Onconova Therapeutics, Inc.
Form S-1/A
April 25, 2018
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As filed with the Securities and Exchange Commission on April 25, 2018

Registration No. 333-224315

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 2

To

FORM S-l

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Onconova Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**22-3627252**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

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

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

Ramesh Kumar, Ph.D.
President and Chief Executive Officer
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375 Pheasant Run
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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 the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. o

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

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

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

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

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

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

Large accelerated filer	o	Accelerated filer	o
Non-accelerated filer	o (Do not check if a smaller reporting company)	Smaller reporting company	x
		Emerging growth company	x

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities To Be Registered	**Proposed Maximum Aggregate Offering Price(1)(2)**	**Amount of Registration Fee(2)**
Units, each Unit consisting of one share of common stock, par value $0.01 per share (Common Stock), and one warrant (Warrant) to purchase [0.025] share of Series B Convertible Preferred Stock, par value $0.01 per share (Series B Preferred Stock)(3)	$ 17,250,000	$ 2,147.63
(i) Common Stock included in the Units(4)	Included with the Units above	
(ii) Warrants included in the Units(4)	Included with the Units above	
Pre-Funded Units in lieu of Units, each Pre-Funded Unit consisting of one pre-funded warrant (Pre-Funded Warrant) to purchase one share of Common Stock and one Warrant to purchase [0.025] share of Series B Preferred Stock(3)	Included with the Units above	
(i) Pre-Funded Warrants included in the Pre-Funded Units(4)	Included with the Units above	
(ii) Warrants included in the Pre-Funded Units(4)	Included with the Units above	
Shares of Series B Preferred Stock underlying Warrants included in the Units and Pre-Funded Units	$ 17,250,000	$ 2,147.63
Shares of Common Stock underlying Pre-Funded Warrants included in the Pre-Funded Units(3)	Included with the Units above	
Total	$ 34,500,000	$ 4,295.25(5)

(1) Estimated solely for purposes of computing the amount of the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended (the Securities Act). Includes securities subject to the underwriter s option to purchase additional securities.

(2) Pursuant to Rule 416 under the Securities Act, the shares of Common Stock registered hereby also include an indeterminate number of additional shares of Common Stock as may, from time to time, become issuable by reason of stock splits, stock dividends, recapitalizations or other similar transactions.

(3) The proposed maximum aggregate offering price of the Units and Pre-Funded Units (including the Common Stock issuable upon exercise of the Pre-Funded Warrants included in the Pre-Funded Units), if any, is $17,250,000 and includes the offering price of any additional shares of Common Stock and Warrants that the underwriter has an option to purchase.

(4) No additional registration fee is payable pursuant to Rule 457(i) under the Securities Act.

(5) The registrant previously paid $4,429.49 in connection with the initial filing of the Registration Statement and the filing of Amendment No. 1.

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

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

Subject to completion, dated April 25, 2018

PRELIMINARY PROSPECTUS

Onconova Therapeutics, Inc.

Up to 26,785,714 Units (each Unit contains one Share of Common Stock and one Warrant to purchase 0.025 share of Series B Convertible Preferred Stock

Up to 26,785,714 Pre-Funded Units (each Pre-Funded Unit contains one Pre-Funded Warrant to purchase one Share of Common Stock and one Warrant to purchase 0.025 share of Series B Convertible Preferred Stock)

(Up to 669,643 Shares of Series B Convertible Preferred Stock Underlying the Warrants) and

(Up to 26,785,714 Shares of Common Stock Underlying the Pre-Funded Warrants)

We are offering up to 26,785,714 Units (Units, each Unit consisting of one share of Common Stock, par value $0.01 per share (Common Stock) and one warrant (the Warrant) to purchase 0.025 share of our Series B Convertible Preferred Stock, par value $0.01 per share (Series B Preferred Stock)). Each Warrant contained in a Unit has an exercise price of $ per share of Common Stock. The Warrants contained in the Units will be exercisable immediately and will expire on the 18-month anniversary of the date (the Charter Amendment Date) on which we publicly announce through the filing of a Current Report on Form 8-K that the amendment to our certificate of incorporation to sufficiently increase our authorized shares of Common Stock to cover the conversion of all outstanding shares of Series B Preferred Stock into Common Stock has been filed with the Secretary of State of the State of Delaware.

We are also offering the shares of Series B Preferred Stock that are issuable from time to time upon exercise of the Warrants contained in the Units. We do not currently have a sufficient number of authorized shares of Common Stock to cover the shares issuable upon the conversion of Series B Preferred Stock. As a result, before any shares of Series B Preferred Stock can become convertible, we need to receive stockholder approval of an amendment (the Charter Amendment) to our Tenth Amended and Restated Certificate of Incorporation, as amended, to sufficiently increase our authorized shares of Common Stock to cover the conversion of all outstanding shares of Series B Preferred Stock into Common Stock. We have agreed in the underwriting agreement for this offering to use our reasonable efforts to obtain such approval within 45 days from the date of this prospectus, and we intend to seek such approval at a special meeting of stockholders or at our 2018 annual meeting of stockholders. We cannot assure you that we will be able to obtain requisite stockholder approval of the Charter Amendment. The Series B Preferred Stock is not convertible until the next business day after the Charter Amendment Date starting at which time each 0.025 share of the Series B Preferred Stock will be convertible into one share of Common Stock. In the event our stockholders do not approve the Charter Amendment, the Series B Preferred Stock will not be convertible into Common Stock and the value of the Warrants and the Series B Preferred Stock may be negatively affected.

