

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 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. 4)*

Aprea Therapeutics, Inc.

(Name of Issuer)

Common Stock, par value \$0.001 per share

(Title of Class of Securities)

03836J102

(CUSIP Number)

Rebecca Lucia
5AM Venture Management, LLC
501 2nd Street, Suite 350
San Francisco, CA 94107
(415) 993-8565

(Name, Address and Telephone Number of Person
Authorized to Receive Notices and Communications)

November 16, 2020

(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 §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

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

1.	Name of Reporting Persons	
	5AM Ventures IV, L.P.	
2.	Check the Appropriate Box if a Member of a Group (see instructions)	
	(a)	o
	(b)	x(1)
3.	SEC USE ONLY	
4.	Source of Funds (see instructions)	
	WC	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Item 2(d) or 2(e)	o
6.	Citizenship or Place of Organization	
	Delaware	
	7. Sole Voting Power	
	0	
	8. Shared Voting Power	
	1,189,592 shares of common stock (2)	
	9. Sole Dispositive Power	
	0	
	10. Shared Dispositive Power	
	1,189,592 shares of common stock (2)	
11.	Aggregate Amount Beneficially Owned by Each Reporting Person	
	1,189,592 shares of common stock (2)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions)	o
13.	Percent of Class Represented by Amount in Row 11	
	5.6% (3)	
14.	Type of Reporting Person (see instructions)	
	PN	

(1) This Schedule 13D is filed by 5AM Partners IV, LLC (“5AM Partners IV”), 5AM Ventures IV, L.P. (“5AM IV”), 5AM Co-Investors IV, L.P. (“5AM Co-Investors IV”), 5AM Opportunities I, L.P. (“5AM Opportunities”), 5AM Opportunities I (GP), LLC (“5AM Opportunities GP”), Dr. John D. Diekman (“Diekman”), Andrew J. Schwab (“Schwab”) and Dr. Scott M. Rocklage (“Rocklage” and, with 5AM Partners IV, 5AM IV, 5AM Co-Investors IV, 5AM Opportunities, 5AM Opportunities GP, Diekman and Schwab, collectively, the “Reporting Persons”). The Reporting Persons expressly disclaim status as a “group” for purposes of this Schedule 13D.

(2) These shares are held by 5AM IV. Diekman, Schwab and Rocklage, as Managing Members of 5AM Partners IV, share voting and investment authority over the shares held by 5AM IV.

(3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer’s Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

1.	Name of Reporting Persons	
	5AM Co-Investors IV, L.P.	
2.	Check the Appropriate Box if a Member of a Group (see instructions)	
	(a)	o
	(b)	x(1)
3.	SEC USE ONLY	
4.	Source of Funds (see instructions)	
	WC	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Item 2(d) or 2(e)	o
6.	Citizenship or Place of Organization	
	Delaware	
	7. Sole Voting Power	
		0
	8. Shared Voting Power	
		49,565 shares of common stock (2)
	9. Sole Dispositive Power	
		0
	10. Shared Dispositive Power	
		49,565 shares of common stock (2)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person	
	49,565 shares of common stock (2)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions)	o
13.	Percent of Class Represented by Amount in Row 11	
	0.2% (3)	
14.	Type of Reporting Person (see instructions)	
	PN	

(1) This Schedule 13D is filed by the Reporting Persons. The Reporting Persons expressly disclaim status as a "group" for purposes of this Schedule 13D.

(2) These shares are held by 5AM Co-Investors IV. Diekman, Schwab and Rocklage, as Managing Members of 5AM Partners IV, share voting and investment authority over the shares held by 5AM Co-Investors IV.

(3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer's Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

1.	Name of Reporting Persons	
	5AM Partners IV, LLC	
2.	Check the Appropriate Box if a Member of a Group (see instructions)	
	(a)	o
	(b)	x(1)
3.	SEC USE ONLY	
4.	Source of Funds (see instructions)	
	AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Item 2(d) or 2(e)	o
6.	Citizenship or Place of Organization	
	Delaware	
	7. Sole Voting Power	
		0
	8. Shared Voting Power	
		1,239,157 shares of common stock (2)
	9. Sole Dispositive Power	
		0
	10. Shared Dispositive Power	
		1,239,157 shares of common stock (2)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person	
	1,239,157 shares of common stock (2)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions)	o
13.	Percent of Class Represented by Amount in Row 11	
	5.8% (3)	
14.	Type of Reporting Person (see instructions)	
	OO	

(1) This Schedule 13D is filed by the Reporting Persons. The Reporting Persons expressly disclaim status as a “group” for purposes of this Schedule 13D.

