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SCHEDULE 13G

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549

Under the Securities Exchange Act of 1934  
(Amendment No. 4)\*

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**BioCryst Pharmaceuticals, Inc.**

(Name of Issuer)

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**Common Stock, par value \$0.01 per share**

(Title of Class of Securities)

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**09058V103**

(CUSIP Number)

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**December 31, 2020**

(Date of Event which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

Rule 13d-1(b)

Rule 13d-1(c)

Rule 13d-1(d)

\*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 (the "Act") or otherwise subject to the liabilities of that section of the Act, but shall be subject to all other provisions of the Act (however, see the Notes).

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<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Baker Bros. Advisors LP		
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
<b>3</b>	<b>SEC USE ONLY</b>		
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware		
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b> 18,100,968 (1)	
	<b>6</b>	<b>SHARED VOTING POWER</b> -0-	
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b> 18,100,968 (1)	
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b> -0-	
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 18,100,968 (1)		
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>		
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 9.95% (1)(2)		
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IA, PN		

- (1) Includes 15,000 shares of the common stock ("Common Stock") of BioCryst Pharmaceuticals, Inc. (the "Issuer") underlying options ("Stock Options") and 5,390,150 shares of Common Stock issuable upon exercise of the Pre-Funded Warrants (as defined in Item 4 below and subject to the limitations as described therein) directly held by the Funds (as defined in Item 4 below).
- (2) Based on 176,565,622 shares of Common Stock outstanding as of October 31, 2020, as reported in the Issuer's Form 10-Q filed with the Securities and Exchange Commission ("SEC") on November 6, 2020, plus 15,000 shares of Common Stock underlying Stock Options and 5,390,150 shares of Common Stock issuable upon the exercise of the Pre-Funded Warrants (as defined in Item 4 below and subject to the limitations as described therein).

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Baker Bros. Advisors (GP) LLC		
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
<b>3</b>	<b>SEC USE ONLY</b>		
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware		
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b> 18,100,968 (1)	
	<b>6</b>	<b>SHARED VOTING POWER</b> -0-	
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b> 18,100,968 (1)	
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b> -0-	
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 18,100,968 (1)		
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>		
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 9.95% (1)(2)		
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> HC,OO		

- (1) Includes 15,000 shares of Common Stock underlying Stock Options and 5,390,150 shares of Common Stock issuable upon exercise of the Pre-Funded Warrants (as defined in Item 4 below and subject to the limitations as described therein) directly held by the Funds (as defined in Item 4 below).
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<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Felix J. Baker		
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
<b>3</b>	<b>SEC USE ONLY</b>		
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States		
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b> 18,178,881 (1)	
	<b>6</b>	<b>SHARED VOTING POWER</b> -0-	
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b> 18,178,881 (1)	
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b> -0-	
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 18,178,881 (1)		
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>		
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 9.99% (1)(2)		
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IN, HC		

- (1) Includes 15,000 shares of Common Stock underlying Stock Options and 5,390,150 shares of Common Stock issuable upon exercise of the Pre-Funded Warrants (as defined in Item 4 below and subject to the limitations as described therein) directly held by the Funds (as defined in Item 4 below).
- (2) Based on 176,565,622 shares of Common Stock outstanding as of October 31, 2020, as reported in the Issuer's Form 10-Q filed with the SEC on November 6, 2020, plus 15,000 shares of Common Stock underlying Stock Options and 5,390,150 shares of Common Stock issuable upon the exercise of the Pre-Funded Warrants (as defined in Item 4 below and subject to the limitations as described therein).

