Onconova Therapeutics, Inc.
Form 424B5
April 20, 2017
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Filed Pursuant To Rule 424(b)(5)

Registration Statement No. 333-199219

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED APRIL 20, 2017

Prospectus Supplement

(to the Prospectus dated November 20, 2014)

Onconova Therapeutics, Inc.

Shares of Common Stock

We are offering shares of our common stock. Our common stock is listed on the NASDAQ Capital Market under the symbol ONTX. On April 20, 2017, the last reported sale price of our common stock on the NASDAQ Capital Market was $2.48 per share.

As of April 19, 2017, the aggregate market value of our outstanding common stock held by non-affiliates, which we may refer to as the public float, was approximately $18,087,000, which was calculated based on 5,617,189 shares of outstanding common stock held by non-affiliates and on a price per share of $3.22, the closing price of our common stock on April 4, 2017. In no event will we sell our common stock in a public primary offering with a value exceeding more than one-third of our public float in any 12 calendar month period so long as our public float remains below $75.0 million. During the 12 calendar month period that ends on, and includes, the date of this prospectus supplement, and

including this offering, we have offered securities with an aggregate market value of approximately $65,600 pursuant to General Instruction I.B.6 of Form S-3.

Investing in our common stock involves risks. See Risk Factors beginning on page S-9 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

(1) We have agreed to reimburse the underwriters for certain expenses. See Underwriting. .The underwriting discount shall be $ per share for shares delivered to certain investors previously identified to the underwriters, for up to a maximum (in aggregate) of 20% of the common stock sold in the offering, and then the underwriting discount shall be $ for any additional shares delivered to these investors above the 20% threshold

We have granted the underwriters an option for a period of 45 days to purchase up to an additional shares of our common stock. If the underwriters exercise their option in full, the total underwriting discounts and commissions payable by us will be $ and the total proceeds to us, before expenses, will be $.

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The underwriters expect to deliver shares of common stock to purchasers on or about April , 2017

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 supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

Laidlaw & Company (UK) Ltd.

The date of this prospectus supplement is April , 2017.

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ABOUT THIS PROSPECTUS SUPPLEMENT

You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwrites have not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled Where You Can Find More Information and Information Incorporated by Reference.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated November 20, 2014, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission (the SEC), before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

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

For purposes of this prospectus, references to Onconova, Onconova Therapeutics, Company, we, us and our refer to Onconova Therapeutics, Inc. and its consolidated subsidiaries.

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

This prospectus supplement, the accompanying prospectus, and the information incorporated by reference herein and therein include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus are the property of their respective owners.

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PROSPECTUS SUPPLEMENT SUMMARY

The following summary highlights certain information contained elsewhere in this prospectus supplement, the accompanying prospectus, any free writing prospectus that we have been authorized to use and the documents incorporated by reference herein and in the accompanying prospectus. This summary does not contain all the information you will need in making your investment decision. You should carefully read this entire prospectus supplement, the accompanying prospectus, any free writing prospectus that we have been authorized to use and the documents incorporated by reference herein and in the accompanying prospectus. You should pay special attention to the Risk Factors section of this prospectus supplement and the accompanying prospectus and the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying 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 an extensive 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 in a randomized controlled Phase 3 clinical trial of intravenous rigosertib rigosertib IV in a population of patients with higher-risk MDS after failure of hypomethylating agent (HMA) therapy. The trial, which we refer to as INSPIRE, is expected to enroll approximately 225 patients at more than 170 sites globally. The primary endpoint of INSPIRE is overall survival, and an interim analysis is anticipated in the second half of 2017. We anticipate reporting topline data from the INSPIRE trial in 2018.