(2) Includes (i) 1,189,592 shares held by 5AM IV; and (ii) 49,565 shares held by 5AM Co-Investors IV. Diekman, Schwab and Rocklage, as Managing Members of 5AM Partners IV, share voting and investment authority over the shares held by 5AM IV and 5AM Co-Investors IV.

(3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer’s Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

1.	Name of Reporting Persons	
	5AM Opportunities I, L.P.	
2.	Check the Appropriate Box if a Member of a Group (see instructions)	
	(a)	o
	(b)	x(1)
3.	SEC USE ONLY	
4.	Source of Funds (see instructions)	
	WC	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Item 2(d) or 2(e)	o
6.	Citizenship or Place of Organization	
	Delaware	
	7. Sole Voting Power	
	0	
	8. Shared Voting Power	
	138,497 shares of common stock (2)	
	9. Sole Dispositive Power	
	0	
	10. Shared Dispositive Power	
	138,497 shares of common stock (2)	
11.	Aggregate Amount Beneficially Owned by Each Reporting Person	
	138,497 shares of common stock (2)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions)	o
13.	Percent of Class Represented by Amount in Row 11	
	0.7% (3)	
14.	Type of Reporting Person (see instructions)	
	PN	

- (1) This Schedule 13D is filed by the Reporting Persons. The Reporting Persons expressly disclaim status as a "group" for purposes of this Schedule 13D.
- (2) These shares are held by 5AM Opportunities. Schwab and Dr. Kush Parmar ("Parmar"), as Managing Members of 5AM Opportunities GP, share voting and investment authority over the shares held by 5AM Opportunities.
- (3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer's Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

1.	Name of Reporting Persons	
	5AM Opportunities I (GP), LLC	
2.	Check the Appropriate Box if a Member of a Group (see instructions)	
	(a)	o
	(b)	x(1)
3.	SEC USE ONLY	
4.	Source of Funds (see instructions)	
	AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Item 2(d) or 2(e)	o
6.	Citizenship or Place of Organization	
	Delaware	
	7. Sole Voting Power	
		0
	8. Shared Voting Power	
		138,497 shares of common stock (2)
	9. Sole Dispositive Power	
		0
	10. Shared Dispositive Power	
		138,497 shares of common stock (2)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person	
	138,497 shares of common stock (2)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions)	o
13.	Percent of Class Represented by Amount in Row 11	
	0.7% (3)	
14.	Type of Reporting Person (see instructions)	
	OO	

(1) This Schedule 13D is filed by the Reporting Persons. The Reporting Persons expressly disclaim status as a "group" for purposes of this Schedule 13D.

(2) Includes 138,497 shares held by 5AM Opportunities. Schwab and Parmar, as Managing Members of 5AM Opportunities GP, share voting and investment authority over the shares held by 5AM Opportunities.

(3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer's Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

1.	Name of Reporting Persons	
	Dr. John D. Diekman	
2.	Check the Appropriate Box if a Member of a Group (see instructions)	
	(a)	o
	(b)	x(1)
3.	SEC USE ONLY	
4.	Source of Funds (see instructions)	
	AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Item 2(d) or 2(e)	o
6.	Citizenship or Place of Organization	
	United States	
	7. Sole Voting Power	
	0	
	8. Shared Voting Power	
	1,239,157 shares of common stock (2)	
	9. Sole Dispositive Power	
	0	
	10. Shared Dispositive Power	
	1,239,157 shares of common stock (2)	
11.	Aggregate Amount Beneficially Owned by Each Reporting Person	
	1,239,157 shares of common stock (2)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions)	o
13.	Percent of Class Represented by Amount in Row 11	
	5.8% (3)	
14.	Type of Reporting Person (see instructions)	
	IN	

(1) This Schedule 13D is filed by the Reporting Persons. The Reporting Persons expressly disclaim status as a "group" for purposes of this Schedule 13D.

(2) Includes (i) 1,189,592 shares held by 5AM IV; and (ii) 49,565 shares held by 5AM Co-Investors IV. Diekman, Schwab and Rocklage, as Managing Members of 5AM Partners IV, share voting and investment authority over the shares held by 5AM IV and 5AM Co-Investors IV.

