

Prospectus Supplement No. 3
To Prospectus dated November 3, 2015



Onconova Therapeutics, Inc.

5,200,000 shares of Common Stock

This Prospectus Supplement No. 3 supplements and amends our prospectus dated November 3, 2015 (the "Prospectus"), relating to the sale, from time to time, of up to 5,200,000 shares of our common stock by Lincoln Park Capital Fund, LLC.

This prospectus supplement is being filed to include the information set forth in our Current Report on Form 8-K filed with the Securities and Exchange Commission on December 8, 2015. This prospectus supplement should be read in conjunction with the Prospectus and any amendments or supplements thereto, which are to be delivered with this prospectus supplement, and is qualified by reference to the Prospectus, except to the extent that the information in this prospectus supplement updates or supersedes the information contained in the Prospectus, including any amendments or supplements thereto.

Our common stock trades on the NASDAQ Global Select Market under the ticker symbol "ONTX." On December 7, 2015, the last reported sale price per share of our common stock was \$1.31 per share.

Investing in our common stock involves risk. Please read carefully the section entitled "Risk Factors" beginning on page 10 of the Prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved these securities or determined if the Prospectus or this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this Prospectus Supplement No. 3 is December 8, 2015.

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, DC 20549

FORM 8-K

**CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934**

Date of Report (Date of earliest event reported): **December 7, 2015**

Onconova Therapeutics, Inc.
(Exact name of Registrant as specified in its charter)

Delaware
(State or Other Jurisdiction
of Incorporation or Organization)

001-36020
(Commission
File Number)

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

375 Pheasant Run

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 8.01. Other Events

On December 7, 2015, Onconova Therapeutics, Inc. (the "Company") issued a press release regarding information presented at the American Society of Hematology (ASH) Annual Meeting. A copy of the press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits.

99.1 Press release issued by the Company dated December 7, 2015.

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SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: December 8, 2015

Onconova Therapeutics, Inc.

By: /s/ Ajay Bansal
Name: Ajay Bansal
Title: Chief Financial Officer

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EXHIBIT INDEX

Exhibit No.	Description
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99.1	Press release issued by the Company dated December 7, 2015.
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Exhibit 99.1



Onconova Presents Positive Data from Phase 2 Combination Trial of Oral Rigosertib and Azacitidine in Higher-Risk Myelodysplastic Syndromes at 2015 ASH Annual Meeting

—Combination Achieved 77% Overall Response Rate in all MDS Patients—
—Overall Response Rate of 84% in treatment-naïve MDS Patients—

NEWTOWN, PA, December 7, 2015 — Onconova Therapeutics, Inc. (NASDAQ: ONTX), a clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, today announced the presentation of data from an ongoing Phase 1/2 clinical trial of oral rigosertib and azacitidine in higher-risk myelodysplastic syndromes (HR-MDS) at the 57th American Society of Hematology (ASH) Annual Meeting in Orlando, Florida.

“The high response rate observed in the 09-08 combination trial is impressive,” said Lewis R. Silverman, M.D., investigator in the trial and Associate Professor of Medicine, Hematology and Medical Oncology, at the Icahn School of Medicine at Mount Sinai. “Furthermore, the tolerability profile of oral rigosertib and azacitidine suggests that this combination could be used in HR-MDS. These results provide strong support for the advancement of oral rigosertib into late-stage clinical trials.”

The 09-08 study, which is fully enrolled, is an open label, multi-site clinical trial evaluating oral rigosertib in combination with the approved dose of injectable azacitidine for patients with MDS and AML. Results from the Phase 1 dose escalation portion of the study, presented at the 2014 ASH Annual Meeting, identified the Recommended Phase Two Dose (RPTD) of oral rigosertib as 560 mg/280 mg twice daily. The Phase 2 portion of the trial was designed to assess whether treatment with the combination (oral rigosertib in combination with injectable azacitidine) reduces the number of bone marrow blasts and improves peripheral blood counts. Accrual in the 09-08 study was recently completed. Clinical trial sites included MD Anderson Cancer Center (Lead Investigator: Dr. Guillermo Garcia-Manero), Mount Sinai School of Medicine (Lead Investigator: Dr. Lewis Silverman) and Hôpital Saint-Louis (Lead Investigator: Dr. Pierre Fenaux).

Summary of Presented Data from the 09-08 Trial

Patient Demographics:

- A total of 37 MDS patients have been treated to date at the RPTD. Thirty of these patients were evaluable for response at the time of this analysis.
- The median age of MDS patients was 64. IPSS risk score (27% INT-1, 41% INT-2 and 32% High) and cytogenetic risk (22% Good, 38% Intermediate, 24% Poor and 16% unknown) were calculated for all MDS patients. Thirteen patients had received prior HMA therapy (ten azacitidine, three decitabine; one received both HMAs serially) and the remaining evaluable patients were HMA-naïve front-line patients.
- This study is now closed for enrollment.

