Registration No. 333-189358

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

PRE-EFFECTIVE AMENDMENT NO. 3 TO

FORM S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

Onconova Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation or organization)

2834 (Primary Standard Industrial Classification Code Number)

22-3627252 (I.R.S. Employer Identification Number)

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 Onconova Therapeutics, Inc. 375 Pheasant Run Newtown, PA 18940 (267) 759-3680

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

Copies to:

David S. Rosenthal, Esq. James J. Marino, Esq. Dechert LLP 1095 Avenue of the Americas New York, New York 10036 (212) 698-3500

Andrew S. Williamson, Esq. Brent B. Siler, Esq. Brian F. Leaf, Esq. Cooley LLP 11951 Freedom Drive Reston, Virginia 20190 (703) 456-8000

Approximate date of commencement of proposed sale to the public:

As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), check the following box. o

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

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

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

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

Large accelerated filer o Accelerated filer o Non-accelerated filer ⊠ Smaller reporting company o

(Do not check if a smaller reporting company)

	is registration statement on such hall thereafter become effective ir on, acting pursuant to said Section			

EXPLANATORY NOTE

This Pre-Effective Amendment No. 3, or Pre-Effective Amendment No. 3, to the Registration Statement on Form S-1 (File No. 333-189358) of Onconova Therapeutics, Inc., or the Registration Statement,
is being filed solely for the purpose of filing Exhibit 5.1 to the Registration Statement. This Pre-Effective Amendment No. 3 does not modify any provision of the prospectus that forms a part of the Registration
Statement. Accordingly, a preliminary prospectus has been omitted.

PART II INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth all costs and expenses, other than underwriting discounts and commissions, paid or payable by us in connection with the sale of the common stock being registered. All amounts shown are estimates except for the SEC registration fee, the Financial Industry Regulatory Authority, or FINRA, filing fee and the initial listing fee for the NASDAQ Global Market.

		Amount
SEC registration fee	\$	10,230
FINRA filing fee		11,750
NASDAQ Global Market listing fee		125,000
Printing expenses		175,000
Legal fees and expenses		1,006,500
Accounting fees and expenses		1,800,000
Transfer agent and registrar fees and expenses		25,000
Miscellaneous expenses		146,520
Total	\$ 3	3,300,000

Item 14. Indemnification of Directors and Officers.

We are incorporated under the laws of the State of Delaware. Section 145 of the Delaware General Corporation Law provides that a Delaware corporation may indemnify any persons who are, or are threatened to be made, parties to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of such corporation), by reason of the fact that such person was an officer, director, employee or agent of such corporation, or is or was serving at the request of such person as an officer, director, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation's best interests and, with respect to any criminal action or proceeding, had no reasonable cause to believe that his or her conduct was illegal. A Delaware corporation may indemnify any persons who are, or are threatened to be made, a party to any threatened, pending or completed action or suit by or in the right of the corporation by reason of the fact that such person was a director, officer, employee or agent of such corporation, or is or was serving at the request of such corporation as a director, officer, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation's best interests except that no indemnification is permitted without judicial approval if the officer or director is adjudged to be liable to the corporation. Where an officer or director is successful on the merits or otherwise in the defense of any action referred to above, the corporation must indemnify him or her against the expenses which such officer or director has actually and reasonably incurred. Our certificate of incorporation and bylaws, each of which will become effective upon consummation of this offering, provide for the indemnification of our directors and officers to the fullest extent permitted under the Delaware General Corporation Law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the

corporation or its stockholders for monetary damages for breach of fiduciary duties as a director, except for liability for any:

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

Our certificate of incorporation includes such a provision. Expenses incurred by any officer or director in defending any such action, suit or proceeding in advance of its final disposition shall be paid by us upon delivery to us of an undertaking, by or on behalf of such director or officer, to repay all amounts so advanced if it shall ultimately be determined that such director or officer is not entitled to be indemnified by us.