(3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer's Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

1.	Name of Reporting Persons	
	Andrew J. Schwab	
2.	Check the Appropriate Box if a Member of a Group (see instructions)	
	(a)	o
	(b)	x(1)
3.	SEC USE ONLY	
4.	Source of Funds (see instructions)	
	AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Item 2(d) or 2(e)	o
6.	Citizenship or Place of Organization	
	United States	
	7. Sole Voting Power	
	0	
	8. Shared Voting Power	
	1,377,654 shares of common stock (2)	
	9. Sole Dispositive Power	
	0	
	10. Shared Dispositive Power	
	1,377,654 shares of common stock (2)	
11.	Aggregate Amount Beneficially Owned by Each Reporting Person	
	1,377,654 shares of common stock (2)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions)	o
13.	Percent of Class Represented by Amount in Row 11	
	6.5% (3)	
14.	Type of Reporting Person (see instructions)	
	IN	

(1) This Schedule 13D is filed by the Reporting Persons. The Reporting Persons expressly disclaim status as a "group" for purposes of this Schedule 13D.

(2) Includes (i) 1,189,592 shares held by 5AM IV; (ii) 49,565 shares held by 5AM Co-Investors IV; and (iii) 138,497 shares held by 5AM Opportunities.

Diekman, Schwab and Rocklage, as Managing Members of 5AM Partners IV, share voting and investment authority over the shares held by 5AM IV and 5AM Co-Investors IV. Schwab and Parmar, as Managing Members of 5AM Opportunities GP, share voting and investment authority over the shares held by 5AM Opportunities.

(3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer's Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

1.	Name of Reporting Persons Dr. Scott M. Rocklage	
2.	Check the Appropriate Box if a Member of a Group (see instructions) (a) (b)	 o x(1)
3.	SEC USE ONLY	
4.	Source of Funds (see instructions) AF	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Item 2(d) or 2(e)	o
6.	Citizenship or Place of Organization United States	
	7. Sole Voting Power 0	
	8. Shared Voting Power 1,239,157 shares of common stock (2)	
	9. Sole Dispositive Power 0	
	10. Shared Dispositive Power 1,239,157 shares of common stock (2)	
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 1,239,157 shares of common stock (2)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions)	o
13.	Percent of Class Represented by Amount in Row 11 5.8% (3)	
14.	Type of Reporting Person (see instructions) IN	

(1) This Schedule 13D is filed by the Reporting Persons. The Reporting Persons expressly disclaim status as a "group" for purposes of this Schedule 13D.

(2) Includes (i) 1,189,592 shares held by 5AM IV; and (ii) 49,565 shares held by 5AM Co-Investors IV. Diekman, Schwab and Rocklage, as Managing Members of 5AM Partners IV, share voting and investment authority over the shares held by 5AM IV and 5AM Co-Investors IV.

(3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer's Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

Explanatory Note: This Amendment No. 4 (the “Amendment”), which amends the Schedule 13D filed with the Securities and Exchange Commission (the “SEC”) on October 17, 2019, as amended by Amendment No. 1 filed May 22, 2020, as amended by Amendment No. 2 filed June 11, 2020 and as amended by Amendment No. 3 filed October 7, 2020 (the “Original Schedule 13D”) is being filed on behalf of 5AM Partners IV, LLC (“5AM Partners IV”), 5AM Ventures IV, L.P. (“5AM IV”), 5AM Co-Investors IV, L.P. (“5AM Co-Investors IV”), 5AM Opportunities I, L.P. (“5AM Opportunities”), 5AM Opportunities I (GP), LLC (“5AM Opportunities GP”), Dr. John D. Diekman (“Diekman”), Andrew J. Schwab (“Schwab”) and Dr. Scott M. Rocklage (“Rocklage”) and, with 5AM Partners IV, 5AM IV, Co-Investors IV, 5AM Opportunities, 5AM Opportunities GP, Diekman and Schwab, collectively, the “Reporting Persons”) in respect of the Common Stock, \$0.001 par value per share of Aprea Therapeutics, Inc., a Delaware corporation (the “Issuer”). This Amendment is being filed by the Reporting Persons to report open market sales of Common Stock on November 16, 2020 and November 18, 2020. Accordingly, the number of securities beneficially owned by the Reporting Persons has decreased as described in Items 4 and 5 below.