We are also offering to each purchaser whose purchase of Units in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding Common Stock immediately following the consummation of this offering, the opportunity to purchase, if the purchaser so chooses, pre-funded units (Pre-Funded Units, each Pre-Funded Unit consisting of one Pre-Funded Warrant (Pre-Funded Warrant) to purchase one share of Common Stock and one Warrant to purchase 0.025 share of Series B Preferred Stock) in lieu of Units that would otherwise result in the purchaser s beneficial ownership exceeding 4.99% of our outstanding Common Stock (or at the election of the purchaser, 9.99%). Each Pre-Funded Warrant contained in a Pre-Funded Unit will be exercisable into one share of Common Stock. The purchase price of each Pre-Funded Unit will equal the price per Unit being sold to the public in this offering minus $0.01, and the exercise price of each Pre-Funded Warrant included in the Pre-Funded Unit will be $0.01 per share of Common Stock. This offering also relates to the shares of Common Stock issuable upon exercise of any Pre-Funded Warrants contained in the Pre-Funded Units sold in this offering. Each Warrant contained in a Pre-Funded Unit has an exercise price of $ per 0.025 share of Series B Preferred Stock. The Warrants contained in the Pre-Funded Units will be exercisable immediately and will expire on the 18-month anniversary of the Charter Amendment Date. We are also offering the shares of Series B Preferred Stock that are issuable from time to time upon exercise of the Warrants contained in the Pre-Funded Units.

Our Common Stock is listed on the Nasdaq Capital Market under the symbol ONTX. On April 20, 2018, the last reported sale price of Common Stock on the Nasdaq Capital Market was $0.56 per share. The actual offering price per Unit and Pre-Funded Unit, and the exercise price of the Warrants, as applicable, will be determined by negotiation between us and the underwriter at the time of pricing, and may be at a discount to the current market price. We do not intend to apply for listing of the Pre-Funded Warrants, the Warrants or Series B Preferred Stock on any securities exchange or other nationally recognized trading system. There is no established public trading market for the Pre-Funded Warrants, the Warrants or Series B Preferred Stock, and we do not expect a market to develop.

For each Pre-Funded Unit we sell, the number of Units we are offering will be decreased on a one-for-one basis. Units and the Pre-Funded Units will not be issued or certificated. The shares of Common Stock or Pre-Funded Warrants, as the case may be, and the Warrants can only be purchased together in this offering but the securities contained in the Units or Pre-Funded Units will be issued separately.

One or more of our directors have indicated interests in purchasing approximately 10% of the Units to be sold in this offering at the public offering price and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriter could determine to sell more, fewer or no Units to our director(s) in this offering, or our director(s) could determine to purchase more, fewer or no Units in this offering.

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

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

	Per Unit	Per Pre-Funded Unit	Total
Public offering price	$	$	$
Underwriting discounts and commissions (1)	$	$	$
Proceeds, before expenses, to us (2)	$	$	$

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

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

We have granted the underwriter the option to purchase up to 4,017,857 additional shares of Common Stock at a purchase price of $ per share and/or Warrants to purchase up to an aggregate of 100,446 shares of Series B Preferred Stock at a purchase price of $0.01 per Warrant with an exercise price of $ per 0.025 share of Series B Preferred Stock, less the underwriting discounts and commissions. The underwriter may exercise its option at any time and from time to time within 30 days from the date of this prospectus. If the underwriter exercises the option in full, the total underwriting discounts and commissions payable by us will be $, and the total proceeds to us, before expenses, will be $.

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

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

Sole Book-Running Manager

H.C. Wainwright & Co.

The date of this prospectus is , 2018.

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ABOUT THIS PROSPECTUS

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

You should rely only on the information contained in this prospectus and any applicable prospectus supplement, including the information incorporated by reference. Neither we nor the underwriter have authorized anyone to provide you with different information. We are not offering to sell or soliciting offers to buy, and will not sell, any securities in any jurisdiction where it is unlawful. You should assume that the information contained in this prospectus or any prospectus supplement, as well as information contained in a document that we have previously filed or in the future will file with the SEC is accurate only as of the date of this prospectus, the applicable prospectus supplement or the document containing that information, as the case may be.

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PROSPECTUS SUMMARY

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

Our Business

Overview

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

In December 2015, we enrolled the first patient into our INSPIRE trial, a randomized controlled Phase 3 clinical trial of intravenous rigosertib (rigosertib IV) in a population of patients with higher-risk MDS after failure of hypomethylating agent (HMA) therapy. The primary endpoint of INSPIRE is overall survival. An interim analysis of the trial was performed in January 2018 and we anticipate reporting topline data from the INSPIRE trial in the first half of 2019.

Our net losses were $24.1 million and $19.7 million for the years ended December 31, 2017 and 2016, respectively. As of December 31, 2017, we had an accumulated deficit of $362.3 million.

Rigosertib

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

Pharma International SA (Pint), which grants Pint certain rights to commercialize rigosertib in Latin America. We have retained development and commercialization rights to rigosertib in the rest of the world, including in the United States and Europe, although we could consider licensing commercialization rights to other territories as we continue to seek additional funding. Previously we were a party to a license and development agreement with Baxalta (as defined below), which granted Baxalta certain rights to commercialize rigosertib in Europe. The Baxalta agreement was terminated on August 30, 2016, at which time the European rights reverted to us at no cost.