Safety/Tolerability:

- The combination of oral rigosertib and azacitidine has been well tolerated to date.
- The median duration of treatment at this time for MDS patients treated in the trial with the combination was four months (range 1 to 27 months to date).
- Adverse events of Grade ≥ 3 experienced across all cycles with the combination included thrombocytopenia (27%), neutropenia (22%), hypokalaemia (5%), hematuria (5%) and diarrhoea (3%).
- Notably, these side effects were similar to the side effects previously reported for azacitidine administered alone.

Efficacy:

- Thirty MDS patients were evaluable for efficacy analysis per IWG 2006 criteria (Cheson et al., *Blood* 2006).
- Twenty-three of 30 (77%) patients responded per IWG, including six patients who had complete remissions (CR).
- Hematologic improvement (HI) per IWG, including tri-lineage response, was noted in 13 patients (50% of the 26 patients evaluable for HI response) and included improvements in erythroid (11 patients), platelet (12 patients) and neutrophil (7 patients) lineages.
- Per IWG, 16 of 19 (84%) evaluable HMA-naïve patients responded to the combination therapy; 7 of 11 (64%) evaluable patients previously treated with HMAs responded.

Following these results, additional data from patients continuing to be treated in the study, and after consultation with key opinion leaders, Onconova intends to seek an end of Phase 2 meeting with U.S. and European regulators in order to discuss next steps for the combination program.

“The results for oral rigosertib in combination with azacitidine support moving this novel therapy towards pivotal trials for patients with MDS and myeloid malignancies,” said Ramesh Kumar, Ph.D., President and CEO of Onconova. “We intend to provide clarity related to timing of further development for oral rigosertib at our upcoming investor event on December 16th.”

Investor Event and Webcast

Onconova will host a live investor event on December 16th in New York, NY at 8:00 AM ET to review the clinical data presented at the ASH Annual Meeting. The event will provide access to key opinion leaders involved with rigosertib clinical trials in MDS. A live webcast can be accessed by visiting “Events & Presentations” in the Investors and Media section of the Company’s website at www.onconova.com.

About Rigosertib

Rigosertib is a small molecule that inhibits cellular signaling by acting as a Ras mimetic. This is believed to be mediated by direct binding of rigosertib to the Ras-binding domain (RBD) found in many Ras effector proteins, including the Raf kinases and PI3K. The initial therapeutic focus for rigosertib is myelodysplastic syndromes (MDS), a group of bone marrow disorders characterized by ineffective formation of blood cells that often converts into acute myeloid leukemia (AML). Clinical trials for rigosertib are being conducted at MDS Centers of Excellence in the United States, Europe, and the Asia-Pacific region.

Intellectual Property

Rigosertib is protected by issued patents (composition of matter with earliest expiration in 2026) and has been awarded Orphan Designation for MDS in the United States, Europe and Japan. The combination of rigosertib and azacitidine is protected by an issued U.S. patent (US 8,664,272 with earliest expiration in 2028) covering the composition of the combination and methods for using the combination to treat MDS and AML.

About Onconova Therapeutics, Inc.

Onconova Therapeutics is a Phase 3 clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer. Onconova's clinical and pre-clinical stage drug development candidates are derived from its extensive chemical library and are designed to work against specific cellular pathways that are important in cancer cells, while causing minimal damage to normal cells. In addition to rigosertib, the Company's most advanced product candidate, two other candidates are clinical stage, and several candidates are in pre-clinical stages. For more information, please visit <http://www.onconova.com>.

Forward Looking Statements

Some of the statements in this release are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. These statements relate to future events or Onconova Therapeutics, Inc.'s future operations, clinical development of Onconova's product candidates and presentation of data with respect thereto, regulatory approvals, expectations regarding the sufficiency of Onconova's cash and other resources to fund operating expenses and capital expenditures, Onconova's anticipated milestones and future expectations and plans and prospects. Although Onconova believes that the expectations reflected in such forward-looking statements are reasonable as of the date made, expectations may prove to have been materially different from the results expressed or implied by such forward-looking statements. Onconova has attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or other words that convey uncertainty of future events or outcomes. These statements are only predictions and involve known and unknown risks, uncertainties, and other factors, including Onconova's need for additional financing and current plans and future needs to scale back operations if adequate financing is not obtained, the success and timing of Onconova's clinical trials and regulatory approval of protocols, and those discussed under the heading "Risk Factors" in Onconova's most recent Annual Report on Form 10-K and quarterly reports on Form 10-Q.

Any forward-looking statements contained in this release speak only as of its date. Onconova undertakes no obligation to update any forward-looking statements contained in this release to reflect events or circumstances occurring after its date or to reflect the occurrence of unanticipated events.

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