
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

SCHEDULE 13D
(Rule 13d-102)

INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT
TO RULE 13d-1(a) AND AMENDMENTS THERETO FILED PURSUANT
TO RULE 13d-2(a)

(Amendment No. 2)*

Aeglea BioTherapeutics, Inc.

(Name of Issuer)

Common Stock, par value \$0.0001 per share

(Title of Class of Securities)

00773J103

(CUSIP number)

Alexandra A. Toohey
Chief Financial Officer
Baker Bros. Advisors LP
860 Washington Street, 3rd Floor
New York, NY 10014
(212) 339-5690

(Name, address and telephone number of person authorized to receive notices and communications)

February 9, 2022

(Date of event which requires filing of this statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of Rule 13d-1(e), 13d-1(f) or 13d-1(g), check the following box ☒.

(Continued on the following pages)

(Page 1 of 9 Pages)

*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 or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act.

1.	NAMES OF REPORTING PERSONS Baker Bros. Advisors LP		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) p (b) p		
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS* OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) o		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 5,044,478 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 5,044,478 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 5,044,478 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* p		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 9.9% (1)(2)		
14.	TYPE OF REPORTING PERSON* IA, PN		

- (1) Includes 1,593,284 shares of Common Stock ("Common Stock") of Aeglea BioTherapeutics, Inc. (the "Issuer") issuable upon exercise of the Pre-Funded Warrants (as defined in Item 5 and subject to the limitations as described therein) directly held by the Funds (as defined below) and 41,088 shares of Common Stock issuable upon exercise of non-qualified options to purchase Common Stock of the Issuer ("Stock Options").
- (2) Based on 49,319,958 shares of Common Stock of the Issuer outstanding as of October 28, 2021, as reported in the Issuer's Form 10-Q filed with the Securities and Exchange Commission ("SEC") on November 4, 2021.

1.	NAMES OF REPORTING PERSONS Baker Bros. Advisors (GP) LLC		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) p (b) p		
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS* OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) o		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 5,044,478 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 5,044,478 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 5,044,478 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* p		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 9.9% (1)(2)		
14.	TYPE OF REPORTING PERSON* HC, OO		

- (1) Includes 1,593,284 shares of Common Stock of the Issuer issuable upon exercise of the Pre-Funded Warrants (as defined in Item 5 and subject to the limitations as described therein) directly held by the Funds (as defined below) and 41,088 shares of Common Stock issuable upon exercise of Stock Options.
- (2) Based on 49,319,958 shares of Common Stock of the Issuer outstanding as of October 28, 2021, as reported in the Issuer's Form 10-Q filed with the SEC on November 4, 2021.

1.	NAMES OF REPORTING PERSONS Felix J. Baker		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) p (b) p		
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS* OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) 0		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION United States		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 5,044,478 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 5,044,478 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 5,044,478 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* p		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 9.9% (1)(2)		
14.	TYPE OF REPORTING PERSON* IN, HC		

- (1) Includes 1,593,284 shares of Common Stock of the Issuer issuable upon exercise of the Pre-Funded Warrants (as defined in Item 5 and subject to the limitations as described therein) directly held by the Funds (as defined below) and 41,088 shares of Common Stock issuable upon exercise of Stock Options.
- (2) Based on 49,319,958 shares of Common Stock of the Issuer outstanding as of October 28, 2021, as reported in the Issuer's Form 10-Q filed with the SEC on November 4, 2021.

1.	NAMES OF REPORTING PERSONS Julian C. Baker		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) p (b) p		
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS* OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) o		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION United States		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 5,044,478 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 5,044,478 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 5,044,478 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* p		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 9.9% (1)(2)		
14.	TYPE OF REPORTING PERSON* IN, HC		

- (1) Includes 1,593,284 shares of Common Stock of the Issuer issuable upon exercise of the Pre-Funded Warrants (as defined in Item 5 and subject to the limitations as described therein) directly held by the Funds (as defined below) and 41,088 shares of Common Stock issuable upon exercise of Stock Options.
- (2) Based on 49,319,958 shares of Common Stock of the Issuer outstanding as of October 28, 2021, as reported in the Issuer's Form 10-Q filed with the SEC on November 4, 2021.

