

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-3
REGISTRATION STATEMENT
UNDER THE SECURITIES ACT OF 1933

BioCryst Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation or organization)

62-1413174
(I.R.S. Employer Identification Number)

4505 Emperor Blvd., Suite 200
Durham, North Carolina 27703
(919) 859-1302
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Jon P. Stonehouse
President and Chief Executive Officer
4505 Emperor Blvd., Suite 200
Durham, North Carolina 27703
(919) 859-1302
(Name, address, including zip code, and telephone number, including area code, of agent for service)

With a copy to:
Brian Lane, Esq.
Robyn Zolman, Esq.
Gibson, Dunn & Crutcher LLP
1050 Connecticut Avenue, NW
Washington, DC 20036
(202) 955-8500

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement, as determined by market conditions.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, check the following box:

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, other than securities offered only in connection with dividend or interest reinvestment plans, please check the following box:

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

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.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer Accelerated filer
Non-accelerated filer Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of Securities Act.

CALCULATION OF REGISTRATION FEE

| Title of Each Class of Securities to be Registered | Amount to be Registered ⁽¹⁾ | Proposed Maximum Offering Price Per Unit ⁽¹⁾⁽²⁾ | Proposed Maximum Aggregate Offering Price ⁽¹⁾ | Amount of Registration Fee ⁽³⁾ |
|--|--|--|--|---|
| Common Stock, \$0.01 par value | | | | |
| Preferred Stock, \$0.01 par value | | | | |
| Depository Shares | | | | |
| Purchase Contracts | | | | |
| Warrants | | | | |
| Debt Securities | | | | |
| Units | | | | |
| Total | (1) | N/A | (1) | (3) |

- (1) There are being registered under this registration statement an indeterminate number of securities of each identified class of the registrant, all at indeterminate prices. Any securities registered under this registration statement may be sold separately or as units with other securities registered hereunder. Separate consideration may or may not be received for securities that are issuable on exercise, conversion or exchange of other securities. Pursuant to Rule 457(i) under the Securities Act, the securities registered hereunder also include such indeterminate number of shares of common stock, preferred stock, depository shares, purchase contracts, warrants, debt securities and units as may be issued upon exercise, settlement, exchange or conversion of any securities registered hereunder that provide for those issuances. In addition, pursuant to Rule 416 under the Securities Act, the securities registered hereunder include such indeterminate number of securities as may be issuable with respect to the securities being registered hereunder as a result of stock splits, stock dividends or similar transactions.
- (2) The proposed maximum offering price per unit is not specified as to each class of securities to be registered, pursuant to General Instruction II.D of Form S-3 under the Securities Act. The proposed maximum offering price per unit will be determined from time to time by the registrant in connection with, and at the time of, the issuance of the securities registered hereunder.
- (3) In accordance with Rules 456(b) and 457(r), the registrant is deferring payment of all of the registration fee.



BioCryst Pharmaceuticals, Inc.

**Common Stock
Preferred Stock
Depositary Shares
Purchase Contracts
Warrants
Debt Securities
Units**

By this prospectus, we may from time to time offer securities to the public. We will provide specific terms of these securities in supplements to this prospectus. You should read this prospectus, the applicable prospectus supplement, and the information incorporated by reference in this prospectus and the applicable prospectus supplement carefully before you invest.

Our common stock, par value \$0.01 per share, trades on The Nasdaq Global Select Market under the symbol "BCRX."

We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus or any prospectus supplement. We take no responsibility for, and can provide no assurances as to the reliability of, any information other than the information contained in or incorporated by reference in this prospectus or any prospectus supplement. We are not making or soliciting an offer of any securities other than the securities described in this prospectus and any prospectus supplement. We are not making or soliciting an offer of these securities in any state or jurisdiction where the offer is not permitted or in any circumstances in which such offer or solicitation is unlawful. You should not assume that the information contained or incorporated by reference in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents.

Investing in these securities involves a high degree of risk. See "Risk Factors" on page 2 of this prospectus, in the applicable prospectus supplement we will deliver with this prospectus and in the documents incorporated herein and therein by reference.

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time, or through a combination of these methods. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement. This prospectus may not be used to sell any securities unless accompanied by a prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 1, 2021.

TABLE OF CONTENTS

| | Page |
|--|--------------------|
| ABOUT THIS PROSPECTUS | i |
| PROSPECTUS SUMMARY | 1 |
| RISK FACTORS | 2 |
| INFORMATION REGARDING FORWARD-LOOKING STATEMENTS | 3 |
| USE OF PROCEEDS | 5 |
| DESCRIPTION OF COMMON STOCK, PREFERRED STOCK AND DEPOSITARY SHARES | 6 |
| DESCRIPTION OF PURCHASE CONTRACTS | 10 |
| DESCRIPTION OF WARRANTS | 11 |
| DESCRIPTION OF DEBT SECURITIES | 12 |
| DESCRIPTION OF UNITS | 17 |
| PLAN OF DISTRIBUTION | 18 |
| LEGAL MATTERS | 21 |
| EXPERTS | 21 |
| WHERE YOU CAN FIND MORE INFORMATION | 22 |
| INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE | 22 |

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using a “shelf” registration or continuous offering process. Under this registration statement, we may sell any combination of the securities described in this prospectus from time to time, either separately or in units, in one or more offerings.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement containing specific information about the terms of that offering. That prospectus supplement may add, update or change information contained in this prospectus and will also include the following information:

- the type and amount of securities that we propose to sell;
- the public offering price of the securities;
- the names of any underwriters, agents or dealers through or to which the securities will be sold;
- any compensation of those underwriters, agents or dealers;
- information about any securities exchanges or automated quotation systems on which the securities will be listed or traded;
- any risk factors applicable to the securities that we propose to sell; and
- any other material information about the offering and sale of the securities.

If there is any inconsistency between the information in this prospectus and any prospectus supplement, you should rely on the information in the prospectus supplement. You should read both this prospectus and any prospectus supplement together with the additional information described under the heading “Where You Can Find More Information.” The registration statement containing this prospectus, including the exhibits to the registration statement, provides additional information about us and the securities offered under this prospectus. The registration statement, including the exhibits, can be read at the SEC’s website referenced under the heading “Where You Can Find More Information.”

All references to “Company,” “BioCryst,” “we,” “our,” or “us” refer solely to BioCryst Pharmaceuticals, Inc. and not to the persons who manage us or sit on our Board of Directors. All trade names used in this prospectus are either our registered trademarks or trademarks of their respective holders.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere or incorporated by reference into this prospectus. Because it is a summary, it does not contain all of the information that you should consider before investing in our securities. You should read this entire prospectus carefully, including the section entitled “Risk Factors” and the documents that we incorporate by reference into this prospectus, before making an investment decision.

Business of BioCryst Pharmaceuticals, Inc.

We are a commercial-stage biotechnology company that discovers novel, oral, small-molecule medicines. We focus on oral treatments for rare diseases in which significant unmet medical needs exist and an enzyme plays the key role in the biological pathway of the disease. We integrate the disciplines of biology, crystallography, medicinal chemistry and computer modeling to discover and develop small molecule pharmaceuticals through the process known as structure-guided drug design.

We are a Delaware corporation originally founded in 1986. Our principal executive offices are located at 4505 Emperor Blvd. Suite 200, Durham, North Carolina 27703, and our telephone number is (919) 859-1302. For more information about us, please visit our website at <http://www.biocryst.com>. The information on our website is not incorporated by reference into this prospectus.

RISK FACTORS

Investing in our securities involves risks. Our business is influenced by many factors that are difficult to predict and beyond our control and that involve uncertainties that may materially affect our business, results of operations, financial condition or cash flows, or the value of these securities. These risks and uncertainties are described in the risk factors section of the documents that are incorporated by reference in this prospectus. Any subsequent prospectus supplement may contain a discussion of additional risks applicable to an investment in us and the particular type of securities we are offering under such prospectus supplement. You should carefully consider all of the information contained in or incorporated by reference in this prospectus and in the applicable prospectus supplement before you invest in our securities.

INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any subsequent prospectus supplement, including the information we incorporate by reference, contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”) and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), which are subject to the “safe harbor” created in Section 21E. All statements other than statements of historical facts contained in this prospectus, any subsequent prospectus supplement and the information we incorporate by reference are forward-looking statements. These forward-looking statements can generally be identified by the use of words such as “may,” “will,” “intends,” “plans,” “believes,” “anticipates,” “expects,” “estimates,” “predicts,” “potential,” the negative of these words or similar expressions. Statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

- the preclinical development, clinical development, commercialization, or post-marketing studies of our products and product candidates, including ORLADEYO™ (berotralstat), BCX9930, BCX9250, peramivir, galidesivir, and early stage discovery programs;
- the timing and success of our commercialization of ORLADEYO in the U.S. and elsewhere;
- the potential for government stockpiling orders of our products and product candidates, including the timing or likelihood of entering into any U.S. government stockpile order and our ability to execute any such order;
- the potential funding from our contracts with the Biomedical Advanced Research and Development Authority within the U.S. Department of Health and Human Services and the National Institute of Allergy and Infectious Diseases for the development of galidesivir;
- additional regulatory approvals, or milestones, royalties or profit from sales of our products by us or our partners;
- the implementation of our business model, strategic plans for our business, products, product candidates and technology;
- our ability to establish and maintain collaborations or out-license rights to our products and product candidates;
- plans, programs, progress and potential success of our collaborations, including Torii Pharmaceutical Co., Ltd. for ORLADEYO in Japan, Shionogi & Co., Ltd. and Green Cross Corporation for peramivir in their territories, and Mundipharma International Corporation Limited for mundesine;
- our and our subsidiary guarantors’ ability to satisfy obligations under our \$200.0 million Credit Agreement with Athyrium Opportunities III Co-Invest 1 LP and to comply with the covenants as set forth in the agreements governing our debt obligations;
- the ability of our subsidiary, JPR Royalty Sub LLC, to satisfy its obligations in respect of the Pharma Senior Secured 14.0% Notes due 2020;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products, product candidates, and technology;
- our ability to operate our business without infringing the intellectual property rights of others;
- estimates of our expenses, revenues, capital requirements, annual cash utilization, and our needs for additional financing;
- the timing or likelihood of regulatory filings or regulatory agreements, deferrals, and approvals;
- our ability to manage our liquidity needs, including our ability to raise additional capital to fund our operations or repay our recourse debt obligations;
- our financial performance; and
- competitive companies, technologies, and our industry.

[TABLE OF CONTENTS](#)

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under “Risk Factors” and elsewhere in this prospectus, any subsequent prospectus supplement and the documents incorporated by reference herein and therein. Any forward-looking statement reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

Discussions containing these forward-looking statements are also included in “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” incorporated by reference from our most recent Annual Report on Form 10-K, and in our Current Reports on Form 8-K filed subsequent to the Annual Report, as well as any amendments we make to those filings or any future filings we make with the SEC.

USE OF PROCEEDS

Except as otherwise described in the applicable prospectus supplement, the net proceeds we expect to receive from the sale of any securities offered hereunder will be added to our general funds and used for general corporate purposes, which may include, but are not limited to:

- funding commercialization, development, manufacturing and regulatory activities for ORLADEYO;
- advancing the development of other pipeline compounds for rare disease targets, including paroxysmal nocturnal hemoglobinuria (PNH) and other complement-mediated diseases and fibrodysplasia ossificans progressiva (FOP);
- post-approval commitments for RAPIVAB™;
- funding our research and development efforts; and
- capital expenditures and general working capital needs.

We may also use a portion of the net proceeds to acquire or invest in businesses, assets, products and technologies that are complementary to our own, although we are not currently contemplating or negotiating any such acquisitions or investments.

The amount and timing of these expenditures will depend on a number of factors, including our success in commercializing and achieving market acceptance of ORLADEYO, the progress of our research and development efforts, and amounts received under our existing and any future government contracts and collaboration arrangements, as well as the amount of cash used in our operations. Accordingly, our management will have broad discretion in the application of these proceeds, and investors will be relying on the judgment of our management with regard to the use of these proceeds. Pending application of the net proceeds as described above, we intend to invest the net proceeds in investment grade interest bearing instruments.

DESCRIPTION OF COMMON STOCK, PREFERRED STOCK AND DEPOSITARY SHARES

The following summary of our capital stock is based on and qualified in its entirety by reference to our Third Restated Certificate of Incorporation, as amended (the “Certificate of Incorporation”), and our Amended and Restated Bylaws, as amended (the “Bylaws”), each of which are incorporated by reference into this prospectus. See “Where You Can Find More Information.”

Authorized Capital Stock

Under the Certificate of Incorporation, we are currently authorized to issue up to 450,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share. On February 24, 2021, there were 177,521,693 shares of common stock outstanding and no shares of preferred stock outstanding. The number of authorized shares of common stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the capital stock of the Company entitled to vote.

Common Stock

Holders of our common stock are entitled to one vote per share on all matters submitted to a vote of stockholders. There are no cumulative voting rights. Directors are elected by a plurality of the votes cast by the stockholders entitled to vote. Except as provided otherwise in the Certificate of Incorporation, the Bylaws, or the General Corporation Law of the State of Delaware (the “DGCL”), the holders of a majority of our common stock present in person or represented by proxy and voting on a matter shall decide any matter to be voted upon by the stockholders at a meeting.

Holders of our common stock have the right to receive dividends as and when declared by our Board of Directors (the “Board”) from funds legally available therefor, subject to any preferential dividend rights of any Preferred Stock then outstanding. We have never paid cash dividends on our common stock.

Upon our dissolution or liquidation, whether voluntary or involuntary, holders of our common stock are entitled to receive all assets legally available for distribution to stockholders, subject to any preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive rights and have no rights to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. All outstanding shares of our common stock are validly issued, fully paid and nonassessable.

Preferred Stock

Preferred stock may be issued from time to time in one or more series, each such series to have such terms as determined by the Board. The Board has the authority to determine and fix such voting powers, full or limited, or no voting powers, and such designations, preferences, and relative participating, optional or other special rights, and qualifications, limitations, or restrictions thereof, including without limitation dividend rights, conversion rights, redemption privileges, and liquidation preferences, without further vote or action by our stockholders. We will distribute a prospectus supplement with regard to each particular series of preferred stock that will describe the terms and provisions of that series of preferred stock. The rights of the holders of any Preferred Stock that may be issued may adversely affect the rights of the holders of our common stock. The issuance of Preferred Stock could make it more difficult for third parties to acquire a majority of our outstanding voting stock.

Anti-Takeover Provisions

Some provisions of the Certificate of Incorporation, the Bylaws, and DGCL may have the effect of delaying, discouraging, or preventing a change in control of us or changes in our management. Pursuant to the Certificate of Incorporation and the Bylaws:

- the Board is authorized to issue “blank check” preferred stock without further stockholder approval;
- the Board is classified, with members thereof serving staggered three-year terms;
- stockholders may not cumulate votes in the election of directors;

TABLE OF CONTENTS

- vacancies on the Board may be filled only by the Board;
- stockholders may remove directors only for cause and only by the affirmative vote of the holders of at least 75 percent of the total number of votes entitled to be cast by the holders of all of the shares of our capital stock then entitled to vote generally in the election of directors (a “supermajority vote”);
- stockholders may take action only at a duly called meeting of the stockholders, and stockholders are not permitted to act by written consent;
- special meetings of stockholders may be called only by the Board; and
- stockholders must satisfy advance notice procedures to submit proposals or nominate directors for consideration at a stockholders meeting.

A supermajority vote is required to amend Article NINTH and Article TENTH of the Certificate of Incorporation, which pertain to the number, classification, and removal of our directors, the creation and filling of vacancies on the Board, the requirement that actions of stockholders be taken at a duly called meeting and not by written consent, and the requirement that special meetings only be called by the Board.

In addition, we are subject to the provisions of Section 203 of the DGCL. In general, the statute prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years after the date that the person became an interested stockholder unless, with some exceptions, the business combination or the transaction in which the person became an interested stockholder is approved in a prescribed manner. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the stockholder, and an “interested stockholder” is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of the corporation’s outstanding voting stock. This provision may have the effect of delaying, deferring, or preventing a change in control without further action by the stockholders.

Exclusive Forum for Certain Actions

The Bylaws provide that unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, stockholders, employees, or agents to us or to our stockholders; (iii) any action asserting a claim against us or any of our directors, officers, stockholders, employees, or agents arising out of or relating to any provision of the DGCL, the Certificate of Incorporation, or the Bylaws; or (iv) any action against us or any of our directors, officers, stockholders, employees, or agents governed by the internal affairs doctrine of the State of Delaware. The Bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock will be deemed to have notice of, and to have consented to, this choice of forum provision. This exclusive forum provision may limit a stockholder’s ability to choose its preferred judicial forum for disputes with us or our directors, officers, employees, or agents, which may discourage the filing of lawsuits with respect to such claims. This exclusive forum provision does not apply to establish the Delaware Court of Chancery as the forum for actions or proceedings brought to enforce a duty or liability created by the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction.

Depository Shares

We may, at our option, elect to offer fractional shares of preferred stock, rather than full shares of preferred stock. If we exercise this option, we will issue to the public receipts for depository shares, and each of these depository shares will represent a fraction, to be set forth in the applicable prospectus supplement, of a share of a particular series of preferred stock.

The shares of any series of preferred stock underlying the depository shares will be deposited under a deposit agreement between us and a bank or trust company selected by us. The depository will have its principal office in the United States and a combined capital and surplus of at least \$50,000,000. Subject to the terms of the deposit agreement, each owner of a depository share will be entitled, in proportion to the applicable fraction of a share of preferred stock underlying the depository share, to all the rights and preferences of the preferred stock underlying that depository share. Those rights may include dividend, voting, redemption, conversion and liquidation rights.