The table below summarizes our rigosertib clinical stage programs.

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Rigosertib IV for higher-risk MDS

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

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

Enrollment for the INSPIRE Phase 3 trial for second-line higher-risk MDS patients is highly selective with stringent entry criteria as outlined above. Currently, the INSPIRE study has opened approximately 175 trial sites in 22 countries across four continents, and has enrolled more than 170 patients. Our partner, SymBio Pharmaceuticals, has opened more than 30 sites in Japan. The selection of countries and trial sites is carefully undertaken to ensure availability of appropriate patients meeting eligibility criteria. Since these criteria are purposely designed to be narrow and

selective, extensive site screening and education is integral to our plan. At launch, the INSPIRE trial was expected to enroll 225 patients and the outcome is measured by overall survival.

The INSPIRE trial included a pre-planned interim analysis triggered by 88 events (deaths), which occurred in December 2017. The statistical analysis plan (SAP) for the INSPIRE trial featured an adaptive trial design,

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permitting several options following the interim analysis, which included continuation of the trial as planned, discontinuation of the trial for futility or safety, trial expansion using pre-planned sample size re-estimation, and trial continuation for only the pre-defined treatment subgroup of patients classified as Very High Risk (VHR) based on the IPSS-R.

After review of the interim data, in January 2018 the Independent Data Monitoring Committee (DMC) recommended continuation of the trial with a one-time expansion in enrollment, using a pre-planned sample size re-estimation, consistent with the SAP. As recommended by the DMC, the expanded INSPIRE study will continue to enroll eligible patients based on the current trial criteria of the overall ITT population and will increase enrollment by adding 135 patients to the original target to reach a total enrollment of 360 patients, with the aim of increasing the power of the trial. Due to the adaptive trial design and the DMC s assessment, the INSPIRE trial will continue to analyze both the ITT and the VHR population for the primary endpoint of overall survival. The design of the trial with the expanded study enrollment will be identical to the current study design and will include the sequential analysis of the overall survival endpoint in the ITT population and if required the pre-specified VHR subgroup. The Company remains blinded to the specific interim analysis results. We anticipate reporting topline data from the INSPIRE trial in the first half of 2019.

Safety and Tolerability of rigosertib in MDS and other hematologic malignancies

A comprehensive analysis of IV and rigosertib oral safety in patients with Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML) was presented in December 2016 at the American Society of Hematology (ASH) Annual Meeting. The most commonly reported treatment-emergent adverse events (TEAEs) in ≥ 10% of patients with MDS/AML (n= 335) receiving rigosertib intravenous (IV) monotherapy were fatigue (33%), nausea (33%), diarrhea (27%), constipation (25%), anaemia (24%) and pyrexia (24%). The most common ≥ Grade 3 AEs were anaemia (21%), febrile neutropenia (13%), pneumonia (12%) and thrombocytopenia (11%). The most common serious AEs were febrile neutropenia (10%), pneumonia (9%), and sepsis (7%). The most common AEs leading to discontinuation of IV rigosertib were sepsis and pneumonia (3% each).

Rigosertib oral in combination with azacitidine for higher-risk MDS

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

Response per IWG 2006

	Overall Evaluable (N=33)	**No prior HMA (N-20)**	**Prior HMA (N=13)**
Complete remission (CR)	8(24)%	7(35)%	1(8)%

Marrow CR + hematologic improvement	10(30)%	6(30)%	4(31)%
Marrow CR alone	6(18)%	3(15)%	3(23)%
Hematologic improvement alone	1(3)%	1(5)%	0
Stable disease	8(24)%	3(15)%	5(38)%
Overall IWG response	25(76)%	17(85)%	8(62)%
Clinical benefit response	19(58)%	14(70)%	5(38)%

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

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Safety/Tolerability of the Combination:

Based upon a comprehensive analysis of patients receiving oral rigosertib in combination with azacitidine that was presented in 2016, the combination of rigosertib oral and azacitidine was well tolerated. The most common TEAEs in ≥ 10% of patients with MDS/AML (n=54) receiving rigosertib oral and azacitidine were nausea (41%), fatigue (39%), diarrhea (37%), constipation (37%) and dysuria (28%). The most common serious AEs were pneumonia (11%) and febrile neutropenia (7%). The most common AEs leading to discontinuation were AML (4%) and pneumonia (4%).

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

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

While the Phase 3 trial is being designed, we have expanded the Phase 1/2 trial cohort by enrolling 45 additional patients. Under a protocol expansion, we are using the expanded cohorts to explore dose optimization by increasing the dose of rigosertib oral to a total of 1120 mg in combination with full dose azacitidine and varying the dose administration scheme of rigosertib oral (560 mg 9 AM/560 mg 9 PM and 840 mg 9 AM/280 mg 9 PM) to identify an optimal dose and schedule. During this expansion, we also instituted risk-mitigation strategies, as further described below, in order to address a prior urinary adverse event of interest, hematuria. After amendments were filed with the regulatory agencies, we started the expansion phase of this trial in the U.S. sites that participated in the initial trial. Since the trial initiation, we have added additional US sites to complete enrollment of the expanded trial. The first patient was enrolled in April 2017 and as of April 2017 half of all of the planned patients have been enrolled in the expansion trial; and the trial is ongoing.