Rigosertib

Rigosertib is a small molecule which we believe blocks cellular signaling by targeting RAS effector pathways. This is believed to be mediated by the binding 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 as a single agent and in combination with azacitidine, in clinical trials of patients with MDS. We have enrolled more than 1,200 patients in rigosertib clinical trials for MDS and other conditions. We were a party to a license and development agreement with Baxalta (as defined below), which granted Baxalta certain rights to commercialize rigosertib in Europe. The Baxalta agreement was terminated on August 30, 2016, at which time the European rights reverted to us at no cost. We are party to a collaboration agreement with SymBio, which grants SymBio certain rights to commercialize rigosertib in Japan and Korea. We have retained development and commercialization rights to rigosertib in the rest of the world, including in the United States and Europe, although we could consider licensing commercialization rights to other territories as we continue to seek additional funding.

Rigosertib IV for higher-risk MDS

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

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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 will enroll higher-risk MDS patients under 82 years of age who have progressed on, or failed to respond to, previous treatment with HMAs within nine months or nine cycles over the course of one year after initiation of HMA therapy, and had their last dose of HMA within six months prior to enrollment in the trial. The primary endpoint of this study is overall survival of all randomized patients in the intent-to-treat (ITT) population and the IPSS-R Very High Risk subgroup. An interim analysis is planned after fifty percent of the total death events have occurred. This randomized trial of approximately 225 patients is expected to be conducted at more than 170 sites globally. The first patient in the INSPIRE trial was enrolled at the MD Anderson Cancer Center in December 2015, the first patient in Europe was enrolled in March, 2016, and the first patient in Japan was enrolled in July, 2016.

Enrollment for the INSPIRE Phase 3 trial for second-line higher-risk MDS patients is highly selective and required us to search extensively to identify appropriate candidates meeting the stringent entry criteria. We are encouraged that the enrollment is on track, with trial sites across 17 countries on four continents. Our partner SymBio Pharmaceuticals has opened 33 sites in Japan collaborating on the INSPIRE protocol. The trial is expected to be active in 19 countries by the end of April following the activation of sites in Switzerland and the Netherlands. We intend to maintain this momentum. We continue to anticipate the pre-planned interim analysis in the second half of 2017 and full enrollment by the first quarter of 2018. The interim analysis will involve a review of the efficacy and safety data for the first half of the trial by our independent data monitoring committee (DMC). This interim analysis may result in the trial continuing as planned, randomization for the Very High Risk MDS subgroup continuing with the other subgroups closed to further accrual, or the trial being stopped for futility. This analysis may also result in an increase to the study s sample size. Our statistical analysis plan is currently under review by the FDA.

Safety and Tolerability of rigosertib in MDS and other hematologic malignancies

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

Rigosertib oral in combination with azacitidine for higher-risk MDS

In December 2016, at the American Society of Hematology (ASH) Annual Meeting, we presented Phase 2 data from an oral rigosertib and azacitidine combination trial in higher-risk MDS. 33 of 40 MDS patients enrolled were evaluable for response at the time of the analysis. The median age of patients was 66, with 73% being male. ECOG performance status was 0 or 1 in 95% of the patients. The ECOG Scale of Performance Status describes a patient s level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). ECOG Performance Status grades include: 0 or Fully active, able to carry on all pre-disease performance without restriction; 1or Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work; 2 or Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours;3 or Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours;4 or Completely disabled; cannot carry on any selfcare; totally confined to bed or chair; 5 or Dead. 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 criteria. Responses were as follows:

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Response per IWG 2006

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

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

Safety/Tolerability of the Combination:

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

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

Following an end of Phase 2 meeting with the Food and Drug Administration (FDA) in September 2016, we began development of a Phase 3 protocol. We expect to submit this protocol for review by regulatory agencies in the US and Europe in the second or third quarter of 2017. The Phase 3 trial will be designed as a 1:1 randomized, placebo-controlled trial of oral rigosertib plus azacitidine compared to azacitidine plus placebo. We plan to use a full dose of azacitidine, as defined in the product insert. The patient population studied in this trial will be first-line (HMA naïve) higher-risk MDS patients. The primary endpoint for assessment of efficacy will be Response Rate of complete remission (CR) + partial remission (PR,) as per the IWG (International Working Group) 2006 Response criteria. Formal FDA review will be sought via the Special Protocol Assessment (SPA) mechanism. Further details, including sample size and other criteria will be available after completion of regulatory review, which is anticipated in the second half of 2017. We will not commence the Phase 3 trial without additional financing.

