

2,758,620 Units

Consisting of One Share of Common Stock and

A Warrant to Purchase One Share of Common Stock

This prospectus supplement, dated February 21, 2023 (this "Supplement"), filed by Windtree Therapeutics, Inc. (the "Company"), modifies and supplements certain information contained in the Company's prospectus filed pursuant to Rule 424(b) under the Securities Act of 1933, as amended, dated May 20, 2020 (the "Prospectus"), as part of the Company's Form S-1 Registration Statement, declared effective by the Securities and Exchange Commission on May 19, 2020. This Supplement is not complete without, and may not be delivered or used except in connection with, the Prospectus, including all amendments and supplements thereto. The Prospectus relates to the offering of 2,758,620 units (the "Units") consisting of one share of Company common stock, par value \$0.001 per share ("Common Stock"), and a warrant to purchase one share of Common Stock (the "Warrant", and collectively the "Warrants") (and the shares of Common Stock issuable from time to time upon exercise of the Warrants) pursuant to the terms of an underwriting agreement that we entered into on May 20, 2020.

On February 21, 2023, the Company entered into warrant amendment agreements with a warrant holder of the Warrants (the "Amendment") whereby the Company agreed to amend the Warrants to purchase up to 275,862 shares of Common Stock held by such holder by reducing the exercise price of the Warrants to \$0.1411 per share of Common Stock.

Accordingly, this Supplement amends and supplements the Prospectus to reflect an amendment of the exercise price of certain of the Warrants to purchase up to 275,862 shares of Common Stock from \$7.975 per share of Common Stock to \$0.1411 per share of Common Stock in accordance with the terms of the Amendment and all references in the Prospectus to the exercise price with respect to Warrants to purchase up to 275,862 shares of Common Stock are hereby amended and restated to reflect an exercise price of \$0.1411 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 \$38,924. The exercise price of all Warrants not so amended shall remain \$7.975 per share of Common Stock.

The information in this Supplement modifies and supersedes, in part, the information contained in the Prospectus. Any information that is modified or superseded in this Supplement shall not be deemed to constitute a part of the Prospectus, except as so modified or superseded by this Supplement. We may further amend or supplement the Prospectus from time to time by filing additional amendments or supplements. You should read the entire Prospectus 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 February 17, 2023, the Nasdaq Official Closing Price (NOCP) of the Company's Common Stock was \$0.1411 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, 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, 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, as well as the other information contained in documents that are incorporated by reference into this Supplement and the Prospectus. The Prospectus, and the documents that are incorporated by reference into the Prospectus, 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 as a result of various factors. Cautionary statements in the "Risk Factors" section of the Prospectus and the documents that are incorporated by reference into 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.

The date of this Supplement is February 21, 2023