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

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

We have an insurance policy covering our officers and directors with respect to certain liabilities, including liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, or otherwise.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of preferred stock and convertible promissory notes issued and options granted by us within the past three years that were not registered under the Securities Act. Also included is the consideration, if any, received by us for such shares, notes and options and information relating to the section of the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

(a) Issuances of Capital Stock:

- (1) On September 21, 2010, we issued an aggregate of 668,602 shares of our Series H convertible preferred stock at a price per share of \$9.79 for an aggregate purchase price of \$6,545,613.58.
- (2) On November 4, 2010, we issued an aggregate of 299,797 shares of our Series H convertible preferred stock at a price per share of \$9.79 for an aggregate purchase price of \$2,935,012.63.
- (3) On December 22, 2010, we issued an aggregate of 225,696 shares of our Series H convertible preferred stock at a price per share of \$9.79 for an aggregate purchase price of \$2,209,563.84.
- (4) On February 17, 2011, we issued 71,488 shares of our Series H convertible preferred stock at a price per share of \$9.79 for an aggregate purchase price of \$699,867.52.
- (5) On June 6, 2011, we issued an aggregate of 135,391 shares of our Series H convertible preferred stock at a price per share of \$9.79 for an aggregate purchase price of \$1,325,477.89.

- (6) On September 19, 2011, we issued an aggregate of 612,450 shares of our Series H convertible preferred stock at a price per share of \$9.79 for an aggregate purchase price of \$5,995,885.50.
- (7) On July 25, 2012, \$26,444,316.00 aggregate principal amount and accrued interest thereon of our convertible promissory notes were converted into 2,433,328 shares of our Series I convertible preferred stock at a price per share of \$11.00.
- (8) On July 27, 2012, we issued an aggregate of 3,030,303 shares of our Series J convertible preferred stock at a price per share of \$16.50 for an aggregate purchase price of \$49,999,999.50.
- (9) Since May 1, 2010, we issued an aggregate of 417,404 shares of our Series G convertible preferred stock at a price per share of \$9.79 for an aggregate purchase price of \$4,086,385 pursuant to the exercise of warrants.
- (10) Since May 1, 2010, we issued an aggregate of 1,116,967 shares of our common stock at prices ranging from \$0.75 to \$5.65 per share to certain of our employees, consultants and directors pursuant to the exercise of stock options under the Onconova Therapeutics, Inc. 2007 Equity Compensation Plan, for an aggregate purchase price of \$1,808,850.

(b) Issuance of Convertible Notes

- (1) On April 27, 2012, we sold \$7,050,000.00 aggregate principal amount of our convertible promissory notes for an aggregate purchase price of \$7.050.000.00.
- (2) On June 29, 2012, we sold \$4,619,000.00 aggregate principal amount of our convertible promissory notes for an aggregate purchase price of \$4,619,000.00.
- (3) On July 18, 2012, we sold \$14,775,316.00 aggregate principal amount of our convertible promissory notes for an aggregate purchase price of \$14,775,316.00.

(c) Grants of Stock Options:

(1) Since May 1, 2010, we have granted stock options to purchase an aggregate of 2,610,812 shares of our common stock with exercise prices ranging from \$4.60 to \$11.06 per share, to certain of our employees, consultants and directors in connection with services provided by such parties to us.

We deemed the offers, sales and issuances of the securities described in paragraphs (a)(1) through (a)(9) and (b)(1) through (b)(3) above to be exempt from registration under the Securities Act in reliance on Section 4(2) of the Securities Act, including in some cases, Regulation D and Rule 506 promulgated thereunder and/or Regulation S promulgated thereunder, relative to transactions by an issuer not involving a public offering, to the extent an exemption from such registration was required.

We deemed the issuance of the securities described in paragraph (a)(10) above and the grant of stock options described in paragraph (c)(1) above to be exempt from registration under the Securities Act in reliance on Rule 701 promulgated under the Securities Act as offers and sales of securities under written compensatory benefit plans and contracts relating to compensation in compliance with Rule 701 promulgated under the Securities Act and/or Section 4(2) of the Securities Act, relative to transactions by an issuer not involving a public offering, to the extent an exemption from such registration was required. Each of the recipients of securities in any transaction exempt from registration either received or had adequate access, through employment, business or other relationships, to information about us.

All purchasers of securities in transactions exempt from registration pursuant to Regulation D promulgated under the Securities Act described above represented to us in connection with their purchase that they were accredited investors and were acquiring the securities for investment purposes

only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from the registration requirements of the Securities Act.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. The certificates representing the issued securities described in this Item 15 included appropriate legends setting forth that the applicable securities have not been registered and reciting the applicable restrictions on transfer. There were no underwriters employed in connection with any of the transactions set forth in this Item 15.