TABLE OF CONTENTS

The depositary shares will be evidenced by depositary receipts issued under a deposit agreement. Depositary receipts will be distributed to those persons purchasing the fractional shares of preferred stock underlying the depositary shares, in accordance with the terms of the offering. The following description of the material terms of the deposit agreement, the depositary shares and the depositary receipts is only a summary and you should refer to the forms of the deposit agreement and depositary receipts that will be filed with the SEC in connection with the offering of the specific depositary shares.

Pending the preparation of definitive engraved depositary receipts, the depositary, upon our written order, may issue temporary depositary receipts substantially identical to the definitive depositary receipts but not in definitive form. These temporary depositary receipts would entitle their holders to all the rights of definitive depositary receipts. Temporary depositary receipts would be exchangeable for definitive depositary receipts at our expense.

Dividends and Other Distributions. The depositary will distribute all cash dividends or other cash distributions received with respect to the underlying stock to the record holders of depositary shares in proportion to the number of depositary shares owned by those holders.

If there were a distribution other than in cash, the depositary would distribute property received by it to the record holders of depositary shares that are entitled to receive the distribution, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary, with our approval, would sell the property and distribute the net proceeds from the sale to the applicable holders.

Withdrawal of Underlying Preferred Stock. Unless we provide otherwise in a prospectus supplement, holders may surrender depositary receipts at the principal office of the depositary and, upon payment of any unpaid amount due to the depositary, would be entitled to receive the number of whole shares of underlying preferred stock and all money and other property represented by the related depositary shares. We will not issue any partial shares of preferred stock. If the holder delivers depositary receipts evidencing a number of depositary shares that represent more than a whole number of shares of preferred stock, the depositary will issue a new depositary receipt evidencing the excess number of depositary shares to that holder.

Redemption of Depositary Shares. If a series of preferred stock represented by depositary shares were subject to redemption, the depositary shares would be redeemed from the proceeds received by the depositary resulting from the redemption, in whole or in part, of that series of underlying stock held by the depositary. The redemption price per depositary share would be equal to the applicable fraction of the redemption price per share payable with respect to that series of underlying stock. Whenever we redeem shares of underlying stock that are held by the depositary, the depositary will redeem, as of the same redemption date, the number of depositary shares representing the shares of underlying stock so redeemed. If fewer than all the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or proportionately, as may be determined by the depositary.

Voting. Upon receipt of notice of any meeting at which the holders of the underlying stock are entitled to vote, the depositary will mail the information contained in the notice to the record holders of the depositary shares underlying the preferred stock. Each record holder of the depositary shares on the record date, which will be the same date as the record date for the underlying stock, will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the amount of the underlying stock represented by that holder's depositary shares. The depositary will then try, as far as practicable, to vote the number of shares of preferred stock underlying those depositary shares in accordance with those instructions, and we will agree to take all actions which may be deemed necessary by the depositary to enable the depositary to do so. The depositary will not vote the underlying shares to the extent it does not receive specific instructions from the holders of depositary shares underlying the preferred stock.

Conversion of Preferred Stock. If the prospectus supplement relating to the depositary shares provides that the deposited preferred stock is convertible into or exchangeable for common stock or preferred stock of another series of BioCryst or securities of any third party, the following will apply. The depositary shares, as such, will not be convertible into or exchangeable for any securities of BioCryst or any third party. Rather, any holder of the depositary shares may surrender the related depositary receipts to the depositary with written instructions to instruct us to cause conversion or exchange of the preferred stock represented by the depositary shares into or for whole shares of common stock or shares of another series of preferred stock of BioCryst or securities of the relevant third party, as applicable. Upon receipt of those instructions and any amounts payable by the holder in

TABLE OF CONTENTS

connection with the conversion or exchange, we will cause the conversion or exchange using the same procedures as those provided for conversion or exchange of the deposited preferred stock. If only some of the depositary shares are to be converted or exchanged, a new depositary receipt or receipts will be issued for any depositary shares not to be converted or exchanged.

Amendment and Termination of the Depositary Agreement. The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended at any time by agreement between us and the depositary. However, any amendment which materially and adversely alters the rights of the holders of depositary shares will not be effective unless the amendment has been approved by the holders of at least a majority of the depositary shares then outstanding. The deposit agreement may be terminated by us or by the depositary only if (a) all outstanding depositary shares have been redeemed or converted or exchanged for any other securities into which the underlying preferred stock is convertible or exchangeable or (b) there has been a final distribution of the underlying stock in connection with our liquidation, dissolution or winding up and the underlying stock has been distributed to the holders of depositary receipts.

Charges of Depositary. We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will also pay charges of the depositary in connection with the initial deposit of the underlying stock and any redemption of the underlying stock. Holders of depositary receipts will pay other transfer and other taxes and governmental charges and those other charges, including a fee for any permitted withdrawal of shares of underlying stock upon surrender of depositary receipts, as are expressly provided in the deposit agreement to be for their accounts.

Reports. The depositary will forward to holders of depositary receipts all reports and communications from us that we deliver to the depositary and that we are required to furnish to the holders of the underlying stock.

Limitation on Liability. Neither we nor the depositary will be liable if either of us is prevented or delayed by law or any circumstance beyond our control in performing our respective obligations under the deposit agreement. Our obligations and those of the depositary will be limited to performance in good faith of our respective duties under the deposit agreement. Neither we nor the depositary will be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or underlying stock unless satisfactory indemnity is furnished. We and the depositary may rely upon written advice of counsel or accountants, or upon information provided by persons presenting underlying stock for deposit, holders of depositary receipts or other persons believed to be competent and on documents believed to be genuine.

Resignation and Removal of Depositary. The depositary may resign at any time by delivering notice to us of its election to resign. We may remove the depositary at any time. Any resignation or removal will take effect upon the appointment of a successor depositary and its acceptance of the appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having a combined capital and surplus of at least \$50,000,000.

DESCRIPTION OF PURCHASE CONTRACTS

The following is a general description of the terms of the purchase contracts we may issue from time to time. Particular terms of any purchase contracts we offer will be described in the prospectus supplement relating to such purchase contracts. Material U.S. federal income tax considerations applicable to the purchase contracts will also be discussed in the applicable prospectus supplement. You should refer to the form of purchase contract and purchase certificate that we will file with the SEC in connection with the offering of the specific purchase contracts for more complete information.

We may issue purchase contracts, including contracts obligating holders to purchase from us, and obligating us to sell to holders, shares of common stock, preferred stock, depositary shares or debt securities at a future date. The consideration for such common stock, preferred stock, depositary shares or debt securities may be fixed at the time that the purchase contracts are issued or may be determined by reference to a specific formula set forth in the purchase contracts. Any purchase contract may include anti-dilution provisions to adjust the number of shares issuable pursuant to such purchase contract upon the occurrence of certain events.

The applicable prospectus supplement will describe the terms of any purchase contracts in respect of which this prospectus is being delivered, including, to the extent applicable, the following:

- whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;
- whether the purchase contracts are to be prepaid or not;
- whether the purchase contracts will be issued as part of a unit and, if so, the other securities comprising the unit;
- whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance, or level of the securities subject to purchase under the purchase contract;
- any acceleration, cancellation, termination, or other provisions relating to the settlement of the purchase contracts; and
- whether the purchase contracts will be issued in full registered or global form.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase our preferred stock, depository shares, common stock or debt securities or any combination thereof. Warrants may be issued independently or together with any other securities in the form of units, and may be attached to, or separate from, such securities. The terms of any warrants to be issued and a description of the material provisions of the applicable warrant agreement will be set forth in the applicable prospectus supplement. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. You should refer to the form of warrant agreement and warrant that we file with the SEC in connection with the offering of the specific warrants for more complete information.

