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**SECURITIES AND EXCHANGE COMMISSION**  
WASHINGTON, DC 20549

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**SCHEDULE 13D/A**

**Under the Securities Exchange Act of 1934**  
**(Amendment No. 1)\***

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**SPRUCE BIOSCIENCES, INC.**

(Name of Issuer)

**Common Stock, par value \$0.001 per share**  
(Title of Class of Securities)

**85209E109**  
(CUSIP Number)

**Jay W. Schmelter**  
**101 S. Hanley Road, Suite 1850**  
**St. Louis, MO 63105**  
**(314) 726-6700**

**With copy to:**

**Gloria M. Skigen, Esq.**  
**Holland & Knight LLP**  
**One Stamford Plaza 263 Tresser Boulevard Suite 1400**  
**Stamford, CT 06901**  
**(203) 905-4526**

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

**February 16, 2023**  
(Date of Event which Requires Filing of this Statement)

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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 (however, see the Notes).

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1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)  RiverVest Venture Fund III, L.P.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  WC	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware, USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  1,641,077 <sup>(1)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  1,641,077 <sup>(1)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,641,077 <sup>(1)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  4.0% <sup>(2)</sup>	
14	TYPE OF REPORTING PERSON  PN	

- (1) Represents (i) 1,528,834 shares of Common Stock (as defined below) and (ii) currently exercisable warrants to acquire 112,243 shares of Common Stock at an exercise price of \$3.96 per share.
- (2) Based upon (i) 23,560,250 shares of common stock, par value \$0.001 per share (“Common Stock”), of Spruce Biosciences, Inc., a Delaware corporation (the “Issuer”), outstanding as of November 4, 2022, as reported in the Issuer’s Form 10-Q filed with the Securities and Exchange Commission (the “SEC”) on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) 112,243 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest Venture Fund III, L.P., a Delaware limited partnership (“RiverVest III”).

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)  RiverVest Venture Fund III (Ohio), L.P.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  WC	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware, USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  87,099 <sup>(3)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  87,099 <sup>(3)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  87,099 <sup>(3)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  0.2% <sup>(4)</sup>	
14	TYPE OF REPORTING PERSON  PN	

(3) Represents (i) 81,142 shares of Common Stock, and (ii) currently exercisable warrants to acquire 5,957 shares of Common Stock at an exercise price of \$3.96 per share.

(4) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest Venture Fund III (Ohio), L.P., a Delaware limited partnership ("RiverVest III (Ohio)")

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)  RiverVest Venture Partners III (Ohio), LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware, USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  87,099 <sup>(5)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  87,099 <sup>(5)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  87,099 <sup>(5)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  0.2% <sup>(6)</sup>	
14	TYPE OF REPORTING PERSON  OO	

(5) Represents (i) 81,142 shares of Common Stock owned by RiverVest III (Ohio) and (ii) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest Fund III (Ohio) at an exercise price of \$3.96 per share. RiverVest Venture Partners III (Ohio), LLC, a Delaware limited liability company (“RiverVest Partners III (Ohio)”), is the general partner of RiverVest III (Ohio).

(6) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer’s Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest Fund III (Ohio).

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)  RiverVest Venture Partners III, L.P.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware, USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  1,728,176 <sup>(7)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  1,728,176 <sup>(7)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,728,176 <sup>(7)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  4.2% <sup>(8)</sup>	
14	TYPE OF REPORTING PERSON  PN	

(7) Represents (i) 1,528,834 shares of Common Stock owned by RiverVest III, (ii) 112, 243 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III, (iii) 81,142 shares of Common Stock owned by RiverVest III (Ohio), and (iv) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III (Ohio). RiverVest Venture Partners III, L.P., a Delaware limited partnership ("RiverVest Partners III"), is the general partner of RiverVest III and the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio).

(8) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, (iii) 112, 243 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III, and (iv) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III (Ohio).