Item 16. Exhibits and Financial Statement Schedules.

- (a) Exhibits. See the Index to Exhibits attached to this registration statement, which is incorporated by reference herein.
- (b) Financial statement schedule. No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or notes.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes to provide to the underwriter at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant has duly caused this pre-effective amendment no. 3 to the registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Newtown, Commonwealth of Pennsylvania, on the 23rd day of July, 2013.

ONCONOVA THERAPEUTICS, INC.

By: /s/ RAMESH KUMAR, PH.D.

Ramesh Kumar, Ph.D.

President and Chief Executive Officer

Pursuant to the requirements of the Securities Act, this pre-effective amendment no. 3 to the registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	<u>Title</u>	<u>Date</u>	
/s/ RAMESH KUMAR, PH.D. Ramesh Kumar, Ph.D.	Director, President and Chief Executive Officer (Principal Executive Officer)	July 23, 2013	
/s/ AJAY BANSAL	Director and Chief Financial Officer (Principal Financial Officer)	July 23, 2013	
Ajay Bansal	i manciai Officer)		
/s/ JAMES R. ALTLAND	Senior Vice President, Finance & Corporate	July 23, 2013	
James R. Altland	Development (Principal Accounting Officer)		
*	Chairman, Board of Directors	July 23, 2013	
Michael B. Hoffman			
*	Director	July 23, 2013	
Henry S. Bienen, Ph.D.			
*	Director	July 23, 2013	
Viren Mehta			

Signature		<u>Title</u>	<u>Date</u>
	*		
	Sarath Naru *	Director Director	July 23, 2013 July 23, 2013
	Pankaj R. Patel		
	*	Director	July 23, 2013
	E. Premkumar Reddy, Ph.D.		
	*	Director	July 23, 2013
	Alan R. Williamson, Ph.D.		
*By:	/s/ RAMESH KUMAR PH.D.		
_	Ramesh Kumar Ph.D. Attorney-in-fact		

INDEX TO EXHIBITS

Exhibit Number	Exhibit Description			
1.1††	Form of Underwriting Agreement.			
3.1††	Form of Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc., to be effective upon consummation of this offering.			
3.2††	Form of Amended and Restated Bylaws of Onconova Therapeutics, Inc., to be effective upon consummation of this offering.			
4.1††	Form of Certificate of Common Stock.			
4.2††	Eighth Amended and Restated Stockholders' Agreement, effective as of July 27, 2012, by and among Onconova Therapeutics, Inc. and certain stockholders named therein.			
4.3††	Amendment No. 1 to Eighth Amended and Restated Stockholders' Agreement, effective as of July 9, 2013.			
5.1	Opinion of Dechert LLP regarding the validity of the securities being registered.			
10.1*††	Development and License Agreement, effective as of September 19, 2012, by and between Onconova Therapeutics, Inc. and Baxter Healthcare SA.			
10.2*††	License Agreement, effective as of July 5, 2011, by and between Onconova Therapeutics, Inc. and SymBio Pharmaceuticals Limited.			
10.3*††	First Amendment to License Agreement, effective as of September 2, 2011, by and between Onconova Therapeutics, Inc. and SymBio Pharmaceuticals Limited.			
10.4*††	License Agreement, effective as of January 1, 1999, by and between Onconova Therapeutics, Inc. and Temple University—Of The Commonwealth System of Higher Education.			
10.5*††	Amendment to License Agreement, effective as of September 1, 2000, by and between Temple University—Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc.			
10.6*††	Amendment #1 to Exclusive License Agreement, effective as of March 21, 2013, by and between Temple University—Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc.			
10.7*††	Definitive Agreement, effective as of May 12, 2010, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society.			
10.8*††	First Amendment to Definitive Agreement, effective as of June 23, 2011, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society.			
10.9*††	Second Amendment to Definitive Agreement, effective as of May 29, 2012, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society.			
10.10*††	Third Amendment to Definitive Agreement, effective as of January 5, 2013, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society.			
10.11††	Termination of Agreement, effective as of February 5, 2013, by and between Onconova Therapeutics, Inc. and The Leukemia and Lymphoma Society.			
10.12*††	Limited Liability Company Agreement of GBO, LLC, dated as of December 12, 2012, by and between Onconova Therapeutics, Inc. and GVK Biosciences Private Limited.			
10.13+††	Onconova Therapeutics, Inc. 2007 Equity Compensation Plan, and forms of agreement thereunder.			

