by and between Onconova Therapeutics, Inc. and Ramesh Kumar, Ph.D. ( <i>Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on February 17, 2016</i> ).                                                                                 |
| 10.16                 | + Amended and Restated Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Thomas McKearn, M.D., Ph.D. ( <i>Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on July 8, 2015</i> ).                                                        |
| 10.17                 | + Amended and Restated Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Ajay Bansal. ( <i>Incorporated by reference to Exhibit 10.4 to the Company's Current Report on Form 8-K filed on July 8, 2015</i> ).                                                                       |
| 10.18                 | + Consulting Agreement, effective as of January 1, 2012, by and between Onconova Therapeutics, Inc. and E. Premkumar Reddy, Ph.D., including Consultant Agreement Renewal, dated February 27, 2013 ( <i>Incorporated by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ). |
| 10.19                 | + Form of Indemnification Agreement entered into by and between Onconova Therapeutics, Inc. and each director and executive officer ( <i>Incorporated by reference to Exhibit 10.24 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013</i> ).                                  |
| 10.20                 | + Onconova Therapeutics, Inc. 2013 Equity Compensation Plan, and forms of agreement thereunder ( <i>Incorporated by reference to Exhibit 10.25 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013</i> ).                                                                       |
| 10.21                 | + Onconova Therapeutics, Inc. 2013 Performance Bonus Plan ( <i>Incorporated by reference to Exhibit 10.26 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013</i> ).                                                                                                            |
| 10.22                 | + Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Dr. Manoj Manair ( <i>Incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed on July 8, 2015</i> ).                                                                                        |

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| Exhibit<br>Number | Exhibit Description                                                                                                                                                                                                                                     |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10.23             | + Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Mark Guerin<br><i>(Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on February 17, 2016).</i>          |
| 10.24             | + Amended and Restated Employment Agreement between Onconova Therapeutics, Inc. and Steven Fruchtman, M.D.<br><i>(Incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed on August 13, 2015).</i>               |
| 10.25             | Purchase Agreement between Onconova Therapeutics, Inc. and Lincoln Park Capital Fund, LLC, dated October 8, 2015<br><i>(Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 8, 2015).</i>            |
| 10.26             | Registration Rights Agreement between Onconova Therapeutics, Inc. and Lincoln Park Capital Fund, LLC, dated October 8, 2015<br><i>(Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on October 8, 2015).</i> |
| 10.27             | Form of Securities Purchase Agreement between Onconova Therapeutics and the Investor party thereto, dated January 5, 2016<br><i>(Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 6, 2016).</i>   |
| 21.1              | Subsidiaries of Onconova Therapeutics, Inc. <i>(Incorporated by reference to Exhibit 21.1 to the Company's Annual Report on Form 10-K filed on March 28, 2016).</i>                                                                                     |
| 23.1              | Consent of Ernst & Young, LLP.                                                                                                                                                                                                                          |
| 23.2              | Consent of Pepper Hamilton LLP (included in Exhibit 5.1)                                                                                                                                                                                                |
| 24.1              | Power of Attorney (included on signature page) ◇                                                                                                                                                                                                        |

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+ Indicates management contract or compensatory plan.

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

◇ Previously filed.

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**Item 17. Undertakings**

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933 (the Act );

(ii) To reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and

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

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

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

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



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

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

(h) Insofar as indemnification for liabilities arising under the Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against

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such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

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**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, Onconova Therapeutics, Inc. has duly caused this Post-Effective Amendment to be signed on its behalf by the undersigned, thereunto duly authorized, in the Township of Newtown, Commonwealth of Pennsylvania, on the 25th day of April, 2016.

ONCONOVA THERAPEUTICS, INC.

By: /s/ Ramesh Kumar, Ph.D.  
Ramesh Kumar, Ph.D.  
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this Post-Effective Amendment has been signed by the following persons in the capacities and on the dates indicated

| <b>Signature</b>                               | <b>Title</b>                                                                                                           | <b>Date</b>    |
|------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|----------------|
| /s/ Ramesh Kumar, Ph.D.<br>Ramesh Kumar, Ph.D. | Director, President and Chief Executive Officer<br>(Principal Executive Officer)                                       | April 25, 2016 |
| /s/ Mark Guerin<br>Mark Guerin                 | Vice President, Financial Planning and<br>Accounting (Principal Financial Officer and Principal<br>Accounting Officer) | April 25, 2016 |
| *<br>Henry S. Bienen, Ph.D.                    | Director                                                                                                               | April 25, 2016 |
| *<br>Jerome E. Groopman, M.D.                  | Director                                                                                                               | April 25, 2016 |
| *<br>Michael B. Hoffman                        | Chairman, Board of Directors                                                                                           | April 25, 2016 |
| *<br>James J. Marino                           | Director                                                                                                               | April 25, 2016 |
| *<br>Viren Mehta, Pharm.D                      | Director                                                                                                               | April 25, 2016 |
| *<br>E. Premkumar Reddy, Ph.D                  | Director                                                                                                               | April 25, 2016 |
| *<br>Anne M. VanLent                           | Director                                                                                                               | April 25, 2016 |

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\*The undersigned by signing his name hereto signs and executes this Amendment No. 2 to Registration Statement on Form S-1 pursuant to the Powers of Attorney executed by the above named signatories and previously filed with the Securities and Exchange Commission on February 3, 2015.

