

Free Writing Prospectus

Diffusion Pharmaceuticals Inc. (the “Company”) has filed a registration statement on Form S-3 (including a prospectus) with the Securities and Exchange Commission (the “SEC”) for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement, the preliminary prospectus supplement dated February 11, 2021, the information incorporated therein by reference, and the other documents the Company has filed with the SEC for more complete information about the Company and the offering.

The information in this free writing prospectus supplements the preliminary prospectus supplement dated February 11, 2021, as follows:

DIFFUSION PHARMACEUTICALS INCREASES PREVIOUSLY ANNOUNCED BOUGHT DEAL OFFERING OF COMMON STOCK TO \$30 MILLION

CHARLOTTESVILLE, Va., February 11, 2021 -- **Diffusion Pharmaceuticals Inc. (NASDAQ: DFFN)** (“Diffusion” or the “Company”), an innovative clinical stage biopharmaceutical company developing novel therapies to enhance the diffusion of oxygen to tissues with low oxygen levels, announced today that, due to demand, the underwriter has agreed to increase the size of the previously announced public offering and purchase on a firm commitment basis 29,268,294 shares of common stock of the Company at a price to the public of \$1.025 per share, less underwriting discounts and commissions. The closing of the offering is expected to occur on or about February 17, 2021, subject to satisfaction of customary closing conditions.

H.C. Wainwright & Co. is acting as the sole book-running manager for the offering.

The Company also has granted to the underwriter a 30-day option to purchase up to an additional 4,390,244 shares of common stock at the public offering price, less underwriting discounts and commission.

The gross proceeds of the offering are expected to be approximately \$30,000,000, before deducting underwriting discounts and commissions and offering expenses payable by Diffusion and assuming no exercise of the option to purchase additional shares. Diffusion intends to use the net proceeds of the offering to fund research and development of our lead product candidate, TSC, including the TCOM Study, the DLCO Study, and other clinical trial activities, and for general corporate purposes.

The shares of common stock described above are being offered by the Company pursuant to a "shelf" registration statement on Form S-3 (File No. 333-249057) filed with the Securities and Exchange Commission (SEC) and declared effective on October 2, 2020 and the accompanying prospectus contained therein. The offering of the shares of common stock is being made only by means of a prospectus, including a prospectus supplement, forming a part of the effective registration statement. A preliminary prospectus supplement and the accompanying prospectus relating to this offering were filed with the SEC and are available on the SEC's website at www.sec.gov. Electronic copies of the preliminary prospectus supplement and the accompanying prospectus relating to this offering, and the final prospectus supplement and the accompanying prospectus relating to this offering when filed, may also be obtained by contacting H.C. Wainwright & Co., LLC at 430 Park Avenue, 3rd Floor, New York, NY 10022, by e-mail at placements@hcwco.com or by calling 646-975-6996.

This announcement is neither an offer to sell, nor a solicitation of an offer to buy, any of these securities and shall not constitute an offer, solicitation or sale in any state or jurisdiction in which such offer, solicitation or sale is unlawful. Any offer, if at all, will be made only by means of the prospectus forming a part of the effective registration statement.

About Diffusion Pharmaceuticals Inc.

Diffusion Pharmaceuticals Inc. is an innovative biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to the areas where it is needed most. Diffusion's lead product candidate, TSC, is being developed to enhance the diffusion of oxygen to tissues with low oxygen levels, also known as hypoxia, a serious complication of many of medicine's most intractable and difficult-to-treat conditions. In addition to TSC, Diffusion's product candidate DFN-529, a novel PI3K/Akt/mTOR pathway inhibitor, is in early-stage development. For more information, please visit us at www.diffusionpharma.com.

Forward-Looking Statements

This press release includes express and implied forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including regarding the anticipated timing, size, pricing, and closing of the offering. The Company may, in some cases, use terms such as "believes", "estimates", "anticipates", "expects", "plans", "intends", "may", "could", "might", "will", "should", "approximately", or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Although the Company believes that it has a reasonable basis for each forward-looking statement contained herein, forward-looking statements by their nature involve risks and uncertainties, known and unknown, many of which are beyond the Company's control, and as a result the Company's actual results could differ materially from those expressed or implied in any forward-looking statement. Particular risk and uncertainties include, among other things, those related to: market and other conditions, the completion of the offering, the satisfaction of customary closing conditions related to the offering and the intended use of net proceeds from the public offering; the Company's ability to design, initiate, execute, and complete its ongoing and planned studies evaluating TSC; the Company's ability to obtain additional financing; the Company's ability to develop and commercialize TSC or any other product candidate; the ongoing COVID-19 pandemic; general economic, political, business, industry, and market conditions; and the other factors discussed under the heading "Risk Factors" in the Company's filings with the U.S. Securities and Exchange Commission ("SEC"). Any forward-looking statements in this press release speak only as of the date hereof (or such earlier date as may be identified) and, except as required by applicable law, rule, or regulation, the Company undertakes no obligation to update any such statements after the date hereof.

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