In March 2018, at the 6th International Bone Marrow Failure Disease Symposium, we presented data on the incidence of hematuria in 37 higher-risk MDS patients receiving rigosertib oral in combination with azacitidine as part of the Phase 1/2 expanded cohort . In the first part of the Phase 1/2 study, prior to the study expansion, of 42 patients studied with oral rigosertib 840 mg total and azacitidine, the incidence of hematuria was 48%. In 37 patients studied with oral rigosertib 1120 mg total and azacitidine in the Phase 1/2 expanded cohort, with the use of risk-mitigating strategies to minimize hematuria, the incidence of hematuria was 11%. The study is ongoing. The risk-mitigating strategies employed are as follows:

Risk-Mitigation Strategies to Minimize Hematuria:

The comparison of the hematuria results from the two parts of this study are presented below:

Hematuria Comparison Between Rigosertib Combination Therapy Parts 1 and 2:

All Patients on Combination Part 1 (Rigosertib 840 mg total & Azacitidine)	42
Patients with hematuria	20 (48%)
Patients with grade 1 or 2 hematuria	17 (40%)
Patients with grade ≥3 hematuria	5 (12%)
All Patients on Combination Part 2 (Rigosertib 1120 mg total) & Azacitidine) with risk-mitigation strategies	37
Patients with hematuria	4 (11%)
Patients with grade 1 or 2 hematuria	4 (11%)
Patients with grade ≥3 hematuria	0 (0%)

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

Upon completion of our Phase 1/2 study, we will submit the study results to the applicable regulatory authorities. The final results of this study may differ from the results presented above and the applicable regulatory authorities may not agree with our analyses. We will not commence the Phase 3 trial of oral rigosertib in combination with azacitidine for higher-risk MDS or AML without additional financing.

Rigosertib oral for lower-risk MDS

We are also developing rigosertib oral as a single agent treatment for lower risk MDS. Higher-risk MDS patients suffer from a shortfall in normal circulating blood cells, or cytopenias, as well as elevated levels of cancer cells, or blasts in their bone marrow and sometimes in their peripheral blood with a significant rate of transformation to acute leukemia. 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; but have a lower rate of acute leukemic transformation.

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 2017, we presented data at the Annual ASH Meeting from the 09-05 Phase 2 trial. This data demonstrated a 44% rate of achieving transfusion independence in the cohort of Lower -risk MDS patients treated with rigosertib oral at a dose of 560 mg BID (1120 mg over 24 hrs). To date, Phase 2 clinical data has indicated that further study of single agent rigosertib oral in transfusion-dependent, lower-risk MDS patients is warranted. Rigosertib has been generally well tolerated, except for urinary side effects at higher dose levels. Future clinical trials

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

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

As presented at the December 2016 ASH Annual Meeting, rigosertib oral as a monotherapy was evaluated in four Phase 1 and 2 studies in MDS and other hematologic malignancies. One study is completed and a clinical study report is available. The most common TEAEs in ≥ 10% of patients with MDS/AML (n=168) were pollakiuria (increased urinary frequency) (35%), fatigue (32%), diarrhea (26%), dysuria (29%) and haematuria (24%). The most common ≥ Grade 3 AEs were anaemia (17%), thrombocytopenia (5%), haematuria (4%) and urinary tract infection (4%). The most common serious AE was pneumonia (6%). The most common AEs leading to discontinuation of patients receiving rigosertib oral as monotherapy were dysuria (8%), urinary tract pain (7%), haematuria (5%) and urinary frequency (5%).

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

Rare Disease Program in RASopathies

Based on new mechanism of action data published last year, we are initiating a collaborative development program focusing on a group of rare diseases with a well-defined molecular basis in expression or defects involving the Ras Effector Pathways. Since RASopathies are rare diseases affecting young children, we are embarking on a multifaceted collaborative program involving patient advocacy, government and academic organizations. The RASopathies are a group of rare diseases which share a well-defined molecular basis in expression or defects involving Ras Effector Pathways. They are usually caused by germline mutations in genes that alter the RAS subfamily and mitogen-activated protein kinases that control signal transduction, and are among the most common genetic syndromes. Together, this group of diseases can impact more than 1 in 1000 individuals, according to RASopathiesNet.

In January 2018, we entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI), part of the National Institutes of Health (NIH). Under the terms of the CRADA, the NCI will conduct research, including preclinical laboratory studies and a clinical trial, on rigosertib in pediatric cancer associated RASopathies.

As part of the CRADA, we will provide rigosertib supplies and initial funding towards non-clinical studies. The NCI will fund the majority of the research, including the cost of the clinical trial, which is expected to start in 2018. A clinical trial protocol has been developed and will be

reviewed by the Institutional Review Board.

While the NCI will conduct a trial for RASopathy related cancers in pediatric patients, Onconova will focus on initiating a trial as well in Juvenile Myelomonocytic Leukemia (JMML), a well-described RASopathy affecting children which is incurable without an allogenic hematopoietic stem cell transplant.

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Other Programs

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

Briciclib

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

Recilisib

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

Preclinical Product Candidates

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

Positive preclinical data was announced at the American Association for Cancer Research (AACR) annual meeting, which took place April 1-5, 2017 in Washington, DC, for ON 123300, a first-in-class dual inhibitor of CDK4/6 + ARK5, and for ON 150030, a novel Type 1 inhibitor of FLT3 and Src pathways. We believe our CDK inhibitor is differentiated from other agents in the market (Palbociclib, Ribociclib and Abemaciclig) or in development (such as the compounds being developed by G1 Therapeutics) by its dual inhibition of CDK4/6 + ARK5. We are party to a license and collaboration agreement with HanX Biopharmaceuticals, Inc. (HanX), which grants HanX certain rights to commercialize ON 123300 in China. We continue to carry out research to enhance the pre-clinical data package for this compound in an attempt to seek additional partners outside of China for co-development of this novel compound.