\* By: /s/ Ramesh Kumar, Ph.D  
Ramesh Kumar, Ph.D, Attorney-in-Fact

April 25, 2016

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**EXHIBIT INDEX**

| <b>Exhibit Number</b> | <b>Exhibit Description</b>                                                                                                                                                                                                                                                                                                         |
|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 3.1                   | Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc. <i>(Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 25, 2013).</i>                                                                                                                       |
| 3.2                   | Amended and Restated Bylaws of Onconova Therapeutics, Inc. <i>(Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 25, 2013).</i>                                                                                                                                                   |
| 4.1                   | Form of Certificate of Common Stock <i>(Incorporated by reference to Exhibit 4.1 to Pre-Effective Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on July 11, 2013.)</i>                                                                                                                                 |
| 4.2                   | Eighth Amended and Restated Stockholders' Agreement, effective as of July 27, 2012, by and among Onconova Therapeutics, Inc. and certain stockholders named therein <i>(Incorporated by reference to Exhibit 4.2 to Pre-Effective Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on July 11, 2013).</i> |
| 4.3                   | Amendment No. 1 to Eighth Amended and Restated Stockholders' Agreement, effective as of July 9, 2013 <i>(Incorporated by reference to Exhibit 4.2 to Pre-Effective Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on July 11, 2013).</i>                                                                |
| 4.4                   | Form of Warrant <i>(Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on January 6, 2016).</i>                                                                                                                                                                                            |
| 5.1                   | Opinion of Pepper Hamilton LLP                                                                                                                                                                                                                                                                                                     |
| 10.1                  | * Development and License Agreement, effective as of September 19, 2012, by and between Onconova Therapeutics, Inc. and Baxter Healthcare SA <i>(Incorporated by reference to Exhibit 10.1 to Pre-Effective Amendment No. 2 to the Company's Registration Statement on Form S-1 filed on July 18, 2013).</i>                       |
| 10.2                  | * License Agreement, effective as of July 5, 2011, by and between Onconova Therapeutics, Inc. and Symbio Pharmaceuticals Limited <i>(Incorporated by reference to Exhibit 10.2 to Pre-Effective Amendment No. 2 to the Company's Registration Statement on Form S-1 filed on July 18, 2013).</i>                                   |
| 10.3                  | * First Amendment to License Agreement, effective as of September 2, 2011, by and between Onconova Therapeutics, Inc. and Symbio Pharmaceuticals Limited <i>(Incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 filed on June 14, 2013).</i>                                            |
| 10.4                  | * License Agreement, effective as of January 1, 1999, by and between Onconova Therapeutics, Inc. and Temple University Of The Commonwealth System of Higher Education <i>(Incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 filed on June 14, 2013).</i>                               |
| 10.5                  | * Amendment to License Agreement, effective as of September 1, 2000, by and between Temple University Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc. <i>(Incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 filed on June 14, 2013).</i>                |
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| Exhibit Number | Exhibit Description                                                                                                                                                                                                                                                                                                                  |
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| 10.7           | * Definitive Agreement, effective as of May 12, 2010, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ).                                                              |
| 10.8           | * First Amendment to Definitive Agreement, effective as of June 23, 2011, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ).                                          |
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| 10.10          | * Third Amendment to Definitive Agreement, effective as of January 5, 2013, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ).                                       |
| 10.11          | Termination of Agreement, effective as of February 5, 2013, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society ( <i>Incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ).                                                       |
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| 10.18          | + Consulting Agreement, effective as of January 1, 2012, by and between Onconova Therapeutics, Inc. and E. Premkumar Reddy, Ph.D., including Consultant Agreement Renewal, dated February 27, 2013 ( <i>Incorporated by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 filed on June 14, 2013</i> ). |
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| 10.20          | + Onconova Therapeutics, Inc. 2013 Equity Compensation Plan, and forms of agreement thereunder                                                                                                                                                                                                                                       |





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| 21.1              | Subsidiaries of Onconova Therapeutics, Inc. <i>(Incorporated by reference to Exhibit 21.1 to the Company's Annual Report on Form 10-K filed on March 28, 2016).</i>                                                                                  |
| 23.1              | Consent of Ernst & Young, LLP.                                                                                                                                                                                                                       |
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| 24.1              | Power of Attorney (included on signature page) ◊                                                                                                                                                                                                     |

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+ Indicates management contract or compensatory plan.

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

◊ Previously filed.