While the Phase 3 trial is being designed, we plan to expand the trial cohort by up to 40 subjects with the view of further studying the investigational therapy. Under a protocol amendment, we anticipate using the expanded cohorts to explore dose optimization by increasing the dose and varying the dose administration scheme of oral rigosertib to identify an optimal dose. We are currently in discussions with FDA concerning the trial expansion.

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.

We have explored single agent rigosertib oral as a treatment for lower-risk MDS in two Phase 2 clinical trials, 09-05 and 09-07. In December 2013, we presented data at the Annual ASH Meeting from the 09-05 Phase 2 trial. To date, Phase 2 clinical data has indicated that further study of single agent oral rigosertib in transfusion-dependent, lower-risk MDS patients is warranted. Rigosertib has been generally well tolerated, except for urinary

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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. To date, a biomarker which would predict response has not been identified. Further testing and development of oral rigosertib for lower-risk MDS will be required. We will not commence further development of oral rigosertib for lower-risk MDS without additional financing.

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 clinical study report is available. The most common TEAEs in ≥ 10% of patients 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 oral rigosertib as monotherapy were dysuria (8%), urinary tract pain (7%), haematuria (5%) and urinary frequency (5%).

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

Other Programs

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

Briciclib

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

Recilisib

Recilisib is a product candidate being developed in collaboration with the U.S. Department of Defense for acute radiation syndromes. We have completed four Phase 1 trials to evaluate the safety and pharmacokinetics of recilisib in healthy human adult subjects using both subcutaneous and oral formulations. We have also conducted animal studies and clinical trials of recilisib under the FDA s Animal 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. Use of government funds to finance the research and development in whole or in part means any future effort to

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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.

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

Common stock offered by us	Shares
Common stock to be outstanding after this offering	shares (or shares if the underwriters exercise in full their option to purchase additional shares)
Option to purchase additional shares	We have granted the underwriters an option to purchase up to an additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 45 days from the date of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds from this offering to fund the development of our clinical and preclinical programs, for other research and development activities and for general corporate purposes, which may include capital expenditures and funding working capital needs. See Use of Proceeds on page S-15.
Risk factors	You should read the Risk Factors section of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement for a discussion of factors to consider before deciding to invest in our common stock.
NASDAQ Capital Market symbol	ONTX.
Underwriting Discount	The underwriting discount shall be $ per share for shares delivered to certain investors previously identified to the underwriters, for up to a maximum (in aggregate) of 20% of the common stock sold in the offering, and then the underwriting discount shall be $ for any additional shares delivered to these investors above the 20% threshold.

The number of shares of our common stock outstanding after the offering is based on 6,759,895 shares outstanding as of December 31, 2016, and excludes as of such date:

- 746,353 shares of common stock issuable upon the exercise of stock options outstanding at December 31, 2016 with a weighted average exercise price of approximately $53.50 per share;

- 3,525,771 shares of common stock issuable upon the exercise of outstanding warrants at December 31, 2016 with a weighted average exercise price of approximately $4.77 per share;

- 6,275 shares of common stock reserved for future issuance under our 2013 Equity Compensation Plan at December 31, 2016; and

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

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Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase up to an additional shares of our common stock.

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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 filed with the SEC, which is incorporated by reference into this prospectus supplement, 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 supplement.

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

Risks Associated with this Offering

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

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

You will experience immediate dilution.

Since the price per share of our common stock being offered is higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of $ per share, and after deducting the underwriting discount and estimated offering expenses payable by us, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $ per share in the net tangible book value of the common stock as of December 31, 2016. See the section entitled Dilution in this prospectus supplement for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors.

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

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

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

Sales of a substantial number of shares of our common stock in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity

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securities. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

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

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

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain forward-looking statements within the meaning of Section 27A of 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 supplement, the accompanying prospectus and the documents incorporated by reference herein and therein 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, approxi that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements appear in a number of places throughout this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, 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 supplement, the accompanying prospectus and in documents incorporated by reference herein and therein, 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 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