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

In December 2017, we entered into a license and collaboration agreement with HanX Biopharmaceuticals, Inc. (HanX), a company focused on development of novel oncology products, for the further development, registration and commercialization of ON 123300 in Greater China. Under the terms of the agreement, we received an upfront payment, and would receive regulatory and commercial milestone payments, as well as royalties on sales in the Greater China territory. The key feature of the collaboration is that HanX will provide all funding required for Chinese IND enabling studies necessary for filing an IND with the Chinese Food and Drug Administration. The studies would be conducted to meet the Good Laboratory Practice (GLP) requirements of FDA such that we could simultaneously file an IND with the US FDA. We and HanX will oversee the IND enabling studies. We will maintain global rights outside of China.

In March 2018, Onconova and HanX completed the pre-Investigational New Drug, or pre-IND, consultation with FDA. These discussions provided guidance for the manufacturing of ON 123300 and the pre-clinical development plan for the submission of an IND application.

In April 2018, at the American Association for Cancer Research 2018 Annual Meeting, we announced an advance in pre-clinical development and the presentation of new pre-clinical data for ON 123300. The data from preclinical studies demonstrates that there is a differential metabolism of ON 123300 in male versus female rodents. As a result, the drug exposure is almost 2-3 fold higher in female rats. Based upon preclinical animal liver microsome studies, this differential effect appears to be limited to rodents, and is not observed in preclinical studies with human liver microsomes. Based on the preclinical liver microsome metabolism data from other species, relevant species have been selected along with the dosing strategy to be implemented in GLP toxicological studies to be conducted by HanX.

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CORPORATE INFORMATION

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

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THE OFFERING

Units offered by us in this offering	Up to 26,785,714 Units, each consisting of one share of Common Stock and one Warrant to purchase 0.025 share of Series B Preferred Stock.
Pre-Funded Units offered by us in this offering	We are also offering to each purchaser whose purchase of Units in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding Common Stock immediately following the consummation of this offering, the opportunity to purchase, if the purchaser so chooses, Pre-Funded Units (each Pre-Funded Unit consisting of one Pre-Funded Warrant to purchase one share of Common Stock and one Warrant to purchase 0.025 share of Series B Preferred Stock) in lieu of Units that would otherwise result in the purchaser s beneficial ownership exceeding 4.99% of our outstanding Common Stock (or at the election of the purchaser, 9.99%). Each Pre-Funded Warrant contained in a Pre-Funded Unit will be exercisable for one share of Common Stock. The purchase price of each Pre-Funded Unit will equal the price per Unit being sold to the public in this offering minus $0.01, and the exercise price of each Pre-Funded Warrant included in the Pre-Funded Unit will be $0.01 per share of Common Stock. This offering also relates to the shares of Common Stock issuable upon exercise of any Pre-Funded Warrants contained in the Pre-Funded Units sold in this offering. For each Pre-Funded Unit we sell, the number of Units we are offering will be decreased on a one-for-one basis. Because we will issue a Warrant as part of each Unit or Pre-Funded Unit, the number of Warrants sold in this offering will not change as a result of a change in the mix of the Units and Pre-Funded Units sold.
Warrants offered by us in this offering	Warrants to purchase an aggregate of up to 669,643 shares of Series B Preferred Stock. Each Unit and each Pre-Funded Unit includes a Warrant to purchase 0.025 share of Series B Preferred Stock. Each Warrant contained in a Unit or Pre-Funded Unit has an exercise price of $ per 0.025 share of Series B Preferred Stock, will be immediately separable from the Common Stock or Pre-Funded Warrant, as the case may be, will be exercisable immediately and will expire on the 18-month anniversary of the Charter Amendment Date.
Series B Preferred Stock	This prospectus also relates to the offering of the shares of Series B Preferred Stock issuable upon the exercise of the Warrants. The Series B Preferred Stock is not convertible until the next business day after the Charter Amendment Date, starting at which time each 0.025 share of the Series B Preferred Stock is convertible into one share of Common Stock. Notwithstanding the foregoing, we shall not effect any conversion of the Series B Preferred Stock, to the extent that, after giving effect to an attempted conversion, the holder of shares of Series B Preferred Stock (together with such holder s affiliates, and any persons acting as a group together with such holder or any of such holder s affiliates) would beneficially own a number of shares of Common Stock in excess of 4.99% of the shares of Common Stock then outstanding after giving effect to such exercise. In the event our stockholders do not approve the Charter Amendment, the Series B Preferred Stock will not be convertible into Common Stock and the value of the Warrants and the Series B Preferred Stock may be negatively affected. For additional information, see the subsection entitled Description of Securities We Are Offering Series B Convertible Preferred Stock in this prospectus.
Insider Participation	One or more of our directors have indicated interests in purchasing approximately 10% of the Units to be sold in this offering at the public offering price and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriter could determine to sell more, fewer or no Units to our director(s) in this offering, or our director(s) could determine to purchase more, fewer or no Units in this offering.
Offering Price	

