PROSPECTUS SUPPLEMENT Dated September 23, 2019 (To Prospectus Dated February 8, 2018)



Onconova Therapeutics, Inc.

Warrant to purchase 261,890 Share of Series A Convertible Preferred Stock

261,890 Shares of Series A Convertible Preferred Stock Underlying the Warrants

This prospectus supplement ("Supplement") modifies, supersedes and supplements certain information contained in, and should be read in conjunction with, that certain prospectus (the "Original Prospectus") filed with the Securities and Exchange Commission (the "SEC") by Onconova Therapeutics, Inc. (the "Company"), dated February 8, 2018, related to the public offering (the "February 2018 Offering") of the Company's common stock, pre-funded warrants to purchase shares of common stock, warrants (the "February 2018 Preferred Stock Warrants") to purchase shares of the Company's Series A Convertible Preferred Stock ("Series A Preferred Stock"), shares of common stock issuable upon the exercise of the pre-funded warrants and shares of Series A Preferred Stock issuable upon the exercise of the February 2018 Preferred Stock Warrants, as supplemented by a prospectus supplement dated May 1, 2018 filed with the SEC by the Company on May 1, 2018 (the "May 2018 Prospectus Supplement" and, the Original Prospectus, as supplemented by the May 2018 Prospectus Supplement, the "Prospectus"). This Supplement is not complete without, and may not be delivered or used except in connection with, the Prospectus.

The Company's common stock is listed on the Nasdaq Capital Market under the symbol "ONTX." On September 20, 2019, the last reported sale price of the Company's common stock on the Nasdaq Capital Market was \$1.60 per share.

The information contained in this Supplement modifies and supersedes, in part, the information in the Prospectus. Any information that is modified or superseded in the Prospectus shall not be deemed to constitute a part of the Prospectus, except as modified or superseded by this Supplement.

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

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

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

FORWARD-LOOKING STATEMENTS

You should carefully consider the risk factors set forth in the Prospectus, as well as the other information contained in this Supplement and the Prospectus. This Supplement and the Prospectus contains forward-looking statements regarding events, conditions, and financial trends that may affect our plan of operation, business strategy, operating results, and financial position. You are cautioned that any forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties. Actual results may differ materially from those included within the forward-looking statements as a result of various factors. Cautionary statements in the "Risk Factors" section of the Prospectus identify important risks and uncertainties affecting our future, which could cause actual results to differ materially from the forward-looking statements made or included in this Supplement and the Prospectus.

AMENDMENTS TO CERTAIN FEBRUARY 2018 PREFERRED STOCK WARRANTS

On September 25, 2019, in connection with the securities purchase agreements the Company entered into with certain institutional and accredited investors dated September 23, 2019, we filed a prospectus supplement (the "Registered Direct Prospectus Supplement") and the accompanying base prospectus with the SEC under our registration statement on Form S-3 (Registration No. 333-221684) in accordance with Rule 424(b)(5) of the Securities Act. Pursuant to the securities purchase agreements and the Registered Direct Prospectus Supplement, the Company offered 2,198,938 shares of the Company's common stock, at a purchase price of \$1.60 per share of common stock (the "Registered Direct Offering"). The Registered Direct Offering is anticipated to close on or about September 25, 2019, subject to satisfaction of customary closing conditions.

Each investor in the Registered Direct Offering is a holder of the February 2018 Preferred Stock Warrants and/or a holder of warrants to purchase shares of our Series B Convertible Preferred Stock issued on May 1, 2018 (the "May 2018 Preferred Stock Warrants"). In connection with the Registered Direct Offering, the Company has agreed that such investor may choose to amend either the such investor's February 2018 Preferred Stock Warrants, or such investor's May 2018 Preferred Stock Warrants.

This Supplement is being filed to disclose the following:

To the extent an investor chose to amend such investor's February 2018 Preferred Stock Warrants, then for each share of common stock the investor purchased in the Registered Direct Offering, (1) the exercise price of the investor's February 2018 Preferred Stock Warrant to purchase one share of common stock on an as-exercised and as-converted basis will be reduced from \$1.01 per 0.1 share of Series A Preferred Stock to \$0.10667 per 0.1 share of Series A Preferred Stock which, on an as-converted basis, which equals to \$1.60 per share of common stock, and (2) the expiration date of such February 2018 Preferred Stock Warrant will be extended to December 31, 2022. The price for amending the February 2018 Preferred Stock Warrants was \$0.125 per share (on an as-converted basis per share of common stock). As of the date hereof, February 2018 Preferred Stock Warrants to purchase an aggregate of 261,890 shares of Series A Preferred Stock, or 392,834 shares of common stock on an as-converted basis, were amended accordingly.

The date of this Prospectus Supplement is September 23, 2019.