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)	
	RiverVest Venture Partners III, LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware, USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  1,728,176 <sup>(9)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  1,728,176 <sup>(9)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,728,176 <sup>(9)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  4.2% <sup>(10)</sup>	
14	TYPE OF REPORTING PERSON  OO	

(9) Represents (i) 1,528,834 shares of Common Stock owned by RiverVest III, (ii) 112, 243 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III, (iii) 81,142 shares of Common Stock owned by RiverVest III (Ohio), and (iv) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III (Ohio). RiverVest Venture Partners III, LLC, a Delaware limited liability company, is the general partner of RiverVest Partners III, which is (a) the general partner of RiverVest III and (b) the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio).

(10) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, (iii) 112, 243 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III, and (iv) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III (Ohio).

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)  RiverVest Venture Fund IV, L.P.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  WC	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware, USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  1,799,105 <sup>(11)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  1,799,105 <sup>(11)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,799,105 <sup>(11)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  4.4% <sup>(12)</sup>	
14	TYPE OF REPORTING PERSON  PN	

(11) Represents (i) 1,326,305 shares of Common Stock owned by RiverVest Venture Fund IV, L.P., a Delaware limited partnership (“RiverVest IV”), and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest IV at an exercise price of \$3.96 per share.

(12) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer’s Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) 472,800 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest IV.

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)  RiverVest Venture Partners IV, L.P.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware, USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  1,799,105 <sup>(13)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  1,799,105 <sup>(13)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,799,105 <sup>(13)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  4.4% <sup>(14)</sup>	
14	TYPE OF REPORTING PERSON  PN	

(13) Represents (i) 1,326,305 shares of Common Stock owned by RiverVest IV, and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest IV. RiverVest Venture Partners IV, L.P., a Delaware limited partnership (“RiverVest Partners IV”), is the general partner of RiverVest IV.

(14) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer’s Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) 472,800 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest IV.



1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)  RiverVest Venture Partners IV, LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware, USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  1,799,105 <sup>(15)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  1,799,105 <sup>(15)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,799,105 <sup>(15)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  4.4% <sup>(16)</sup>	
14	TYPE OF REPORTING PERSON  OO	

(15) Represents (i) 1,326,305 shares of Common Stock owned by RiverVest IV, and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest IV. RiverVest Venture Partners IV, LLC, a Delaware limited liability company, is the general partner of RiverVest Partners IV, which is the general partner of RiverVest IV.

(16) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) 472,800 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest IV.

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)	
	John P. McKearn, Ph.D.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  3,527,281 <sup>(17)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  3,527,281 <sup>(17)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  3,527,281 <sup>(17)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  8.6% <sup>(18)</sup>	
14	TYPE OF REPORTING PERSON  IN	

- (17) Represents (i) an aggregate of 2,936,281 shares of Common Stock owned collectively by RiverVest III, RiverVest III (Ohio) and RiverVest IV, and (ii) an aggregate of 591,000 additional shares of Common Stock issuable upon the exercise of the warrants held collectively by RiverVest III, RiverVest III (Ohio) and RiverVest IV, in each case at an exercise price of \$3.96 per share.

Dr. McKearn is a member of RiverVest Venture Partners III, LLC, which is the general partner of RiverVest Partners III. RiverVest Partners III is (a) the general partner of RiverVest III and (b) the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio).

Dr. McKearn is a member of RiverVest Venture Partners IV, LLC, which is the general partner of RiverVest Partners IV. RiverVest Partners IV is the general partner of RiverVest IV.

- (18) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) an aggregate of 591,000 additional shares of Common Stock issuable upon the exercise of the warrants held collectively by RiverVest III, RiverVest III (Ohio) and RiverVest IV.

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)	
	Jay Schmelter	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  3,527,281 <sup>(19)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  3,527,281 <sup>(19)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  3,527,281 <sup>(19)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  8.6% <sup>(20)</sup>	
14	TYPE OF REPORTING PERSON  IN	

- (19) Represents (i) an aggregate of 2,936,281 shares of Common Stock owned collectively by RiverVest III, RiverVest III (Ohio) and RiverVest IV, and (ii) an aggregate of 591,000 additional shares of Common Stock issuable upon the exercise of the warrants held collectively by RiverVest III, RiverVest III (Ohio) and RiverVest IV, in each case at an exercise price of \$3.96 per share

Mr. Schmelter is a member of RiverVest Venture Partners III, LLC, which is the general partner of RiverVest Partners III. RiverVest Partners III is (a) the general partner of RiverVest III and (b) the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio).