The prospectus supplement will describe the terms of any warrants being offered, including:

- the title and the aggregate number of warrants;
- the price or prices at which the warrants will be issued;
- the currency or currencies in which the price of the warrants will be payable;
- the securities or other rights, including rights to receive payment in cash or securities based on the value, rate or price of one or more specified commodities, currencies, securities or indices, or any combination of the foregoing, purchasable upon exercise of the warrants;
- the price at which, and the currency or currencies in which, the securities or other rights purchasable upon exercise of such warrants may be purchased;
- the periods during which, and places at which, the warrants are exercisable;
- the date or dates on which the warrants shall commence and the date or dates on which the warrants will expire;
- the terms of any mandatory or optional call provisions;
- the price or prices, if any, at which the warrants may be redeemed at the option of the holder or will be redeemed upon expiration;
- whether the warrants will be sold separately or with other securities as part of a unit;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- any provisions for the adjustment of the number or amount of securities receivable upon exercise of warrants;
- the identity of the warrant agent;
- the exchanges, if any, on which the warrants may be listed;
- the maximum or minimum number of warrants which may be exercised at any time;
- if applicable, a discussion of any material United States federal income tax considerations;
- whether the warrants shall be issued in book-entry form; and
- any other terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under an indenture to be entered into between us and U.S. Bank National Association, or another trustee chosen by us that is qualified to act as such under the Trust Indenture Act of 1939, as amended (the “Trust Indenture Act”), and appointed under an indenture. The indenture will be qualified under the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture. We urge you to read the applicable prospectus supplement and any related free writing prospectus related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

TABLE OF CONTENTS

- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$2,000 and multiples of \$1,000 in excess thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depository for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Events of Default and Remedies

Unless otherwise described in the applicable prospectus supplement, an event of default with respect to any series of debt securities will be defined in the indenture or applicable supplemental indenture or authorizing resolution as being:

- our failure to pay interest on any debt security of such series when the same becomes due and payable and the continuance of any such failure for a period of 30 days;
- our failure to pay the principal or premium of any debt security of such series when the same becomes due and payable at maturity, upon acceleration, redemption or otherwise;
- our failure or the failure of any restricted subsidiary to comply with any of its agreements or covenants in, or provisions of, the debt securities of such series or the indenture (as they relate thereto) and such failure continues for a period of 90 days after our receipt of notice of the default from the trustee or from the holders of at least 25% in aggregate principal amount of the then outstanding debt securities of that series (except in the case of a default with respect to the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of our assets (or any other provision specified in the applicable supplemental indenture or authorizing resolution), which will constitute an event of default with notice but without passage of time); or
- certain events of bankruptcy, insolvency or reorganization occur with respect to us.

The indenture will provide that the trustee may withhold notice to the holders of any series of debt securities of any default, except a default in payment of principal or interest, if any, with respect to such series of debt securities, if the trustee considers it in the interest of the holders of such series of debt securities to do so.

The indenture will provide that if any event of default has occurred and is continuing with respect to any series of debt securities, the trustee or the holders of not less than 25% in principal amount of such series of debt securities then outstanding may declare the principal of all the debt securities of such series to be due and payable immediately. However, the holders of a majority in principal amount of the debt securities of such series then outstanding by notice to the trustee may waive any existing default and its consequences with respect to such series of debt securities, other than any event of default in payment of principal or interest. Holders of a majority in principal amount of the then outstanding debt securities of any series may rescind an acceleration with respect to such series and its consequences, except an acceleration due to nonpayment of principal or interest on such series, if the rescission would not conflict with any judgment or decree and if all existing events of default with respect to such series have been cured or waived.

The holders of a majority of the outstanding principal amount of the debt securities of any series will have the right to direct the time, method and place of conducting any proceedings for any remedy available to the trustee with respect to such series, subject to limitations specified in the indenture.

Defeasance

The indenture will permit us to terminate all our respective obligations under the indenture as they relate to any particular series of debt securities, other than the obligation to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal of and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

The indenture will also permit us to terminate all of our respective obligations under the indenture as they relate to any particular series of debt securities, including the obligations to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

TABLE OF CONTENTS

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that (A) we have received from, or there has been published by, the Internal Revenue Service a ruling, or (B) since the date such series of debt securities were originally issued, there has been a change in the applicable federal income tax law, in either case to the effect that, and based thereon such opinion of counsel shall state that, holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

In addition, the indenture will permit us to terminate substantially all our respective obligations under the indenture as they relate to a particular series of debt securities by depositing with the trustee money or government obligations sufficient to pay all principal and interest on such series at its maturity or redemption date if the debt securities of such series will become due and payable at maturity within one year or are to be called for redemption within one year of the deposit.

Transfer and Exchange Rights

A holder will be able to transfer or exchange debt securities only in accordance with the indenture. The registrar may require a holder, among other things, to furnish appropriate endorsements and transfer documents, and to pay any taxes and fees required by law or permitted by the indenture.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, lease, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Amendment, Supplement and Waiver

Without notice to or the consent of any holder, we and the trustee may amend or supplement the indenture or the debt securities of a series to:

- cure any ambiguity, omission, defect or inconsistency;
- comply with the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of our assets;
- provide that specific provisions of the indenture shall not apply to a series of debt securities not previously issued or to make a change to specific provisions of the indenture that only applies to any series of debt securities not previously issued or to additional debt securities of a series not previously issued;
- create a series and establish its terms;
- provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- release a guarantor in respect of any series of debt securities which, in accordance with the terms of indenture applicable to the particular series, ceases to be liable in respect of its guarantee;
- add a guarantor subsidiary in respect of any series of debt securities;
- secure any series of debt securities;
- comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act;
- make any change that does not adversely affect the rights of any holder; or
- conform the provisions of the indenture to the final offering document in respect of any series of debt securities.

TABLE OF CONTENTS

With the exceptions discussed below, we and the trustee may amend or supplement the indenture or the debt securities of a particular series with the written consent of the holders of at least a majority in principal amount of the debt securities of such series then outstanding. In addition, the holders of a majority in principal amount of the debt securities of such series then outstanding may waive any existing default under, or compliance with, any provision of the debt securities of a particular series or of the indenture relating to a particular series of debt securities, other than any event of default in payment of interest or principal. These consents and waivers may be obtained in connection with a purchase of, or tender offer or exchange offer for, debt securities.

Without the consent of each holder affected, we and the trustee may not:

- reduce the amount of debt securities of such series whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest, including defaulted interest;
- reduce the principal of or extend the fixed maturity of any debt security or alter the provisions with respect to redemptions or mandatory offers to repurchase debt securities;
- make any change that adversely affects any right of a holder to convert or exchange any debt security into or for shares of our common shares or other securities, cash or other property in accordance with the terms of such security;
- modify the ranking or priority of the debt securities;
- make any change to any provision of the indenture relating to the waiver of existing defaults, the rights of holders to receive payment of principal and interest on the debt securities, or to the provisions regarding amending or supplementing the indenture or the debt securities of a particular series with the written consent of the holders of such series;
- waive a continuing default or event of default in the payment of principal of or interest on the debt securities; or
- make any debt security payable at a place or in money other than that stated in the debt security, or impair the right of any holder of a debt security to bring suit as permitted by the indenture.

The right of any holder to participate in any consent required or sought pursuant to any provision of the indenture, and our obligation to obtain any such consent otherwise required from such holder, may be subject to the requirement that such holder shall have been the holder of record of debt securities with respect to which such consent is required or sought as of a record date fixed by us in accordance with the indenture.

Governing Law

The laws of the State of New York will govern the indenture and the debt securities.

DESCRIPTION OF UNITS

We may issue units consisting of one or more of the other securities described in this prospectus in any combination, as described in a prospectus supplement. We may issue units in one or more series, which will be described in a prospectus supplement. We will issue the units or hybrid securities under one or more unit agreements, each referred to as a unit agreement, to be entered into between us and a bank or trust company, as unit agent. You should refer to the form of unit agreement and unit certificate that we file with the SEC in connection with the offering of the specific units for more complete information.

The applicable prospectus supplement will describe:

- the designation and the terms of the units and of the securities constituting the units, including whether and under what circumstances the securities comprising the units may be traded separately;
- any additional terms of the governing unit agreement;
- any additional provisions for the issuance, payment, settlement, transfer or exchange of the units or of the preferred stock, common stock, stock purchase contracts, depositary shares, warrants or debt securities constituting the units; and
- any applicable United States federal income tax consequences.

PLAN OF DISTRIBUTION

We may sell the securities being offered hereby at prices and under terms then prevailing, at prices related to the then current market price or in negotiated transactions from time to time in one or more of the following ways:

- directly to one or more purchasers;
- through one or more underwriters on a firm commitment or best-efforts basis;
- through broker-dealers, who may act as agents or principals, including a block trade in which a broker or dealer so engaged will attempt to sell as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- through agents;
- through remarketing firms;
- in privately negotiated transactions; or
- in any combination of these methods of sale.

We will set forth in a prospectus supplement the terms of the offering of securities, including:

- the name or names of any underwriters, dealers or agents;
- the number of securities and purchase price of the securities being offered and the proceeds we will receive from the sale;
- any underwriting discounts and commissions or agency fees and other items constituting underwriters' or agents' compensation;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any delayed delivery arrangements;
- any discounts or concessions allowed or re-allowed or paid to dealers; and
- any securities exchange on which the securities may be listed.

The distribution of the securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, at market prices prevailing at the time of sale, at prices related to the prevailing market prices or at negotiated prices.

We may designate agents who agree to use their reasonable efforts to solicit purchases for the period of their appointment or to sell securities on a continuing basis. Agents may receive compensation in the form of commissions, discounts or concessions from us. Agents may also receive compensation from the purchasers of the securities for whom they sell as principals. Each particular agent will receive compensation in amounts negotiated in connection with the sale, which might be in excess of customary commissions. Agents and any other participating broker-dealers may be deemed to be "underwriters" within the meaning of Section 2(11) of the Securities Act of 1933 (the "Securities Act") in connection with sales of the securities. Accordingly, any commission, discount or concession received by them and any profit on the resale of the securities purchased by them may be deemed to be underwriting discounts or commissions under the Securities Act. We have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their securities. As of the date of this prospectus, there are no special selling arrangements between any broker-dealer or other person and us. No period of time has been fixed within which the securities will be offered or sold.

