SCHEDULE 13G

SECURITIES AND EXCHANGE COMMISSION WASHINGTON, DC 20549

Under the Securities Exchange Act of 1934 (Amendment No. 2)*

| | BioCryst Pharmaceuticals, Inc. | |
|---------------------------|--|---------------|
| | (Name of Issuer) | |
| | Common Stock, par value \$0.01 per share | |
| | (Title of Class of Securities) | |
| | 09058V103 | |
| | (CUSIP number) | |
| | December 31, 2018 | |
| | (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) | | |
| | rer page shall be filled out for a reporting person's initial filing on this form with respect to the subj mendment containing information which would alter disclosures provided in a prior cover page. | ject class of |
| | on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of e "Act") or otherwise subject to the liabilities of that section of the Act, but shall be subject to all ot | |
| | Page 1 of 10 Pages | |

| 1 | NAMES OF REPORTING PERSONS | | |
|---------------------|--|------------------------------------|-------|
| | Baker Bros. | Advisors LP | |
| 2 | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) [| | |
| | | | (b) 🗆 |
| 3 | SEC USE ONLY | | |
| | | | |
| 4 | 4 CITIZENSHIP OR PLACE OF ORGANIZATION | | |
| | Delaware | | |
| | 5 | SOLE VOTING POWER | |
| | | 15,148,081 (1) | |
| NUMBER OF SHARES | 6 | SHARED VOTING POWER | |
| BENEFICIALLY | | -0- | |
| OWNED BY EACH | 7 | SOLE DISPOSITIVE POWER | |
| REPORTING PERSON | | 15,148,081 (1) | |
| WITH | 8 | SHARED DISPOSITIVE POWER | |
| | | -0- | |
| 9 | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON | | |
| | 15,148,081 (1) | | |
| 10 | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES | | |
| | (See Instructions) | | |
| 11 | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | |
| | 13.8% (1)(2) | | |
| 12 | 1 | EPORTING PERSON (See Instructions) | |
| 12 | | | |
| | IA. PN | | |

(1) Includes 45,000 shares of the common stock of BioCryst Pharmaceuticals, Inc. (the "Issuer") underlying options.

⁽²⁾ Based on 109,641,044 shares of Common Stock of the Issuer outstanding as of October 31, 2018, as reported in the Issuer's Form 10-Q filed with the Securities and Exchange Commission ("SEC") on November 8, 2018.

| 1 | NAMES OF REPORTING PERSONS | | | |
|--------------------------|---|--------------------------|----------------|--|
| | Baker Bros. Advisors (GP) LLC | | | |
| 2 | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) | | | |
| | | | (a) □ (b) □ | |
| 3 | SEC USE ONLY | | | |
| | | | | |
| 4 | CITIZENSHIP OR PLACE OF ORGANIZATION | | | |
| | Delaware | | | |
| | 5 | SOLE VOTING POWER | | |
| | | 15,148,081 (1) | | |
| NUMBER OF SHARES | 6 | SHARED VOTING POWER | | |
| BENEFICIALLY OWNED BY | | -0- | | |
| EACH | 7 | SOLE DISPOSITIVE POWER | | |
| REPORTING PERSON | | 15,148,081 (1) | | |
| WITH | 8 | SHARED DISPOSITIVE POWER | | |
| | | -0- | | |
| 9 | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON | | | |
| | 15,148,081 (1) | | | |
| 10 | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES ☐ (See Instructions) | | | |
| 11 | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | | |
| | 13.8% (1)(2) | | | |
| 12 | TYPE OF REPORTING PERSON (See Instructions) | | | |
| | HC, OO | | | |

(1) Includes 45,000 shares of the Common Stock of the Issuer underlying options.
(2) Based on 109,641,044 shares of Common Stock of the Issuer outstanding as of October 31, 2018, as reported in the Issuer's Form 10-Q filed with the SEC on November 8, 2018.

| 1 | NAMES OF REPORTING PERSONS | | |
|---------------------|--|--------------------------|----------------|
| | Felix J. Baker | | |
| 2 | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) | | |
| | | | (a) □ (b) □ |
| 3 | SEC USE ONLY | | |
| | | | |
| 4 | CITIZENSHIP OR PLACE OF ORGANIZATION | | |
| | United States | | |
| | 5 | SOLE VOTING POWER | |
| | | 15,171,540 (1) | |
| NUMBER OF SHARES | 6 | SHARED VOTING POWER | |
| BENEFICIALLY | | -0- | |
| OWNED BY EACH | 7 | SOLE DISPOSITIVE POWER | |
| REPORTING PERSON | | 15,171,540 (1) | |
| WITH | 8 | SHARED DISPOSITIVE POWER | |
| | | -0- | |
| 9 | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON | | |
| | 15,171,540 (1) | | |
| 10 | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES □ | | |
| | (See Instructions) | | |
| 11 | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | |
| | 13.8% (1)(2) | | |
| 12 | TYPE OF REPORTING PERSON (See Instructions) | | |
| | IN, HC | | |