Mr. Schmelter is a member of RiverVest Venture Partners IV, LLC, which is the general partner of RiverVest Partners IV. RiverVest Partners IV is the general partner of RiverVest IV.

- (20) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) an aggregate of 591,000 additional shares of Common Stock issuable upon the exercise of the warrants held collectively by RiverVest III, RiverVest III (Ohio) and RiverVest IV.

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)	
	Thomas C. Melzer	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  0
	8	SHARED VOTING POWER  1,728,176 <sup>(21)</sup>
	9	SOLE DISPOSITIVE POWER  0
	10	SHARED DISPOSITIVE POWER  1,728,176 <sup>(21)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,728,176 <sup>(21)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  4.2% <sup>(22)</sup>	
14	TYPE OF REPORTING PERSON  IN	

(21) Represents (i) 1,528,834 shares of Common Stock owned by RiverVest III, (ii) 112, 243 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III, (iii) 81,142 shares of Common Stock owned by RiverVest III (Ohio), and (iv) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III (Ohio).

Mr. Melzer is a member of RiverVest Venture Partners III, LLC, which is the general partner of RiverVest Partners III. RiverVest Partners III is (a) the general partner of RiverVest III and (b) the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio).

(22) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, (iii) 112, 243 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III, and (iv) 5,957 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III (Ohio).

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. (ENTITIES ONLY)	
	Niall O'Donnell, Ph.D.	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS  AF	
5	CHECK IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) OR 2(e)  <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION  USA	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER  32,500 <sup>(23)</sup>
	8	SHARED VOTING POWER  1,799,105 <sup>(24)</sup>
	9	SOLE DISPOSITIVE POWER  32,500 <sup>(23)</sup>
	10	SHARED DISPOSITIVE POWER  1,799,105 <sup>(24)</sup>
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  1,799,105 <sup>(24)</sup>	
12	CHECK IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES  <input checked="" type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)  4.4% <sup>(25)</sup>	
14	TYPE OF REPORTING PERSON  IN	

(23) Represents 32,500 shares of Common Stock options owned by Mr. O'Donnell.

(24) Represents (i) 1,326,305 shares of Common Stock owned by RiverVest IV, and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest IV.

Mr. O'Donnell is a member of RiverVest Venture Partners IV, LLC, which is the general partner of RiverVest Partners IV. RiverVest Partners IV is the general partner of RiverVest IV.

(25) Based upon (i) 23,560,250 shares of Common Stock outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) 472,800 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest IV.

This amendment (“Amendment No. 1”) amends the Schedule 13D originally filed with the SEC on October 23, 2020 (the “Schedule”), and relates to the Common Stock. All capitalized terms contained herein but not otherwise defined shall have the meanings ascribed to such terms in the Schedule.

**Item 1. Security and Issuer.**

No change.

**Item 2. Identity and Background.**

No change.

**Item 3. Source and Amount of Funds or Other Consideration.**

Item 3 amends and supplements Item 3 in the Schedule as follows:

On February 8, 2023, RiverVest III, RiverVest III (Ohio) and RiverVest IV, among other parties, entered into a Securities Purchase Agreement with the Issuer. Pursuant to the Securities Purchase Agreement, RiverVest III, RiverVest III (Ohio) and RiverVest IV purchased an aggregate of 2,936,281 shares of the Common Stock (“Shares”) and 591,000 warrants to purchase the Common Stock with an exercise price of \$3.96 per Share (“Warrants”), for a combined price of \$3.17 per share of common stock, and total consideration of \$2,419,160. At the closing of the transaction on February 16, 2023, the Issuer sold and issued, in a private placement, the Shares and Warrants to RiverVest III, RiverVest III (Ohio) and RiverVest IV, respectively. The foregoing description is qualified in its entirety by the Securities Purchase Agreement incorporated by reference in this filing.