If required under applicable state securities laws, we will sell the securities only through registered or licensed brokers or dealers. In addition, in some states, we may not sell securities unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and complied with.

If we use underwriters for a sale of securities, the underwriters will acquire the securities for their own account. The underwriters may resell the securities in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the

TABLE OF CONTENTS

underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may change from time to time any initial public offering price and any discounts or concessions the underwriters allow or re-allow or pay to dealers. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement naming the underwriter the nature of any such relationship.

We may use a remarketing firm to offer to sell the securities in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own account or as agents for us. These remarketing firms will offer or sell the securities pursuant to the terms of the securities. A prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket.

If we offer and sell securities through a dealer, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. Any such dealer may be deemed to be an underwriter of the securities so offered and sold. The name of the dealer and the terms of the transactions will be set forth in the applicable prospectus supplement.

We may also sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act.

We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers and agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act. Underwriters, dealers and agents may engage in transactions with or perform services for us in the ordinary course of their businesses.

We may authorize agents, dealers or underwriters to solicit offers to purchase securities at the public offering price under delayed delivery contracts. The terms of these delayed delivery contracts, including when payment for and delivery of the securities sold will be made under the contracts and any conditions to each party's performance set forth in the contracts, will be described in the applicable prospectus supplement. The compensation received by underwriters, agents or dealers soliciting purchases of securities under delayed delivery contracts will be described in the applicable prospectus supplement.

We may enter into derivative or other hedging transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. We may also loan or pledge securities covered by this prospectus and the applicable prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and the applicable prospectus supplement.

Unless otherwise specified in the related prospectus supplement, all securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We may apply to list any series of securities on an exchange, but we are not obligated to do so. Therefore, no assurance can be given as to the liquidity of, or the trading market for, any series of securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by

TABLE OF CONTENTS

the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on The Nasdaq Global Select Market or otherwise.

Any underwriters who are qualified market makers on The Nasdaq Global Select Market may engage in passive market making transactions in the common stock on The Nasdaq Global Select Market in accordance with Rule 103 of Regulation M, during the business day before the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

We will bear all costs, expenses and fees in connection with the registration of the securities, as well as the expense of all commissions and discounts, if any, attributable to sales of the securities by us.

LEGAL MATTERS

Gibson, Dunn & Crutcher LLP has rendered an opinion with respect to the validity of the securities being offered by this prospectus. We have filed this opinion as an exhibit to the registration statement of which this prospectus is a part. If counsel for any underwriters passes on legal matters in connection with an offering made by this prospectus, we will name that counsel in the prospectus supplement relating to that offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2020, and the effectiveness of our internal control over financial reporting as of December 31, 2020, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and our management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2020 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file electronically with the SEC our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements and other information. We make available on or through our website, <http://www.biocryst.com>, free of charge, copies of these filings as soon as reasonably practicable after we electronically file them with or furnish them to the SEC. The information on our website is not incorporated by reference into this prospectus. You can also request copies of such documents by contacting our Investor Relations Department at 4505 Emperor Blvd., Suite 200, Durham, North Carolina 27703 or sending an email to investorrelations@biocryst.com.

The SEC also maintains a website that contains reports, proxy and information statements, and other information about issuers, like BioCryst, that file electronically with the SEC. The address of that site is <http://www.sec.gov>. Unless specifically listed below under “Incorporation of Certain Documents by Reference” the information contained on the SEC website is not incorporated by reference into this prospectus.

We have filed with the SEC a registration statement on Form S-3 that registers the securities we are offering. The registration statement, including the attached exhibits and schedules, contains additional relevant information about us and our securities. The rules and regulations of the SEC allow us to omit certain information included in the registration statement from this prospectus.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information into this prospectus. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus, except for any information that is superseded by information that is included directly in this document.

This prospectus includes by reference the documents listed below that we have previously filed with the SEC and that are not included in or delivered with this document. They contain important information about us and our financial condition.

- Our [Annual Report on Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 1, 2021 (the “2020 Form 10-K”);
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 from our [Definitive Proxy Statement](#) (other than information furnished rather than filed) for our 2020 Annual Meeting of Stockholders, which was filed with the SEC on March 31, 2020; and
- The description of our common stock that is contained in our Registration Statement on Form 8-A (File No. 000-23186) filed with the SEC on January 7, 1994, together with the amendment thereto filed with the SEC on March 14, 1994, as updated by the description of our common stock filed as [Exhibit 4.1](#) to our 2020 Form 10-K, and any other amendments or reports filed for the purpose of updating such description.

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and prior to the termination of our offering of securities shall be deemed to be incorporated by reference herein and to be a part of this prospectus from the date of filing of such documents, excluding any information furnished under Item 2.02 or Item 7.01 of any Current Report on Form 8-K and exhibits filed on such form that are related to such items. Any statement contained in a document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

[TABLE OF CONTENTS](#)

You can obtain any of the documents incorporated by reference in this prospectus from us without charge, excluding any exhibits to those documents unless the exhibit is specifically incorporated by reference as an exhibit to this prospectus. You can obtain documents incorporated by reference in this prospectus at no cost by requesting them in writing or by telephone from us at the following address:

Investor Relations
BioCryst Pharmaceuticals, Inc.
4505 Emperor Blvd., Suite 200
Durham, North Carolina 27703
(919) 859-1302

We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus or any prospectus supplement. We take no responsibility for, and can provide no assurances as to the reliability of, any information other than the information contained in or incorporated by reference in this prospectus or any prospectus supplement. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this document are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you.



BioCryst Pharmaceuticals, Inc.

**Common Stock
Preferred Stock
Depository Shares
Stock Purchase Contracts
Warrants
Debt Securities
Units**

PROSPECTUS

March 1, 2021

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.

The following table sets forth all expenses payable by the registrant in connection with the issuance and distribution of the securities, other than underwriting discounts and commissions. The registrant will bear all of such expenses. All the amounts shown are estimates except the registration fee.

| | |
|------------------------------|-------------|
| Registration fee | \$* |
| Accounting fees and expenses | ** |
| Legal fees and expenses | ** |
| Printing and engraving | ** |
| Miscellaneous | ** |
| Total | <u>\$**</u> |

* Deferred in accordance with Rules 456(b) and 457(r) under the Securities Act of 1933.

** These fees are calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Section 145 of the Delaware General Corporation Law (the “DGCL”) sets forth the circumstances in which a Delaware corporation is permitted and/or required to indemnify its directors and officers. The DGCL permits a corporation to indemnify its directors and officers in certain proceedings if the director or officer has complied with the standard of conduct set out in the DGCL. The standard of conduct requires that the director or officer must have acted in good faith, in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to matters in a criminal proceeding, the director or officer must have had no reason to believe that his or her conduct was unlawful. With respect to suits by or in the right of the corporation, the DGCL permits indemnification of directors and officers if the person meets the standard of conduct, except that it precludes indemnification of directors and officers who are adjudged liable to the corporation, unless the Court of Chancery or the court in which the corporation’s action or suit was brought determines that the director or officer is fairly and reasonably entitled to indemnity for expenses. To the extent that a present or former director or officer of the corporation is successful on the merits or otherwise in his or her defense of a proceeding, the corporation is required to indemnify the director or officer against reasonable expenses incurred in defending himself or herself. The rights provided in Section 145 of the DGCL are not exclusive, and the corporation may also provide for indemnification under bylaw, agreement, vote of stockholders or disinterested directors or otherwise.

The registrant’s Third Restated Certificate of Incorporation, as amended (the “Certificate of Incorporation”), provides for indemnification of any director or officer who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he is or was, or has agreed to become, a director or officer of the registrant, or is or was serving, or agreed to serve, at the request of the registrant, as a director, officer or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf in connection with such action, suit or proceeding and any appeal therefrom, in each case to the fullest extent permitted by the DGCL. The registrant shall not indemnify any person seeking indemnification in connection with a proceeding or part thereof initiated by such person unless the initiation was approved by the Board of Directors of the registrant. The Certificate of Incorporation further provides for permissible indemnification of employees and other agents to the maximum extent permitted by the DGCL and the Certificate of Incorporation with respect to directors and officers.

Section 102(b)(7) of the DGCL provides that a corporation may relieve its directors from personal liability to the corporation or its stockholders for monetary damages for any breach of their fiduciary duty as directors except for (i) a breach of the duty of loyalty; (ii) acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law; (iii) willful or negligent violations of certain provisions in the DGCL

TABLE OF CONTENTS

imposing certain requirements with respect to stock repurchases, redemptions and dividends; or (iv) for any transactions from which the director derived an improper personal benefit. The registrant's Certificate of Incorporation provides that no directors of the registrant shall be liable to the registrant or its stockholders for monetary damages for breach of fiduciary duty as a director to the fullest extent permitted by the DGCL.