	$ per Unit $ per Pre-Funded Unit
Option to purchase additional securities	The underwriter has the option to purchase up to 4,017,857 additional shares of Common Stock at a purchase price of $ per share and/or Warrants to purchase up to an aggregate of 100,446 shares of Series B Preferred Stock at a purchase price of $0.01 per Warrant with an exercise price of $ per 0.025 share of Series B Preferred Stock, less the underwriting discounts and commissions. The underwriter may exercise its option at any time and from time to time within 30 days from the date of this prospectus.
Common stock to be outstanding after this offering	46,211,877 shares of Common Stock (assuming no sale of any Pre-Funded Units), or 50,229,734 shares of Common Stock if the underwriter exercises its option to purchase additional Units in full (assuming no sale of any

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	Pre-Funded Units).
Use of proceeds	We estimate that the net proceeds to us from this offering will be approximately $13.4 million ($15.4 million if the underwriter s option to purchase additional Units is exercised in full), based on an assumed public offering price per Unit of $0.56, the last reported sale price of Common Stock on the Nasdaq Capital Market on April 20, 2018, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to fund the development of our clinical and preclinical programs, for other research and development activities and for general corporate purposes, which may include capital expenditures and funding working capital needs. See Use of Proceeds on page 16.
Risk factors	You should read the Risk Factors section of this prospectus and in the documents incorporated by reference into this prospectus for a discussion of factors to consider before deciding to invest in our securities.
Listing	Common Stock is listed on the Nasdaq Capital Market under the symbol ONTX. We do not intend to apply for listing of the Pre-Funded Warrants, the Warrants or Series B Preferred Stock on any securities exchange or other nationally recognized trading system. There is no established public trading market for the Pre-Funded Warrants, the Warrants or Series B Preferred Stock, and we do not expect a market to develop.

The number of shares of Common Stock outstanding after the offering is based on 19,426,163 shares outstanding as of March 31, 2018, and excludes as of such date:

- 1,118,849 shares of Common Stock issuable upon the exercise of stock options outstanding at March 31, 2018 with a weighted average exercise price of approximately $25.00 per share;

- 15,232,146 shares of Common Stock issuable upon the exercise of outstanding or issuable warrants at March 31, 2018 with a weighted average exercise price of approximately $1.82 per share (includes Common Stock issuable for warrants which are exercisable for our Series A Convertible Preferred Stock, which is convertible to Common Stock); to the extent the preferred stock warrant repricing described under Underwriting Company Lock-up Waiver Agreement occurs, preferred stock warrants to purchase an aggregate of 994,750 shares of our Series A Convertible Preferred Stock, which are convertible into an aggregate of 9,947,500 shares of Common Stock, will be repriced, and the weighted average exercise price of all outstanding or issuable warrants at March 31, 2018 taking into account such repricing will be approximately $1.55 per share based on an assumed public offering price per Unit of $0.56, the last reported sale price of Common Stock on the Nasdaq Capital Market on April 20, 2018;

- 0 shares of Common Stock issuable upon the conversion of our Series A Convertible Preferred Stock at March 31, 2018 (no shares of Series A Preferred Stock were issued and outstanding and 1,044,488 shares of Series A Preferred Stock were reserved for issuance upon the exercise of outstanding preferred stock warrants as of March 31, 2018);

- 33,779 shares of Common Stock reserved for future issuance under our 2013 Equity Compensation Plan at March 31, 2018; and

- any additional shares of Common Stock that we may issue to Lincoln Park Capital Fund, LLC (Lincoln Park), pursuant to a purchase agreement we entered into on October 8, 2015, which provides that, upon the terms and subject to the conditions and limitation set forth therein, Lincoln Park is committed to purchase up to an aggregate of an additional $15 million of shares of Common Stock over the term of the purchase agreement, should we elect to sell shares to Lincoln Park.

As of April 20, 2018, the total number of our outstanding shares of Common Stock was 20,243,108.

Unless otherwise indicated, all information contained in this prospectus assumes (i) no exercises by the underwriter of its option to purchase additional securities and (ii) no sale of any Pre-Funded Warrants.

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RISK FACTORS

Our business is influenced by many factors that are difficult to predict, and that involve uncertainties that may materially affect actual operating results, cash flows and financial condition. Before making an investment decision, you should carefully consider these risks, including those set forth below and those described in the Risk Factors section of our Annual Report on Form 10-K, as filed with the SEC on March 16, 2018, which is incorporated by reference into this prospectus, as well as any amendment or update to our risk factors reflected in subsequent filings with the SEC, and you should also carefully consider any other information we include or incorporate by reference in this prospectus.

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

Risks Associated with this Offering

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

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

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

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

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

Since the effective price per share of Common Stock included in the Units or issuable upon exercise of the Pre-Funded Warrants being offered is substantially higher than the net tangible book deficit per share of Common Stock outstanding prior to this offering, you will suffer immediate and substantial dilution in the net tangible book value of Common Stock included in the Units or issuable upon the exercise of the Pre-Funded Warrants issued in this offering. See the section titled Dilution below for a more detailed discussion of the dilution you will incur if you purchase Units in this offering. To the extent outstanding stock options or warrants to purchase Common Stock are exercised, or outstanding warrants to purchase shares of our Series A Convertible Preferred Stock are exercised and the resulting shares of Series A Convertible Preferred Stock are converted into shares of Common Stock, there will be further dilution to new investors.

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Our shareholders may experience significant dilution as a result of future equity offerings or issuances.