Exhibit Number	Exhibit Description
	Employment Agreement, effective as of April 1, 2007, by and between Onconova Therapeutics, Inc. and Ramesh Kumar, Ph.D., including extension letter, dated April 10, 2010, and Employment Agreement Renewal, dated January 10, 2013.
10.15+††	Amendment to Employment Agreement, effective as of December 21, 2012, by and between Onconova Therapeutics, Inc. and Ramesh Kumar, Ph.D.
10.16+††	Employment Agreement, effective as of September 1, 2012, by and between Onconova Therapeutics, Inc. and Thomas McKearn, M.D., Ph.D.
10.17+††	Amendment to Employment Agreement, effective as of April 9, 2013, by and between Onconova Therapeutics, Inc. and Thomas McKearn, M.D., Ph.D.
10.18+††	Employment Agreement, effective as of April 17, 2008, by and between Onconova Therapeutics, Inc. and François Wilhelm, M.D., including Employment Agreement Renewals, dated March 30, 2010 and January 10, 2013.
10.19+††	Amendment to Employment Agreement, effective as of December 21, 2012, by and between Onconova Therapeutics, Inc. and Francois Wilhelm, M.D.
10.20+††	Employment Agreement, effective as of January 1, 2007, by and between Onconova Therapeutics, Inc. and Dr. Manoj Maniar, including Employment Agreement Renewals, dated March 30, 2010 and January 10, 2013.
10.21+††	Amendment to Employment Agreement, effective as of December 21, 2012, by and between Onconova Therapeutics, Inc. and Dr. Manoj Maniar.
10.22+††	Employment Agreement, effective as of March 20, 2013, by and between Onconova Therapeutics, Inc. and Ajay Bansal.
10.23+††	Consulting Agreement, effective as of January 1, 2012, by and between Onconova Therapeutics, Inc. and E. Premkumar Reddy, Ph.D., including Consultant Agreement Renewal, dated February 27, 2013.
10.24+††	Form of Indemnification Agreement to be entered into by and between Onconova Therapeutics, Inc. and each director and executive officer.
10.25+††	Onconova Therapeutics, Inc. 2013 Equity Compensation Plan, and forms of agreement thereunder.
10.26+††	Onconova Therapeutics, Inc. 2013 Performance Bonus Plan.
16.1††	Letter from EisnerAmper LLP, as to the change in certifying accountant, dated as of June 14, 2013.
21.1††	Subsidiaries of Onconova Therapeutics, Inc.
23.1††	Consent of Ernst & Young LLP.
23.2††	Consent of EisnerAmper LLP.
23.3	Consent of Dechert LLP (included in Exhibit 5.1).
24.1††	Power of Attorney.
99.1††	Consent of Director Nominee Jerome E. Groopman.
99.2††	Consent of Director Nominee Anne M. VanLent.

^{††} Previously filed.

⁺ Indicates management contract or compensatory plan.

^{*} Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

QuickLinks

EXPLANATORY NOTE

PART II INFORMATION NOT REQUIRED IN PROSPECTUS

<u>Item 13. Other Expenses of Issuance and Distribution.</u>

Item 14. Indemnification of Directors and Officers.

Item 15. Recent Sales of Unregistered Securities.

Item 16. Exhibits and Financial Statement Schedules.

Item 17. Undertakings.

SIGNATURES

INDEX TO EXHIBITS



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July 23, 2013

Onconova Therapeutics, Inc. 375 Pheasant Run Newtown, PA 18940

Re: <u>REGISTRATION STATEMENT ON FORM S-1</u>,

REGISTRATION NO. 333-189358

Ladies and Gentlemen:

We have acted as counsel to Onconova Therapeutics, Inc. a Delaware corporation (the "Company"), in connection with the filing with the Securities and Exchange Commission (the "Commission") of a Registration Statement on Form S-1 (the "Registration Statement") for the purpose of registering under the Securities Act of 1933, as amended (the "Securities Act"), 5,307,692 shares of its common stock, par value \$0.01 per share (the "Common Stock"), all of which will be sold by the Company (the "Securities"), and which includes 692,307 shares subject to an over-allotment option granted by the Company to the underwriters. The term "Securities" shall include any additional Securities registered by the Company pursuant to Rule 462(b) under the Securities Act in connection with the offering contemplated by the Registration Statement.