In addition, the registrant currently maintains liability insurance for its directors and officers insuring them against certain liabilities asserted against them in their capacities as directors or officers or arising out of such status.

The indemnification provisions noted above may be sufficiently broad to permit indemnification of the registrant's officers and directors for liabilities arising under the Securities Act.

ITEM 16. EXHIBITS.

| <u>Exhibit No.</u> | <u>Description</u> |
|------------------------|--|
| 1.1* | Form of Underwriting Agreement. |
| 4.1 | Third Restated Certificate of Incorporation of the Company. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed December 22, 2006 (File No. 000-23186). |
| 4.2 | Certificate of Amendment to the Third Restated Certificate of Incorporation of the Company. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed July 24, 2007 (File No. 000-23186). |
| 4.3 | Certificate of Amendment to the Third Restated Certificate of Incorporation of the Company. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed May 7, 2014 (File No. 000-23186). |
| 4.4 | Certificate of Increase of Authorized Number of Shares of Series B Junior Participating Preferred Stock. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed November 4, 2008 (File No. 000-23186). |
| 4.5 | Certificate of Increase of Authorized Number of Shares of Series B Junior Participating Preferred Stock of the Company. Incorporated by reference to Exhibit 3.2 to the Company's Form 8-K filed May 7, 2014 (File No. 000-23186). |
| 4.6 | Certificate of Elimination of the Series B Junior Participating Preferred Stock. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed May 13, 2020 (File No. 000-23186). |
| 4.7 | Certificate of Amendment to the Third Restated Certificate of Incorporation of BioCryst Pharmaceuticals, Inc. Incorporated by reference to Exhibit 3.2 to the Company's Form 8-K filed May 13, 2020 (File No. 000-23186). |
| 4.8 | Amended and Restated Bylaws of the Company effective October 29, 2008. Incorporated by reference to Exhibit 3.2 to the Company's Form 8-K filed November 4, 2008 (File No. 000-23186). |
| 4.9 | Amendment to Amended and Restated Bylaws of the Company effective January 21, 2018. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed January 22, 2018. (File No. 001-23186). |
| 4.10 | Specimen Certificate for Registrant's Common Stock. Incorporated by reference to Exhibit 4.7 to the Company's Form S-3 filed November 28, 2008 (File No. 333-155783). |
| 4.11 | Form of Indenture. Incorporated by reference to Exhibit 4.9 to the Company's Form S-3 filed April 24, 2020 (File No. 333-237820). |
| 4.11* | Form of Supplemental Indenture or Officers' Certificate. |
| 4.12* | Form of Global Debt Security. |
| 4.13* | Certificate of Designation of Preferred Stock. |
| 4.14* | Form of Warrant Agreement (including form of Warrant). |
| 4.15* | Form of Deposit Agreement with respect to Depository Shares (including form of Depository Receipt). |
| 4.16* | Form of Purchase Contract (including form of Purchase Certificate). |
| 4.17* | Form of Unit Agreement (including form of Unit Certificate). |
| (5.1) | Opinion of Gibson, Dunn & Crutcher LLP. |
| (23.1) | Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm. |
| (23.2) | Consent of Gibson, Dunn & Crutcher LLP (included in Exhibit 5.1). |
| (24.1) | Power of Attorney (included on the signature page of this Registration Statement). |
| (25.1) | Statement of eligibility of trustee for debt securities on Form T-1. |

* To be filed by amendment hereto or pursuant to a Current Report on Form 8-K to be incorporated herein by reference.

() Filed herewith.

ITEM 17. UNDERTAKINGS.

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (a) To include any prospectus required by Section 10(a)(3) of the Securities Act;
 - (b) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
 - (c) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

Provided, however, that paragraphs (1)(a), (1)(b) and (1)(c) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment 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.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act to any purchaser:
 - (a) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (b) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however,* that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

TABLE OF CONTENTS

- (5) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
- (a) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
 - (b) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
 - (c) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
 - (d) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (6) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act that is incorporated by reference in the registration statement 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.
- (7) 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 described in Item 15, or otherwise, the registrant has been advised that in the opinion of the Commission 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.
- (8) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of section 310 of the Trust Indenture Act ("Act") in accordance with the rules and regulations prescribed by the Commission under section 305(b)(2) of the Act.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Durham, State of North Carolina, on March 1, 2021.

BioCryst Pharmaceuticals, Inc.

By: /s/ Jon P. Stonehouse

Jon P. Stonehouse

President and Chief Executive Officer

POWER OF ATTORNEY

Each of the undersigned officers and directors of BioCryst Pharmaceuticals, Inc. hereby severally constitutes and appoints Jon P. Stonehouse, Anthony Doyle, and Alane Barnes, and each of them singly, his or her true and lawful attorneys-in-fact and agent, with full power to them and each of them singly, with full and several power of substitution and resubstitution, to sign for him or her in his or her name in the capacities indicated below, any and all amendments (including post-effective amendments), and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission; granting unto said attorneys-in-fact and agents, and each of them, full power and authority to perform any other act on behalf of the undersigned required to be done in the premises, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their substitutes or resubstitutes, lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities indicated on March 1, 2021.

| <u>Name</u> | <u>Title</u> |
|---|---|
| <u>/s/ Jon P. Stonehouse</u> Jon P. Stonehouse | President, Chief Executive Officer and Director (Principal Executive Officer) |
| <u>/s/ Anthony Doyle</u> Anthony Doyle | Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer) |
| <u>/s/ Michael L. Jones</u> Michael L. Jones | Executive Director, Finance and Principal Accounting Officer (Principal Accounting Officer) |
| <u>/s/ George B. Abercrombie</u> George B. Abercrombie | Director |
| <u>/s/ Stephen J. Aselage</u> Stephen J. Aselage | Director |
| <u>/s/ Theresa M. Heggie</u> Theresa M. Heggie | Director |
| <u>/s/ Nancy Hutson, Ph.D.</u> Nancy Hutson, Ph.D. | Director |
| <u>/s/ Robert A. Ingram</u> Robert A. Ingram | Director |

TABLE OF CONTENTS

| <u>Name</u> | <u>Title</u> |
|---|--------------|
| <u>/s/ Kenneth B. Lee, Jr.</u> Kenneth B. Lee, Jr. | Director |
| <u>/s/ Alan G. Levin</u> Alan G. Levin | Director |
| <u>/s/ Helen Thackray, M.D.</u> Helen Thackray, M.D. | Director |

[Letterhead of Gibson, Dunn & Crutcher LLP]

March 1, 2021

BioCryst Pharmaceuticals, Inc.
4505 Emperor Blvd., Suite 200
Durham, North Carolina 27703

Re: BioCryst Pharmaceuticals, Inc.
Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as counsel to BioCryst Pharmaceuticals, Inc., a Delaware corporation (the "Company"), in connection with the preparation and filing with the Securities and Exchange Commission (the "Commission") of a Registration Statement on Form S-3 (the "Registration Statement") under the Securities Act of 1933, as amended (the "Securities Act"), relating to the registration under the Securities Act and the proposed issuance and sale from time to time pursuant to Rule 415 under the Securities Act, together or separately and in one or more series (if applicable) of:

- (i) the Company's unsecured debt securities (the "Debt Securities");
 - (ii) shares of the Company's common stock, par value \$0.01 per share (the "Common Stock");
 - (iii) shares of the Company's preferred stock, par value \$0.01 per share (the "Preferred Stock");
 - (iv) depositary shares each representing a fraction of a share of a particular series of Preferred Stock (the "Depositary Shares");
 - (v) contracts for the purchase or sale of Debt Securities, Common Stock, Preferred Stock or Depositary Shares (the "Purchase Contracts");
 - (vi) warrants for the purchase of Common Stock, Preferred Stock, Depositary Shares, Debt Securities or any combination thereof (the "Warrants"); and
 - (vii) units of the Company comprised of any combination of Common Stock, Preferred Stock, Depositary Shares, Purchase Contracts, Debt Securities or Warrants (the "Units").
-

The Debt Securities, Common Stock, Preferred Stock, Depositary Shares, Purchase Contracts, Warrants and Units are collectively referred to herein as the “Securities.” The Debt Securities are to be issued under an indenture to be entered into between the Company and U.S. Bank National Association, as indenture trustee (the “Base Indenture”).

In arriving at the opinions expressed below, we have examined originals, or copies certified or otherwise identified to our satisfaction as being true and complete copies of the originals, of the form of Base Indenture, the specimen Common Stock certificate and such other documents, corporate records, certificates of officers of the Company and of public officials and other instruments as we have deemed necessary or advisable to enable us to render these opinions. In our examination, we have assumed the genuineness of all signatures, the legal capacity and competency of all natural persons, the authenticity of all documents submitted to us as originals and the conformity to original documents of all documents submitted to us as copies. As to any facts material to these opinions, we have relied to the extent we deemed appropriate and without independent investigation upon statements and representations of officers and other representatives of the Company and others.