RiverVest III, RiverVest III (Ohio) and RiverVest IV purchased the Shares and Warrants set forth in this Schedule 13D using funds from working capital.

**Item 4. Purpose of the Transaction.**

Item 4 of the Schedule is supplemented as follows:

The information set forth in Item 3 and Item 6 of this Schedule 13D is incorporated by reference to this Item 4.

**Item 5. Interest in Securities of the Issuer.**

(a) and (b)

<u>Entity or Individual</u>	<u>Shares Held Directly</u>	<u>Sole Voting Power</u>	<u>Shared Voting Power</u>	<u>Sole Dispositive Power</u>	<u>Shared Dispositive Power</u>	<u>Beneficial Ownership</u>	<u>Percentage of Class<sup>(*)</sup></u>
RiverVest Venture Fund III, L.P.	1,641,077	0	1,641,077	0	1,641,077	1,641,077	4.0%
RiverVest Venture Fund III (Ohio), L.P.	87,099	0	87,099	0	87,099	87,099	0.2%
RiverVest Venture Partners III (Ohio), LLC <sup>(1)</sup>	0	0	87,099	0	87,099	87,099	0.2%
RiverVest Venture Partners III, L.P. <sup>(2)</sup>	0	0	1,728,176	0	1,728,176	1,728,176	4.2%
RiverVest Venture Partners III, LLC <sup>(3)</sup>	0	0	1,728,176	0	1,728,176	1,728,176	4.2%

RiverVest Venture Fund IV, L.P.	1,799,105	0	1,799,105	0	1,799,105	1,799,105	4.4%
RiverVest Venture Partners IV, L.P. (4)	0	0	1,799,105	0	1,799,105	1,799,105	4.4%
RiverVest Venture Partners IV, LLC(5)	0	0	1,799,105	0	1,799,105	1,799,105	4.4%
John P. McKearn, Ph.D.(6)	0	0	3,527,281	0	3,527,281	3,527,281	8.6%
Jay Schmelter(7)	0	0	3,527,281	0	3,527,281	3,527,281	8.6%
Thomas C. Melzer(8)	0	0	1,728,176	0	1,728,176	1,728,176	4.2%
Niall O'Donnell(9)	32,500	32,500	1,799,105	32,500	1,799,105	1,799,105	4.4%

- (\*) Based upon (i) 23,560,250 shares of Common Stock, of the Issuer, outstanding as of November 4, 2022, as reported in the Issuer's Form 10-Q filed with the SEC on November 10, 2022, plus (ii) the 16,916,000 additional shares of Common Stock sold and issued by the Issuer pursuant to the Securities Purchase Agreement described herein, and (iii) 112,243 additional shares of Common Stock issuable upon the exercise of the warrants held by RiverVest III.
- (1) RiverVest Partners III (Ohio) is the general partner of RiverVest III (Ohio), and as a result, may be deemed to beneficially own the (i) 81,142 shares of Common Stock, and (ii) currently exercisable warrants to acquire 5,957 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III (Ohio).
- (2) RiverVest Partners III is the general partner of RiverVest III and the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio), and as a result, may be deemed to beneficially own the (i) 1,528,834 shares of Common Stock, and (ii) currently exercisable warrants to acquire 112,243 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III and the (i) 81,142 shares of Common Stock, and (ii) currently exercisable warrants to acquire 5,957 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III (Ohio).
- (3) RiverVest Venture Partners III, LLC is the general partner of RiverVest Partners III, which is (a) the general partner of RiverVest III and (b) the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio), and as a result, may be deemed to beneficially own the (i) 1,528,834 shares of Common Stock, and (ii) currently exercisable warrants to acquire 112,243 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III and the (i) 81,142 shares of Common Stock, and (ii) currently exercisable warrants to acquire 5,957 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III (Ohio).
- (4) RiverVest Partners IV is the general partner of RiverVest IV, and as a result, may be deemed to beneficially own the (i) 1,326,305 shares of Common Stock, and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of warrants held at an exercise price of \$3.96 beneficially owned by RiverVest IV.
- (5) RiverVest Venture Partners IV, LLC is the general partner of RiverVest Partners IV, which is the general partner of RiverVest IV, and as a result, may be deemed to beneficially own the (i) 1,326,305 shares of Common Stock, and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of warrants held at an exercise price of \$3.96 beneficially owned by RiverVest IV.
- (6) Dr. McKearn is a member of RiverVest Venture Partners III, LLC, which is the general partner of RiverVest Partners III. RiverVest Partners III is (a) the general partner of RiverVest III and (b) the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio). As a result, Dr. McKearn may be deemed to beneficially own the (i) 1,528,834 shares of Common Stock, and (ii) currently exercisable warrants to acquire 112,243 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III and the (i) 81,142 shares of Common Stock, and (ii) currently exercisable warrants to acquire 5,957 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III (Ohio).