Includes 45,000 shares of the Common Stock of the Issuer underlying options.
 Based on 109,641,044 shares of Common Stock of the Issuer outstanding as of October 31, 2018, as reported in the Issuer's Form 10-Q filed with the SEC on November 8, 2018.

| 1 | NAMES OF REPORTING PERSONS | | |
|---------------------|---|--------------------------|----------------|
| | Julian C. Baker | | |
| 2 | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) | | |
| | | | (a) □ (b) □ |
| 3 | SEC USE ONLY | | |
| | | | |
| 4 | CITIZENSHIP OR PLACE OF ORGANIZATION | | |
| | United States | | |
| | 5 | SOLE VOTING POWER | |
| | | 15,171,540 (1) | |
| NUMBER OF SHARES | 6 | SHARED VOTING POWER | |
| BENEFICIALLY | | -0- | |
| OWNED BY EACH | 7 | SOLE DISPOSITIVE POWER | |
| REPORTING PERSON | | 15,171,540 (1) | |
| WITH | 8 | SHARED DISPOSITIVE POWER | |
| | | -0- | |
| 9 | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON | | |
| | 15,171,540 (1) | | |
| 10 | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES ☐ (See Instructions) | | |
| 11 | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 | | |
| | 13.8% (1)(2) | | |
| 12 | TYPE OF REPORTING PERSON (See Instructions) | | |
| IN, HC | | | |

(1) Includes 45,000 shares of the Common Stock of the Issuer underlying options.
(2) Based on 109,641,044 shares of Common Stock of the Issuer outstanding as of October 31, 2018, as reported in the Issuer's Form 10-Q filed with the SEC on November 8, 2018.

Amendment No. 2 to Schedule 13G

This Amendment No. 2 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 Schedule 13G 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, 3rd 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) | Common Stock, par value \$0.01 per share ("Common Stock") | | |
|-----------|--|----------|--|
| | | | |
| Item 2(e) | | | |
| 09058V103 | | | |
| Item 3. | m 3. If this statement is filed pursuant to §§240.13d-1(b) or (c), check whether the person filing is a: | | nt 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) | \times | 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) | \times | A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G). |

Item 4. Ownership.

(h)

(i)

(j)

Company Act of 1940.

Group, in accordance with Rule 13d-1(b)(1)(ii)(J).

Items 5 through 9 and 11 of each of the cover pages to this Amendment No. 2 are incorporated herein reference. Set forth below is the aggregate number of shares of Common Stock of the Issuer directly held by each of the 667, L.P. and Baker Brothers Life Sciences, L.P. (collectively the "Funds"), which may be deemed to be indirectly beneficially owned by the Reporting Persons. The information set forth below is based upon 109,641,044 shares of Common Stock outstanding as of October 31, 2018, as reported on the Issuer's Form 10-Q filed with the SEC on November 8, 2018. Such percentage figures are calculated in accordance with Rule 13d-3 under the Securities Exchange Act of 1934, as amended.

A savings association as defined in Section 3(b) of the Federal Deposit Insurance Act.

A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment

| | Number of Shares | |
|------------------------------------|--------------------|------------------|
| | of Common Stock | |
| | we own or have the | |
| | right to acquire | Percent of Class |
| Name | within 60 days | Outstanding |
| 667, L.P. | 1,946,184 | 1.8% |
| Baker Brothers Life Sciences, L.P. | 13,136,064 | 12.0% |
| Total | 15,082,248 | 13.8% |

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, and may be deemed to have the power to vote or direct the vote of and the power to dispose or direct the disposition of such securities.

Pursuant to the management agreements, as amended, among the Adviser, the Funds 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 23,459 shares of Common Stock of the Issuer received as part of a pro-rata distribution from 14159, L.P. for no consideration on January 28, 2015.

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 options to purchase 45,000 shares of Common Stock ("Stock Options") and 20,833 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 Reporting Persons disclaim beneficial ownership of the securities of the Issuer held by each of the Funds, and this Amendment No. 2 shall not be deemed an admission that the Reporting Persons are the beneficial owners of such securities for purposes of Section 13(d) or for any other purpose, except to the extent that any such Reporting Persons actually exercises voting or dispositive power with respect to such securities.

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

| If this statement is being filed to report the fact that than five percent of the class of securities, check the following \Box . | at as of the date hereof the reporting person has ceased to be the beneficial owner of more N/A |
|---|---|
| | Page 8 of 10 Pages |

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

The information in Item 4 is incorporated herein by reference.

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 13, 2019

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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