We have assumed without independent investigation that:

(i) at the time any Securities are sold pursuant to the Registration Statement (the “Relevant Time”), the Registration Statement and any supplements and amendments thereto (including post-effective amendments) will be effective and will comply with all applicable laws;

(ii) at the Relevant Time, a prospectus supplement will have been prepared and filed with the Commission describing the Securities offered thereby and all related documentation and will comply with all applicable laws;

(iii) all Securities will be issued and sold in the manner stated in the Registration Statement and the applicable prospectus supplement;

(iv) at the Relevant Time, all corporate or other action required to be taken by the Company to duly authorize each proposed issuance of Securities and any related documentation (including (a) the due reservation of any shares of Common Stock or Preferred Stock for issuance upon exercise, conversion or exchange of any Securities for Common Stock or Preferred Stock (a “Convertible Security”), and (b) the execution (in the case of certificated Securities), delivery and performance of the Securities and any related documentation referred to in paragraphs 1 through 7 below) shall have been duly completed and shall remain in full force and effect;

(v) upon issuance of any Common Stock or Preferred Stock, including upon exercise, conversion or exchange of any Convertible Security, the total number of shares of Common Stock or Preferred Stock issued and outstanding will not exceed the total number of shares of Common Stock or Preferred Stock, as applicable, that the Company is then authorized to issue under its certificate of incorporation and other relevant documents;

(vi) in the case of Debt Securities, at the Relevant Time, the Base Indenture shall have been duly executed and delivered by the Company and all other parties thereto and duly qualified under the TIA;

(vii) at the Relevant Time, a definitive purchase, underwriting or similar agreement and any other necessary agreement with respect to any Securities offered or issued will have been duly authorized by all necessary corporate or other action of the Company and duly executed and delivered by the Company and the other parties thereto.

Based on the foregoing and in reliance thereon, and subject to the assumptions, exceptions, qualifications and limitations set forth herein, we are of the opinion that:

1. With respect to any Debt Securities, when:

- a. the terms and conditions of such Debt Securities have been duly established by supplemental indenture or officers' certificate in accordance with the terms and conditions of the Base Indenture,
- b. any such supplemental indenture has been duly executed and delivered by the Company and the relevant trustee (together with the Base Indenture, the "Indenture"), and
- c. such Debt Securities have been executed (in the case of certificated Debt Securities), delivered and authenticated in accordance with the terms of the applicable Indenture and issued and sold for the consideration set forth in the applicable definitive purchase, underwriting or similar agreement,

such Debt Securities will be legal, valid and binding obligations of the Company, enforceable against the Company in accordance with their respective terms.

2. With respect to any shares of Preferred Stock, when:

- a. the certificate of designations relating to such Preferred Stock (the "Certificate of Designations") has been duly executed and filed with the Office of the Secretary of State of the State of Delaware,
 - b. such shares have been issued either (i) in accordance with the applicable definitive purchase, underwriting or similar agreement and for the consideration therefor provided for therein or (ii) upon exercise, conversion or exchange of any Convertible Security and for any additional consideration specified in such Convertible Security or the instrument governing such Convertible Security providing for such conversion or exercise, which consideration (including any consideration paid for such Convertible Security), on a per-share basis, shall in either event not be less than the par value of the Preferred Stock, and
-

- c. any such Convertible Security was previously validly issued and is fully paid and non-assessable (in the case of an equity Security) or is a legal, valid and binding obligation of the Company, enforceable against the Company in accordance with its terms,

such shares of Preferred Stock will be validly issued, fully paid and non-assessable.

3. With respect to Depositary Shares, when:

- a. a deposit agreement relating to such Depositary Shares ("Deposit Agreement") has been duly executed and delivered by the Company and the depositary appointed by the Company,
- b. the terms of the Depositary Shares have been established in accordance with the Deposit Agreement, and
- c. the depositary receipts representing the Depositary Shares have been duly executed and countersigned (in the case of certificated Depositary Shares), registered and delivered in accordance with the related Deposit Agreement and the applicable definitive purchase, underwriting or similar agreement for the consideration provided therein,

the Depositary Shares will be legally issued and will entitle the holders of such Depositary Shares to the rights specified in the applicable Deposit Agreement and the applicable depositary receipts.

4. With respect to shares of Common Stock, when:

- a. such shares of Common Stock have been duly executed (in the case of certificated shares) and delivered either (i) in accordance with the applicable definitive purchase, underwriting or similar agreement for the consideration provided for therein, or (ii) upon conversion or exercise of any Convertible Security, in accordance with the terms of such Convertible Security or the instrument governing such Convertible Security providing for such conversion or exercise, and for any additional consideration specified therein, which consideration (including any consideration paid for such Convertible Security), on a per-share basis, shall in either event not be less than the par value of the Common Stock, and
 - b. any such Convertible Security was previously validly issued and is fully paid and non-assessable (in the case of an equity Security) or is a legal, valid and binding obligation of the Company, enforceable against the Company in accordance with its terms,
-

such shares of Common Stock will be validly issued, fully paid and non-assessable.

5. With respect to any Purchase Contracts, when:

- a. the related purchase contract agreement (“Purchase Contract Agreement”), if any, has been duly executed by the Company and each other party thereto,
- b. the terms of the Purchase Contracts have been established in accordance with the Purchase Contract Agreement, if any, or the applicable definitive purchase, underwriting or similar agreement,
- c. the terms of any collateral or security arrangements relating to such Purchase Contracts have been established and the agreements thereto have been validly executed and delivered by each of the parties thereto and any collateral has been deposited with the collateral agent, if applicable, in accordance with such arrangements, and
- d. such Purchase Contracts have been executed (in the case of certificated Purchase Contracts) and delivered in accordance with the Purchase Contract Agreement, if any, and the applicable definitive purchase, underwriting or similar agreement for the consideration provided for therein,

such Purchase Contracts will be legal, valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

6. With respect to any Warrants, when:

- a. the warrant agreement relating to such Warrants (the “Warrant Agreement”), if any, has been duly executed and delivered by the Company and each other party thereto,
- b. the terms of the Warrants have been established in accordance with the Warrant Agreement, if any, and the applicable definitive purchase, underwriting or similar agreement, and
- c. the Warrants have been duly executed (in the case of certificated Warrants) and delivered in accordance with the Warrant Agreement, if any, and the applicable definitive purchase, underwriting or similar agreement for the consideration provided for therein,

such Warrants will be legal, valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

7. With respect to any Units, when:

- a. the unit agreement relating to the Units (the "Unit Agreement"), if any, has been duly executed and delivered by the Company and each other party thereto,
- b. the terms of the Units have been duly established in accordance with the Unit Agreement, if any, and the applicable definitive purchase, underwriting or similar agreement, and
- c. the Units have been duly executed (in the case of certificated Units) and delivered in accordance with the Unit Agreement, if any, and the applicable definitive purchase, underwriting or similar agreement for the consideration provided for therein,

the Units will be legal, valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

The opinions expressed above are subject to the following exceptions, qualifications, limitations and assumptions:

A. We render no opinion herein as to matters involving the laws of any jurisdiction other than the State of New York and, for purposes of paragraphs 2 and 4 above, the Delaware General Corporation Law. This opinion is limited to the effect of the current state of the laws of the State of New York, the Delaware General Corporation Law and the facts as they currently exist. We assume no obligation to revise or supplement this opinion in the event of future changes in such laws or the interpretations thereof or such facts.

B. The opinions above with respect to the Indenture, the Debt Securities, depositary receipts representing the Depositary Shares, the Deposit Agreement, the Purchase Contracts, any Purchase Contract Agreement, the Warrants, the Warrant Agreement, the Units and the Unit Agreement (collectively, the "Documents") are each subject to (i) the effect of any bankruptcy, insolvency, reorganization, moratorium, arrangement or similar laws affecting the rights and remedies of creditors generally, including without limitation the effect of statutory or other laws regarding fraudulent transfers or preferential transfers, (ii) general principles of equity, including without limitation concepts of materiality, reasonableness, good faith and fair dealing and the possible unavailability of specific performance, injunctive relief or other equitable remedies regardless of whether enforceability is considered in a proceeding in equity or at law and (iii) the provisions of the sixth article of the Company's Third Restated Certificate of Incorporation, as amended.

C. We express no opinion regarding the effectiveness of (i) any waiver of stay, extension or usury laws; (ii) provisions relating to indemnification, exculpation or contribution, to the extent such provisions may be held unenforceable as contrary to public policy or federal or state securities laws, (iii) any waiver of the right to jury trial or (iv) any provision to the effect that every right or remedy is cumulative and may be exercised in addition to any other right or remedy or that the election of some particular remedy does not preclude recourse to one or more others.