Amendment No. 2 to Schedule 13D

This Amendment No. 2 to Schedule 13D amends and supplements the previously filed Schedule 13D 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.

The Adviser GP is the sole general partner of the Adviser. Pursuant to the management agreements, as amended, among the Adviser, Baker Brothers Life Sciences, L.P. (“Life Sciences”) and 667, L.P. (“667”, and together with Life Sciences, 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 over 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.

All capitalized terms contained herein but not otherwise defined shall have the meanings ascribed to such terms in the Schedule 13D, as amended. Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

Item 4. Purpose of the Transaction.

On February 9, 2022, Sara Brownstein, a full-time employee of the Adviser resigned from the board of directors of Aeglea BioTherapeutics, Inc. (the “Issuer”) (the “Board”). Ms. Brownstein previously served on the Board as a representative of the Funds and served on the Nominating and Corporate Governance Committee.

The Funds hold securities of the Issuer for investment purposes. The Reporting Persons or their affiliates may purchase additional securities or dispose of securities in varying amounts and at varying times depending upon the Reporting Persons’ continuing assessments of pertinent factors, including the availability of shares of Common Stock or other securities for purchase at particular price levels, the business prospects of the Issuer, other business investment opportunities, economic conditions, stock market conditions, money market conditions, the attitudes and actions of the Board and management of the Issuer, the availability and nature of opportunities to dispose of securities of the Issuer and other plans and requirements of the particular entities. The Reporting Persons may discuss items of mutual interest with the Issuer’s management, members of the Board and other investors, which could include items in subparagraphs (a) through (j) of Item 4 Schedule 13D.

Depending upon their assessments of the above factors, the Reporting Persons or their affiliates may change their present intentions as stated above and they may assess whether to make suggestions to the management of the Issuer regarding financing, and whether to acquire additional securities of the Issuer (by means of open market purchases, privately negotiated purchases, exercise of some or all of the Pre-Funded Warrants (as defined in Item 6 below), exercise of some or all of the vested Stock Options, or otherwise) or to dispose of some or all of the securities of the Issuer under their control.

Except as otherwise disclosed herein, at the present time, the Reporting Persons do not have any plans or proposals with respect to any extraordinary corporate transaction involving the Issuer including, without limitation, those matters described in subparagraphs (a) through (j) of Item 4 of Schedule 13D.

ITEM 5. Interest in Securities of the Issuer.

Item 5 of this Schedule 13D is hereby amended and restated in its entirety as follows:

(a) and (b) Items 7 through 11 and 13 of each of the cover pages of this Amendment No. 2 are incorporated herein by reference.

Set forth below is the aggregate number of shares of Common Stock directly held by each of the Funds, which may be deemed to be indirectly beneficially owned by the Reporting Persons, as well as the shares of Common Stock that may be acquired upon exercise of the Pre-Funded Warrants (as defined below), subject to the limitation on exercise described below.

Name	Common Stock	February 2019 Pre-Funded Warrants	April 2020 Pre- Funded Warrants
667, L.P.	315,516	315,047	996,358
Baker Brothers Life Sciences, L.P.	3,094,590	3,434,953	10,863,970
Total	3,410,106	3,750,000	11,860,328