This opinion is being furnished to the Company in connection with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act, and no opinion is expressed herein as to any matter pertaining to the contents of the Registration Statement or the prospectus that is a part of the Registration Statement, other than as expressly stated herein with respect to the Securities.

As your counsel, we have examined such documents and such matters of fact and law that we have deemed necessary for the purpose of rendering the opinion expressed herein. In our examination, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as original documents, and the conformity to original documents of all documents submitted to us as copies, the legal capacity of natural persons who are signatories to the documents examined by us, and the legal power and authority of all persons signing on behalf of parties (other than the Company) to all documents.

Based on the foregoing, we advise you that, in our opinion, when the price at which the Securities are to be sold has been approved by or on behalf of the Board of Directors of the Company, when the Registration Statement has been declared effective by the Commission and when the Securities have been duly issued and delivered against payment therefor in accordance with the terms of the Underwriting Agreement referred to in the prospectus that is a part of the Registration Statement, the Securities will be validly issued, fully paid and non-assessable.

We are members of the Bar of the State of New York and the foregoing opinion is limited to the General Corporation Law of the State of Delaware.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement and further consent to the reference to our name under the caption "Legal Matters" in the prospectus that is a part of the Registration Statement. We further consent to the incorporation by reference of this letter and consent into any registration statement filed pursuant to Rule 462(b) with respect to the Securities. In giving this consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission thereunder.

Very truly yours,

/s/ Dechert LLP

DAVID S. ROSENTHAL

david.rosenthal@dechert.com +1 212 698 3616 Direct +1 212 698 0416 Fax

July 23, 2013

VIA EDGAR

Jeffrey P. Riedler Assistant Director Division of Corporation Finance U.S. Securities & Exchange Commission 100 F Street, NE Washington, D.C. 20549

Re: Onconova Therapeutics, Inc. (the "Company")

Registration Statement on Form S-1 (File No. 333-189358)

Dear Mr. Riedler:

On behalf of Onconova Therapeutics, Inc. (the "<u>Company</u>"), set forth below is the Company's response to the comment letter dated July 22, 2013 provided by the staff of the Division of Corporation Finance (the "<u>Staff</u>") of the Securities and Exchange Commission (the "<u>Commission</u>") to the Company regarding the Company's Pre-Effective Amendment No. 2 ("<u>PEA No. 2</u>") to the Registration Statement on Form S-1 (File No. 333-189358) (the "<u>Registration Statement</u>") and the prospectus included therein (the "<u>Prospectus</u>").

We also describe below the changes that we have made in response to the Staff's comments in Pre-Effective Amendment No. 3 ("<u>PEA No. 3</u>") to the Registration Statement that the Company filed on July 23, 2013. For your convenience, the Staff's comments are numbered and presented in italicized text below, and each comment is followed by the Company's proposed response. The Company will also provide the Staff a courtesy copy of PEA No. 3 as-filed.

Exhibit 5.1

1. We note counsel's opinion that the securities will be validly issued, fully paid and non-assessable is subject to the assumption that the Tenth Amended and Restated Certificate of Incorporation will be filed with the Secretary of State of the State of Delaware. Please either file a revised legal opinion to remove this assumption or confirm that an appropriately unqualified opinion will be filed by post-effective amendment no later than the closing date of the offering. See Sections II.B.2.f and II.B.3.a of Staff Legal Bulletin No. 19.

The Company respectfully acknowledges the Staff's comment and has included a revised legal opinion as Exhibit 5.1 to PEA No. 3 removing the assumption regarding the filing of the Tenth Amended and Restated Certificate of Incorporation.

2. Please also provide a revised legal opinion to modify the statement regarding "the legal power and authority of all persons signing on behalf of parties to all documents," to limit this qualification to persons signing on behalf of parties other than the registrant.

The Company respectfully acknowledges the Staff's comment and has included a revised legal opinion as Exhibit 5.1 to PEA No. 3.

If you have any questions, or if you require additional information, please do not hesitate to contact me at (212) 698-3616.

Sincerely,

/s/ David S. Rosenthal

David S. Rosenthal

Cc: Ramesh Kumar, Ph.D.
Ajay Bansal
Onconova Therapeutics, Inc.
James J. Marino, Esq.
Dechert LLP
Brent B. Siler, Esq.
Cooley LLP