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

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

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

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

Neither the Warrants nor the Pre-Funded Warrants in this offering confer any rights of Common Stock or Series B Preferred Stock ownership on its holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of Common Stock or Series B Preferred Stock at a fixed price, as the case maybe, and, with respect to the Warrants, during a fixed period of time. Specifically, commencing on the date of issuance, holders of the Warrants may exercise their right to acquire Series B Preferred Stock and pay an exercise price of $ per 0.025 share of Series B Preferred Stock, subject to certain adjustments, prior to the expiration of the Warrants.

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

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

We do not currently have a sufficient number of authorized shares of Common Stock to cover the shares issuable upon conversion of the Series B Preferred stock being offered by this prospectus. As a result, before the Series B Preferred Stock can become convertible, we need to receive stockholder approval of the Charter Amendment (which is an amendment to our Tenth Amended and Restated Certificate of Incorporation, as amended, to sufficiently increase our authorized shares of Common Stock to cover the conversion of all outstanding shares of Series B Preferred

Stock into Common Stock). We have agreed in the underwriting agreement for this offering to use our reasonable efforts to obtain such approval within 45 days from the date of this prospectus, and we intend to seek such approval at a special meeting of stockholders or at our 2018 annual meeting of stockholders. We cannot assure you that we will be able to obtain requisite stockholder approval of the Charter Amendment. In the event our stockholders do not approve the Charter Amendment, the Series B Preferred Stock will not be convertible into Common Stock and the value of the Warrants and the Series B Preferred Stock may be negatively affected.

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

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

Upon completion of this offering, based on our shares outstanding as of March 31, 2018, we will have 46,211,877 shares of Common Stock outstanding based on the issuance and sale of 26,785,714 Units in this offering, assuming no sale of any Pre-Funded Units. Of these shares, only 1,604,207 shares are subject to a contractual lock-up with the underwriter for this offering for a period of 90 days following this offering. These shares can be sold, subject to any applicable volume limitations under federal securities laws, after the earlier of the expiration of, or release from, the 90-day lock-up period. The balance of our outstanding shares of Common Stock, including any shares of Common Stock included in the Units, and shares of Common Stock issuable upon the exercise of the Pre-Funded Warrants or issuable upon the conversion of the Series B Preferred Stock underlying the Warrants purchased in this offering, other than shares acquired by our current stockholders who are also subject to the contractual lock-up, may be resold into the public market immediately without restriction, unless owned or purchased by our affiliates. Moreover, some of the holders of Common Stock have the right, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

As of March 31, 2018, there were approximately 1,118,849 shares subject to outstanding options or that are otherwise issuable under our 2013 Equity Compensation Plan, all of which shares we have registered under the Securities Act of 1933, as amended, or the Securities Act, on a registration statement on Form S-8. These shares can be

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freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described above, to the extent applicable.

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

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

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

We have 100,000,000 authorized shares of Common Stock. As of April 20, 2018, we had 20,243,108 shares of Common Stock outstanding, 1,118,849 shares of Common Stock issuable upon the exercise of outstanding stock options, 15,232,146 shares of Common Stock issuable upon the exercise of outstanding warrants, 33,799 shares of Common Stock reserved for future issuance under our 2013 Equity Compensation Plan and 5,200,000 shares of Common Stock reserved for issuance under our effective registration statement on Form S-1 (Filed No. 333-207533) in connection with our agreement with Lincoln Park. As a result, as of April 20, 2018, we had approximately 58.2 million authorized shares of Common Stock available for issuance. If we issue substantially all of our available authorized shares of Common Stock in this offering which we expect to do, we will not be able to issue additional shares for future capital raising transactions or strategic transactions unless we obtain stockholders approval to amend our certificate of incorporation to increase the number of authorized shares of Common Stock. This may cause a delay in our future capital raising, collaboration, partnership or other strategic transactions, and may have a material adverse effect on our business and financial condition.

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

Neither our certificate of incorporation nor the Certificate of Designation for the Series B Preferred Stock prohibits us from issuing additional series of preferred stock that would rank senior or equally to the Series B Preferred Stock as to dividend payments and liquidation preference. Our certificate of incorporation provides that we have the authority to issue up to 5,000,000 shares of preferred stock, 1,044,488 shares have been designated as Series A Convertible Preferred Stock. The Series B Preferred Stock will rank equally with the Series A Convertible Preferred Stock as to dividend payments and liquidation preference. The issuances of other series of preferred stock could have the effect of reducing the amounts available to the Series B Preferred Stock in the event of our liquidation, winding-up or dissolution. It may also reduce cash dividend payments on the Series B Preferred Stock if we do not have sufficient funds to pay dividends on all Series B Preferred Stock outstanding and outstanding parity preferred stock.

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

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

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

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

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

We are required to meet certain qualitative and financial tests to maintain the listing of our securities on The Nasdaq Capital Market. As previously disclosed, as of March 31, 2017, June 30, 2017, September 30, 2017 and December 31, 2017, our total stockholders equity was $(2.7) million, $0.4 million, $(6.1) million and $(10.9) million, respectively. As a result, we did not comply with the Nasdaq s $2.5 million minimum stockholders equity requirement, nor the alternative compliance standards under Nasdaq Listing Rule 5550(b) for the continued listing of our securities on The Nasdaq Capital Market. In addition, as previously disclosed, the Nasdaq Staff notified us of the noncompliance and, after granting a grace period and reviewing our proposed plan to regain compliance, the Nasdaq Staff had determined to seek to delist our securities from Nasdaq unless we requested a hearing before a Nasdaq Hearings Panel (the Panel). Accordingly, we requested and had a hearing on January 18, 2018 before the Panel, which has the authority to grant us an additional extension of time to regain compliance.