Item 4 and 5 of the Original Schedule 13D are hereby amended and supplemented to the extent hereinafter expressly set forth and, except as amended and supplemented hereby, the Original Schedule 13D remains in full force and effect. All capitalized terms used in this Amendment but not defined herein shall have the meanings ascribed thereto in the Original Schedule 13D.

Item 4. Purpose of Transaction

Item 4 of the Original Schedule 13D is hereby amended and supplemented by adding the following paragraphs at the end of Item 4:

On November 16, 2020, 5AM IV sold an aggregate of 288,000 shares of Common Stock in an open market transaction at a price of \$20.10 per share and 5AM Co-Investors IV sold an aggregate of 12,000 shares of Common Stock in an open market transaction at a price of \$20.10 per share.

On November 18, 2020, 5AM IV sold an aggregate of 345,600 shares of Common Stock in an open market transaction at a price of \$19.92 per share and 5AM Co-Investors IV sold an aggregate of 14,400 shares of Common Stock in an open market transaction at a price of \$19.92 per share.

Item 5. Interest in Securities of the Issuer

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

(a) – (b). The following information with respect to the ownership of the Common Stock of the Issuer by the persons filing this statement on Schedule 13D is provided as of November 18, 2020:

Reporting Persons	Shares Held Directly	Sole Voting Power	Shared Voting Power (1)	Sole Dispositive Power	Shared Dispositive Power (1)	Beneficial Ownership	Percentage of Class (3)
5AM IV	1,189,592	0	1,189,592	0	1,189,592	1,189,592	5.6%
5AM Co-Investors IV	49,565	0	49,565	1	49,565	49,565	0.2%
5AM Partners IV (1)	0	0	1,239,157	0	1,239,157	1,239,157	5.8%
5AM Opportunities	138,497	0	138,497	0	138,497	138,497	0.7%
5AM Opportunities GP (2)	0	0	138,497	0	138,497	138,497	0.7%
Diekman (1)	0	0	1,239,157	0	1,239,157	1,239,157	5.8%
Schwab (1) (2)	0	0	1,377,654	0	1,377,654	1,377,654	6.5%
Rocklage (1)	0	0	1,239,157	0	1,239,157	1,239,157	5.8%

(1) Includes 1,189,592 shares of Common Stock held by 5AM IV and 49,565 shares of Common Stock held by 5AM Co-Investors IV. Diekman, Schwab and Rocklage, as Managing Members of 5AM Partners IV, share voting and investment authority over the shares held by 5AM IV and 5AM Co-Investors IV.

(2) Includes 138,497 shares of Common Stock held by 5AM Opportunities. Schwab and Parmar, as Managing Members of 5AM Opportunities GP, share voting and investment authority over the shares held by 5AM Opportunities.

(3) Percentage based on 21,186,827 shares of Common Stock outstanding as of November 6, 2020 as disclosed in the Issuer's Form 10-Q filed with the Securities and Exchange Commission on November 6, 2020.

(c) Except as set forth herein, none of the Reporting Persons has effected any transactions in shares of the Issuer's Common Stock during the last 60 days.

(d) No other person is known to have the right to receive or the power to direct the receipt of dividends from, or any proceeds from the sale of, the shares of Common Stock beneficially owned by any of the Reporting Persons.

(e) Not applicable.

SIGNATURES

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.

Date: November 19, 2020

5AM Ventures IV, L.P.

By: 5AM Partners IV, LLC,
Its General Partner

By: /s/ Andrew J. Schwab
Andrew J. Schwab
Managing Member

5AM Co-Investors IV, L.P.

By: 5AM Partners IV, LLC,
Its General Partner

By: /s/ Andrew J. Schwab
Andrew J. Schwab
Managing Member

5AM Partners IV, LLC

By: /s/ Andrew J. Schwab
Andrew J. Schwab
Managing Member

5AM Opportunities I, L.P.

By: 5AM Opportunities I (GP), LLC,
Its General Partner

By: /s/ Andrew J. Schwab
Andrew J. Schwab
Managing Member

5AM Opportunities I (GP), LLC

By: /s/ Andrew J. Schwab
Andrew J. Schwab
Managing Member

DR. JOHN D. DIEKMAN

By: /s/ Dr. John D. Diekman
Dr. John D. Diekman

ANDREW J. SCHWAB

By: /s/ Andrew J. Schwab
Andrew J. Schwab

DR. SCOTT M. ROCKLAGE

By: /s/ Dr. Scott M. Rocklage
Dr. Scott M. Rocklage