The Funds hold warrants to purchase shares of Common Stock that were issued on February 8, 2019 (the “February 2019 Pre-Funded Warrants”) in the amounts disclosed in the table above that are exercisable on a 1-for-1 basis into Common Stock, subject to the terms of the February 2019 Pre-Funded Warrants. Subject to the Maximum Percentage limitation described in the following sentence, the February 2019 Pre-Funded Warrants are exercisable at any time by delivery of notice to the Issuer, and permit the Funds to purchase Common Stock of the Issuer for \$0.0001 per share (as adjusted from time to time, as provided in the February 2019 Pre-Funded Warrants). February 2019 Pre-Funded Warrants may not be exercised if the holder, together with its affiliates and any persons who are members of a Section 13(d) group with the holders, would beneficially own more than a designated percentage (the “February 2019 Warrant Maximum Percentage”), which currently is 9.9%, of the number of shares of Common Stock outstanding immediately after giving effect to such exercise. A holder may increase or decrease the February 2019 Warrant Maximum Percentage by written notice to the Issuer, provided that any such increase requires at least 61 days’ prior notice to the Issuer.

The Funds hold warrants to purchase shares of Common Stock that were issued on April 30, 2020 (the “April 2020 Pre-Funded Warrants”, and together with the February 2019 Pre-Funded Warrants, the “Pre-Funded Warrants”) in the amounts disclosed in the table above that are exercisable on a 1-for-1 basis into Common Stock, subject to the terms of the April 2020 Pre-Funded Warrants. Subject to the Maximum Percentage limitation described in the following sentence, the April 2020 Pre-Funded Warrants are exercisable at any time by delivery of notice to the Issuer, and permit the Funds to purchase Common Stock of the Issuer for \$0.0001 per share (as adjusted from time to time, as provided in the April 2020 Pre-Funded Warrants). April 2020 Pre-Funded Warrants may not be exercised if the holder, together with its affiliates and any persons who are members of a Section 13(d) group with the holders, would beneficially own more than a designated percentage (the “April 2020 Warrant Maximum Percentage”), which currently is 9.9%, of the number of shares of Common Stock outstanding immediately after giving effect to such exercise. A holder may increase or decrease the April 2020 Warrant Maximum Percentage, but not in excess of 19.99%, by written notice to the Issuer, provided that any such increase requires at least 61 days’ prior notice to the Issuer.

As a result of the above restrictions, 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 is the sole general partner of the Adviser. Pursuant to 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.

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.

(c) Except as disclosed herein and in our previous Schedule 13D, none of the Reporting Persons or their affiliates has effected any other transactions in securities of the Issuer during the past 60 days.

(d) Certain securities of the Issuer are held directly by 667, a limited partnership the sole general partner of which is Baker Biotech Capital, L.P., a limited partnership the sole general partner of which is Baker Biotech Capital (GP), LLC. Julian C. Baker and Felix J. Baker are the controlling members of Baker Biotech Capital (GP), LLC.

Certain securities of the Issuer are held directly by Life Sciences, a limited partnership the sole general partner of which is Baker Brothers Life Sciences Capital, L.P., a limited partnership the sole general partner of which is Baker Brothers Life Sciences Capital (GP), LLC. Julian C. Baker and Felix J. Baker are the controlling members of Baker Brothers Life Sciences Capital (GP), LLC.

(e) Not applicable.

Item 6. Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer.

Item 3 of Schedule 13D is supplemented and amended, as the case may be, as follows:

Ms. Brownstein, as compensation for her previous service on the Board was granted 47,200 options to purchase Common Stock ("Stock Options") at an exercise price of \$7.11 per share, which expire on February 22, 2031, 14,422 of which are vested and 32,778 of which expired as of the date of this filing and 40,000 Stock Options at an exercise price of \$6.80 per share, which expire on June 7, 2031, 26,666 of which are vested and 13,334 of which expired as of the date of this filing. All of the Stock Options expire 3 months after Ms. Brownstein's resignation from the Board.

The policy of the Adviser to the Funds does not permit employees of the Adviser to receive compensation for serving as directors of the Issuer. Therefore, Ms. Brownstein will have no pecuniary interest in the Stock Options or Common Stock received from the exercise of Stock Options received as directors' compensation for her previous service. The Funds are instead entitled to the pecuniary interest in the Stock Options, Common Stock and Common Stock received from the exercise of Stock Options received as directors' compensation.

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 10, 2022

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