D. To the extent relevant to our opinions in paragraphs 3, 5, 6 and 7 and not covered by our opinions in paragraphs 1, 2 or 4, we have assumed that any securities, currencies or commodities underlying, comprising or issuable upon exchange, conversion or exercise of any Depositary Shares, Purchase Contracts, Warrants, or Units are validly issued, fully paid and non-assessable (in the case of an equity security) or a legal, valid and binding obligation of the issuer thereof, enforceable against such issuer in accordance with its terms.

You have informed us that you intend to issue Securities from time to time on a delayed or continuous basis, and we understand that prior to issuing any Securities pursuant to the Registration Statement (i) you will advise us in writing of the terms thereof, and (ii) you will afford us an opportunity to (x) review the operative documents pursuant to which such Securities are to be issued or sold (including the applicable offering documents), and (y) file such supplement or amendment to this opinion (if any) as we may reasonably consider necessary or appropriate.

We consent to the filing of this opinion as an exhibit to the Registration Statement, and we further consent to the use of our name under the caption "Legal Matters" in the Registration Statement and the prospectus that forms a part thereof. In giving these consents, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ Gibson, Dunn & Crutcher LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Form S-3) and related Prospectus of BioCryst Pharmaceuticals, Inc. for the registration of common stock and other securities and to the incorporation by reference therein of our reports dated March 1, 2021, with respect to the consolidated financial statements of BioCryst Pharmaceuticals, Inc., and the effectiveness of internal control over financial reporting of BioCryst Pharmaceuticals, Inc., included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 1, 2021

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM T-1

**STATEMENT OF ELIGIBILITY UNDER
THE TRUST INDENTURE ACT OF 1939 OF A
CORPORATION DESIGNATED TO ACT AS TRUSTEE**

Check if an Application to Determine Eligibility of
a Trustee Pursuant to Section 305(b)(2)

U.S. BANK NATIONAL ASSOCIATION

(Exact name of Trustee as specified in its charter)

31-0841368

I.R.S. Employer Identification No.

| | |
|---|------------|
| 800 Nicollet Mall Minneapolis, Minnesota | 55402 |
| (Address of principal executive offices) | (Zip Code) |

Paul Vaden
U.S. Bank National Association
214 North Tryon Street, 27th Floor
Charlotte, NC 28202-1078
(704) 335-4654
(Name, address and telephone number of agent for service)

BioCryst Pharmaceuticals, Inc.

(Issuer with respect to the Securities)

| | |
|--|--------------------------------------|
| Delaware | 62-1413174 |
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification No.) |

| | |
|---|------------|
| 4505 Emperor Blvd., Suite 200 Durham, North Carolina | 27703 |
| (Address of Principal Executive Offices) | (Zip Code) |

Debt Securities
(Title of the Indenture Securities)

Item 1. GENERAL INFORMATION. Furnish the following information as to the Trustee.

a) *Name and address of each examining or supervising authority to which it is subject.*
Comptroller of the Currency
Washington, D.C.

b) *Whether it is authorized to exercise corporate trust powers.*
Yes

Item 2. AFFILIATIONS WITH THE OBLIGOR. *If the obligor is an affiliate of the Trustee, describe each such affiliation.*
None

Items 3-15 *Items 3-15 are not applicable because to the best of the Trustee's knowledge, the obligor is not in default under any Indenture for which the Trustee acts as Trustee.*

Item 16. LIST OF EXHIBITS: *List below all exhibits filed as a part of this statement of eligibility and qualification.*

1. copy of the Articles of Association of the Trustee.*
2. A copy of the certificate of authority of the Trustee to commence business, attached as Exhibit 2.
3. A copy of the certificate of authority of the Trustee to exercise corporate trust powers, attached as Exhibit 3.
4. A copy of the existing bylaws of the Trustee.**
5. A copy of each Indenture referred to in Item 4. Not applicable.
6. The consent of the Trustee required by Section 321(b) of the Trust Indenture Act of 1939, attached as Exhibit 6.
7. Report of Condition of the Trustee as of September 30, 2020 published pursuant to law or the requirements of its supervising or examining authority, attached as Exhibit 7.

* Incorporated by reference to Exhibit 25.1 to Amendment No. 2 to registration statement on S-4, Registration Number 333-128217 filed on November 15, 2005.

** Incorporated by reference to Exhibit 25.1 to registration statement on form S-3ASR, Registration Number 333-199863 filed on November 5, 2014.

SIGNATURE

Pursuant to the requirements of the Trust Indenture Act of 1939, as amended, the Trustee, U.S. BANK NATIONAL ASSOCIATION, a national banking association organized and existing under the laws of the United States of America, has duly caused this statement of eligibility and qualification to be signed on its behalf by the undersigned, thereunto duly authorized, all in the City of Charlotte, North Carolina on the 24th of February, 2021.

By: /s/ Paul Vaden

Paul Vaden
Vice President



CERTIFICATE OF CORPORATE EXISTENCE

I, Brian Brooks, Acting Comptroller of the Currency, do hereby certify that:

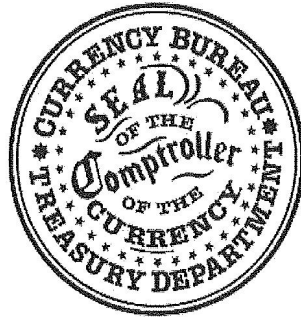
1. The Comptroller of the Currency, pursuant to Revised Statutes 324, et seq, as amended, and 12 USC 1, et seq, as amended, has possession, custody, and control of all records pertaining to the chartering, regulation, and supervision of all national banking associations.

2. "U.S. Bank National Association," Cincinnati, Ohio (Charter No. 24), is a national banking association formed under the laws of the United States and is authorized thereunder to transact the business of banking on the date of this certificate.

IN TESTIMONY WHEREOF, today, June 1, 2020, I have hereunto subscribed my name and caused my seal of office to be affixed to these presents at the U.S. Department of the Treasury, in the City of Washington, District of Columbia

A handwritten signature in black ink, appearing to read 'Brian Brooks', written over a horizontal line.

Acting Comptroller of the Currency



2020-00621-C



CERTIFICATE OF FIDUCIARY POWERS

I, Brian Brooks, Acting Comptroller of the Currency, do hereby certify that:

1. The Office of the Comptroller of the Currency, pursuant to Revised Statutes 324, et seq, as amended, and 12 USC 1, et seq, as amended, has possession, custody, and control of all records pertaining to the chartering, regulation, and supervision of all national banking associations.

2. "U.S. Bank National Association," Cincinnati, Ohio (Charter No. 24), was granted, under the hand and seal of the Comptroller, the right to act in all fiduciary capacities authorized under the provisions of the Act of Congress approved September 28, 1962, 76 Stat. 668, 12 USC 92a, and that the authority so granted remains in full force and effect on the date of this certificate.

IN TESTIMONY WHEREOF, today, June 1, 2020, I have hereunto subscribed my name and caused my seal of office to be affixed to these presents at the U.S. Department of the Treasury, in the City of Washington, District of Columbia.

A handwritten signature in black ink, appearing to read "Brian Brooks", written over a horizontal line.

Acting Comptroller of the Currency



2020-00621-C

Exhibit 6

CONSENT

In accordance with Section 321(b) of the Trust Indenture Act of 1939, the undersigned, U.S. BANK NATIONAL ASSOCIATION hereby consents that reports of examination of the undersigned by Federal, State, Territorial or District authorities may be furnished by such authorities to the Securities and Exchange Commission upon its request therefor.

Dated: February 24, 2021

By: /s/ Paul Vaden

Paul Vaden
Vice President

Exhibit 7
U.S. Bank National Association
Statement of Financial Condition
As of 9/30/2020

(\$000's)

9/30/2020

| | |
|---|-----------------------|
| Assets | |
| Cash and Balances Due From | \$ 43,891,940 |
| Depository Institutions | |
| Securities | 132,530,990 |
| Federal Funds | 898 |
| Loans & Lease Financing Receivables | 307,196,612 |
| Fixed Assets | 7,598,340 |
| Intangible Assets | 12,549,045 |
| Other Assets | 26,728,893 |
| Total Assets | \$ 530,496,718 |
| Liabilities | |
| Deposits | \$ 426,766,411 |
| Fed Funds | 1,460,030 |
| Treasury Demand Notes | 0 |
| Trading Liabilities | 859,917 |
| Other Borrowed Money | 29,719,033 |
| Acceptances | 0 |
| Subordinated Notes and Debentures | 3,850,000 |
| Other Liabilities | 14,732,819 |
| Total Liabilities | \$ 477,388,210 |
| Equity | |
| Common and Preferred Stock | 18,200 |
| Surplus | 14,266,915 |
| Undivided Profits | 38,022,958 |
| Minority Interest in Subsidiaries | 800,435 |
| Total Equity Capital | \$ 53,108,508 |
| Total Liabilities and Equity Capital | \$ 530,496,718 |