

9,230,500 Shares of Common Stock Warrants to Purchase up to 9,230,500 Shares of Common Stock

This prospectus supplement, dated January 20, 2023 (this "Supplement"), filed by Windtree Therapeutics, Inc. (the "Company"), modifies and supplements certain information contained in the Company's prospectus supplement, dated March 23, 2021 (as amended and supplemented from time to time, the "Prospectus Supplement"), as part of the Company's Form S-3 Registration Statement declared effective by the Securities and Exchange Commission on September 29, 2020. This Supplement is not complete without, and may not be delivered or used except in connection with, the Prospectus Supplement, including all amendments and supplements thereto. The Prospectus Supplement relates to the offering of 9,230,500 shares of common stock, par value \$0.001 per share ("Common Stock"), and warrants to purchase up to 9,230,500 shares of our Common Stock, and this Supplement relates to the 9,230,500 warrants that were sold in that offering (the "Warrants") (and the shares of Common Stock issuable from time to time upon exercise of these Warrants) pursuant to the terms of an underwriting agreement that we entered into on March 23, 2021.

On January 20, 2023, the Company entered into warrant amendment agreements with certain warrant holders of the Warrants (the "Amendment") whereby the Company agreed to amend the Warrants to purchase up to 4,450,063 shares of Common Stock held by such holders by reducing the exercise price of the Warrants to \$0.20 per share of Common Stock.

Accordingly, this Supplement amends and supplements the Prospectus Supplement to reflect an amendment of the exercise price of certain of the Warrants to purchase up to 4,450,063 shares of Common Stock from \$3.60 per share of Common Stock to \$0.20 per share of Common Stock in accordance with the terms of the Amendment and all references in the Prospectus Supplement to the exercise price with respect to Warrants to purchase up to 4,450,063 shares of Common Stock are hereby amended and restated to reflect an exercise price of \$0.20 per share of Common Stock. Following the Amendment, if all of the amended Warrants are exercised for cash, we would receive gross proceeds of approximately \$890,013. The exercise price of all Warrants not so amended shall remain \$3.60 per share of Common Stock.

The information in this Supplement modifies and supersedes, in part, the information contained in the Prospectus Supplement. Any information that is modified or superseded in the Supplement shall not be deemed to constitute a part of the Prospectus Supplement, except as so modified or superseded by this Supplement. We may further amend or supplement the Prospectus Supplement from time to time by filing additional amendments or supplements. You should read the entire Prospectus Supplement and any amendments or supplements carefully before you make an investment decision.

The Company's Common Stock is traded on the Nasdaq Capital Market under the symbol "WINT." On January 19, 2023, the Nasdaq Official Closing Price (NOCP) of the Company's Common Stock was \$0.2152 per share.

Investing in our Common Stock involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in the Prospectus Supplement, in our Annual Report on Form 10-K for the year ended December 31, 2021, and in our subsequently filed periodic and current reports and documents incorporated by reference therein and herein, which we file with the Securities and Exchange Commission, which describe specific risks and other information that should be considered before you make an investment decision.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities or determined if the Prospectus Supplement, this Supplement, or any supplements or amendments relating hereto and thereto, 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 Supplement, as well as the other information contained in documents that are incorporated by reference into this Supplement and the Prospectus Supplement. The Prospectus Supplement, and the documents that are incorporated by reference into the Prospectus Supplement, contain forward-looking statements regarding events, conditions, and financial trends that may affect our plans of operations, 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 in the "Risk Factors" section of the Prospectus Supplement and the documents that are incorporated by reference into the Prospectus Supplement 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 Supplement.

The date of this Supplement is January 20, 2023