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Julian C. Baker		
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
<b>3</b>	<b>SEC USE ONLY</b>		
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States		
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b> 18,178,881 (1)	
	<b>6</b>	<b>SHARED VOTING POWER</b> -0-	
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b> 18,178,881 (1)	
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b> -0-	
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 18,178,881 (1)		
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>		
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 9.99% (1)(2)		
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IN, HC		

- (1) Includes 15,000 shares of Common Stock underlying Stock Options and 5,390,150 shares of Common Stock issuable upon exercise of the Pre-Funded Warrants (as defined in Item 4 below and subject to the limitations as described therein) directly held by the Funds (as defined in Item 4 below).
- (2) Based on 176,565,622 shares of Common Stock outstanding as of October 31, 2020, as reported in the Issuer's Form 10-Q filed with the SEC on November 6, 2020, plus 15,000 shares of Common Stock underlying Stock Options and 5,390,150 shares of Common Stock issuable upon the exercise of the Pre-Funded Warrants (as defined in Item 4 below and subject to the limitations as described therein).

#### Amendment No. 4 to Schedule 13G

This Amendment No. 4 to Schedule 13G amends the previously filed Schedule 13G filed by Baker Bros. Advisors LP (the "Adviser"), Baker Bros. Advisors (GP) LLC (the "Adviser GP"), Julian C. Baker and Felix J. Baker (collectively, the "Reporting Persons"). Except as supplemented herein, such statements, as heretofore amended and supplemented, remain in full force and effect.

**Item 1(a) Name of Issuer:**

BioCryst Pharmaceuticals, Inc.

**Item 1(b) Address of Issuer's Principal Executive Offices:**

4505 Emperor Blvd., Ste. 200

Durham, North Carolina 27703

**Item 2(a) Name of Person Filing:**

This Amendment No. 4 is being filed jointly by the Reporting Persons.

**Item 2(b) Address of Principal Business Office or, if None, Residence:**

The business address of each of the Reporting Persons is:

c/o Baker Bros. Advisors LP

860 Washington Street, 3<sup>rd</sup> Floor

New York, NY 10014

(212) 339-5690

**Item 2(c) Citizenship:**

The Adviser is a limited partnership organized under the laws of the State of Delaware. The Adviser GP is a limited liability company organized under the laws of the State of Delaware. The citizenship of each of Julian C. Baker and Felix J. Baker is the United States of America.

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**Item 2(d) Title of Class of Securities**

Common Stock, par value \$0.01 per share (“Common Stock”)

**Item 2(e) CUSIP Number**

09058V103

**Item 3. If this statement is filed pursuant to §§240.13d-1(b) or (c), check whether the person filing is a:**

- (a)  Broker or dealer registered under Section 15 of the Exchange Act.
- (b)  Bank as defined in section 3(a)(6) of the Exchange Act.
- (c)  Insurance company as defined in section 3(a)(19) of the Exchange Act.
- (d)  Investment company registered under section 8 of the Investment Company Act of 1940.
- (e)  An investment adviser in accordance with Rule 13d-1(b)(1)(ii)(E).
- (f)  An employee benefit plan or endowment fund in accordance with Rule 13d-1(b)(1)(ii)(F).
- (g)  A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G).
- (h)  A savings association as defined in Section 3(b) of the Federal Deposit Insurance Act.
- (i)  A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940.
- (j)  Group, in accordance with Rule 13d-1(b)(1)(ii)(J).

**Item 4. Ownership.**

Items 5 through 9 and 11 of each of the cover pages to this Amendment No. 4 are incorporated herein by reference. Set forth below is the aggregate number of shares of Common Stock of the Issuer directly held by each of 667, L.P. (“667”) and Baker Brothers Life Sciences, L.P. (“Life Sciences”, and together with 667, the “Funds”), including 5,390,150 shares of Common Stock issuable upon the exercise of the Pre-Funded Warrants (as defined below), which may be deemed to be indirectly beneficially owned by the Reporting Persons. The information set forth below is based upon 176,565,622 shares of Common Stock outstanding as of October 31, 2020, as reported on the Issuer’s Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020, plus 5,390,150 shares of Common Stock issuable upon the exercise of Pre-Funded Warrants (as defined below). Such percentage figures were calculated in accordance with Rule 13d-3 under the Securities Exchange Act of 1934, as amended (the “Exchange Act”).