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

As of April 13, 2018, we were not able to regain compliance. On April 11, 2018, we submitted a written request to the Panel requesting an extension to May 14, 2018 to regain compliance.

On April 23, 2018, we received a letter from the Panel stating that the Panel has granted us an extension to May 14, 2018 to regain compliance.

There is no assurance that we will regain compliance on or before May 14, 2018, and even if we do, that we will be able to maintain compliance. If we are unable to regain compliance by May 14, 2018 or maintain compliance and our securities are delisted, it could be more difficult to buy or sell our securities and to obtain accurate quotations, and the price of our securities could suffer a material decline. Delisting could also impair our ability to raise capital.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

- our need for additional financing for our INSPIRE trial and other operations, and our ability to obtain sufficient funds on acceptable terms when needed, and our plans and future needs to scale back operations if adequate financing is not obtained;

- our ability to continue as a going concern;

- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;

- the success and timing of our preclinical studies and clinical trials, including site initiation and patient enrollment, and regulatory approval of protocols for future clinical trials;

- our ability to enter into, maintain and perform collaboration agreements with other pharmaceutical companies, for funding and commercialization of our clinical drug product candidates or preclinical compounds, and our ability to achieve certain milestones under those agreements;

- the difficulties in obtaining and maintaining regulatory approval of our product candidates, and the labeling under any approval we may obtain;

- our plans and ability to develop, manufacture and commercialize our product candidates;

- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;

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

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

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

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

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USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately $13.4 million, based on an assumed public offering price per Unit of $0.56, the last reported sale price of Common Stock on the Nasdaq Capital Market on April 20, 2018, assuming the sale of 26,785,714 Units and no sale of any Pre-Funded Units in this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of Warrants issued pursuant to this offering. If the underwriter exercises its option to purchase the additional Units in full, we estimate that the net proceeds will be approximately $15.4 million, based on an assumed public offering price per Unit of $0.56, the last reported sale price of Common Stock on the Nasdaq Capital Market on April 20, 2018, assuming the sale of 30,803,571 Units and no sale of any Pre-Funded Units in this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the Warrants issued pursuant to this offering.

We intend to use the net proceeds from this offering to fund the development of our clinical and preclinical programs, for other research and development activities and for general corporate purposes, which may include capital expenditures and funding our working capital needs. We expect from time to time to evaluate the acquisition of businesses, products and technologies for which a portion of the net proceeds may be used, although we currently are not planning or negotiating any such transactions.

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

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

The actual offering price per Unit and Pre-Funded Unit, and the exercise price of the Warrants, as applicable, will be as determined by negotiation between us and the underwriter at the time of pricing, and may be at a discount to the current market price of Common Stock. These estimates exclude the proceeds, if any, from the exercise of the Warrants in this offering. If all of the Warrants sold in this offering were to be exercised in cash at an assumed exercise price of $0.56 per 0.025 share of Series B Preferred Stock, we would receive additional net proceeds of approximately $15.0 million. However, the Warrants contain a cashless exercise provision that permits exercise of the Warrants on a cashless basis (i) at any time when there is no effective registration statement under the Securities Act of 1933, as amended, covering the issuance of the underlying shares of Series B Preferred Stock or (ii) on the expiration date of the Warrant. We cannot predict when or if the Warrants will be exercised or whether they will be exercised for cash. It is possible that the Warrants may be exercised solely on a cashless basis.

A $0.25 increase or decrease in the assumed public offering price per Unit of $0.56, the last reported sale price of Common Stock on the Nasdaq Capital Market on April 20, 2018, would increase or decrease the net proceeds to us from this offering by $6.2 million, assuming that the number of Units offered by us, as set forth on the cover page of this prospectus, remains the same, assuming no sale of any Pre-Funded Units, after deducting the estimated underwriter discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the Warrants issued pursuant to this offering.

Similarly, each increase or decrease of 1,000,000 Units offered by us would increase or decrease the net proceeds to us by approximately $0.5 million, assuming the assumed public offering price per Unit of $0.56 remains the same, assuming no sale of any Pre-Funded Units, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the Warrants issued pursuant to this offering.

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CAPITALIZATION

The following table presents our cash, cash equivalents and capitalization, as of December 31, 2017:

- on an actual basis;

- on a pro forma basis to give effect to (i) our underwritten public offering (the February 2018 Offering) of 7,005,000 shares of Common Stock, pre-funded warrants to purchase 2,942,500 shares of Common Stock and preferred stock warrants to purchase 994,750 shares of our Series A Convertible Preferred Stock pursuant to an underwriting agreement between us and H.C. Wainwright & Co., LLC dated as of February 8, 2018 and (ii) subsequent exercises of pre-funded warrants to purchase 1,650,000 shares of Common Stock (together with the February 2018 Offering, the Prior Transactions); and

- on a pro forma as adjusted basis to give further effect to the sale of 26,785,714 Units in this offering at an assumed public offering price per Unit of $0.56, the last reported sale price of Common Stock on the Nasdaq Capital Market on April 20, 2018, assuming no sale of any Pre-Funded Warrants, after deducting estimated underwriting discounts and commissions and estimate offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the Warrants issued pursuant to this offering.

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

	December 31, 2017 (unaudited)	
	Actual	Pro Forma	Pro Forma