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Holder	Number of Shares of Common Stock we own or have the right to acquire within 60 days	Percent of Class Outstanding
667, L.P.	1,505,548	0.8%
Baker Brothers Life Sciences, L.P.	16,544,587	9.1%

The warrants have an exercise price of \$0.01 per share and have no expiration date (the “Pre-Funded Warrants”). The Pre-Funded Warrants are only exercisable to the extent that after giving effect to such exercise the holders thereof and their affiliates and any persons who are members of a Section 13(d) group with the holders or their affiliates would beneficially own in the aggregate, for purposes of Rule 13d-3 under the Exchange Act, no more than 9.99% of the outstanding Common Stock (the “Maximum Percentage”). By written notice to the Issuer, the Funds may from time to time increase or decrease the Maximum Percentage applicable to that Fund to any other percentage not in excess of 19.99%. Any such increase will not be effective until the 61st day after such notice is delivered to the Issuer. As a result of this restriction, the number of shares of Common Stock that may be issued upon exercise of the Pre-Funded Warrants by the above holders may change depending upon changes in the outstanding Common Stock.

The Adviser GP, Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, and the Adviser may be deemed to be beneficial owners of securities of the Issuer directly held by the Funds.

The Adviser GP is the sole general partner of the Adviser. Pursuant to the management agreements, as amended, among the Adviser, Life Sciences and 667 and their respective general partners, the Funds’ respective general partners relinquished to the Adviser all discretion and authority with respect to the investment and voting power of the securities held by the Funds, and thus the Adviser has complete and unlimited discretion and authority with respect to the Funds’ investments and voting power over investments.

Julian C. Baker and Felix J. Baker each directly hold and beneficially own 77,913 shares of Common Stock of the Issuer received from pro-rata distributions without consideration.

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Dr. Stephen R. Biggar, an employee of the Adviser, is a former Director of the Issuer. In connection with his previous service on the Board of Directors of the Issuer (the "Board"), Dr. Biggar holds 15,000 non-qualified options to purchase Common Stock of Issuer ("Stock Options") and 35,833 shares of Common Stock received from the exercise of options to purchase Common Stock of the Issuer. Dr. Biggar previously served on the Board as a representative of the Funds. The policy of the Funds and the Adviser does not permit employees of the Adviser to receive compensation for serving as a Director of the Issuer. Therefore, Dr. Biggar has no pecuniary interest in any Stock Options or shares of Common Stock directly held by him. The Funds are instead entitled to the pecuniary interest in any Stock Options and shares of Common Stock received as director compensation.

The Adviser has voting and investment power over the Common Stock, Stock Options, Common Stock underlying such Stock Options and Common Stock received from the exercise of Stock Options by Dr. Biggar as directors' compensation received for past service. The Adviser GP, Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, may be deemed to have the power to vote or direct the vote of and the power to dispose or direct the disposition of the Common Stock, Stock Options, Common Stock received from the exercise of Stock Options and Common Stock underlying such Stock Options received by Dr. Biggar as director's compensation.

**Item 5. Ownership of Five Percent or Less of a Class.**

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following . N/A

**Item 6. Ownership of More than Five Percent on Behalf of Another Person.**

N/A

**Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company or Control Person.**

The information in Item 4 is incorporated herein by reference.

**Item 8. Identification and Classification of Members of the Group.**

N/A

**Item 9. Notice of Dissolution of Group.**

N/A

**Item 10. Certification.**

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

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**SIGNATURE**

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

February 16, 2021

**BAKER BROS. ADVISORS LP**

By: Baker Bros. Advisors (GP) LLC, its general partner

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

**BAKER BROS. ADVISORS (GP) LLC**

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

/s/ Julian C. Baker

Julian C. Baker

/s/ Felix J. Baker

Felix J. Baker

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