Dr. McKearn is a member of RiverVest Venture Partners IV, LLC, which is the general partner of RiverVest Partners IV. RiverVest Partners IV is the general partner of RiverVest IV. As a result, Dr. McKearn may be deemed to beneficially own the (i) 1,326,305 shares of Common Stock, and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of warrants held at an exercise price of \$3.96 beneficially owned by RiverVest IV.

- (7) Mr. Schmelter is a member of RiverVest Venture Partners III, LLC, which is the general partner of RiverVest Partners III. RiverVest Partners III is (a) the general partner of RiverVest III and (b) the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio). As a result, Mr. Schmelter may be deemed to beneficially own the (i) 1,528,834 shares of Common Stock, and (ii) currently exercisable warrants to acquire 112,243 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III and the (i) 81,142 shares of Common Stock, and (ii) currently exercisable warrants to acquire 5,957 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III (Ohio).

Mr. Schmelter is a member of RiverVest Venture Partners IV, LLC, which is the general partner of RiverVest Partners IV. RiverVest Partners IV is the general partner of RiverVest IV. As a result, Dr. McKearn may be deemed to beneficially own the (i) 1,326,305 shares of Common Stock, and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of warrants held at an exercise price of \$3.96 beneficially owned by RiverVest IV.

- (8) Mr. Melzer is a member of RiverVest Venture Partners III, LLC, which is the general partner of RiverVest Partners III. RiverVest Partners III is (a) the general partner of RiverVest III and (b) the sole member of RiverVest Partners III (Ohio), which is the general partner of RiverVest III (Ohio). As a result, Mr. Melzer may be deemed to beneficially own the (i) 1,528,834 shares of Common Stock, and (ii) currently exercisable warrants to acquire 112,243 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III and the (i) 81,142 shares of Common Stock, and (ii) currently exercisable warrants to acquire 5,957 shares of Common Stock at an exercise price of \$3.96 per share beneficially owned by RiverVest III (Ohio).
- (9) Mr. O'Donnell is a member of RiverVest Venture Partners IV, LLC, which is the general partner of RiverVest Partners IV. RiverVest Partners IV is the general partner of RiverVest IV. As a result, Mr. O'Donnell may be deemed to beneficially own the (i) 1,326,305 shares of Common Stock, and (ii) 472,800 additional shares of Common Stock issuable upon the exercise of warrants held at an exercise price of \$3.96 beneficially owned by RiverVest IV.

By virtue of the relationships described herein, the Reporting Persons may be deemed to constitute a "group" for purposes of Section 13(d) (3) of the Act. The filing of this Statement shall not be construed as an admission that the Reporting Persons are a group, or have agreed to act as a group. Each Reporting Person expressly disclaims beneficial ownership of the securities reported herein, except to the extent such Reporting Person actually exercises voting or dispositive power with respect to such securities.

(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.

#### **Item 6. Contracts, Arrangements, Understandings or Relationships With Respect to Securities of the Issuer.**

Item 6 is amended and supplemented as follows:

On February 8, 2023, the Issuer and certain other purchasers including RiverVest III, RiverVest III (Ohio) and RiverVest IV entered into a Securities Purchase Agreement pursuant to which the Issuer agreed to sell and issue (i) 16,116,000 of the Common Stock, (ii) pre-funded warrants to purchase 800,000 Shares of the Common Stock, and (iii) 12,687,000 standard warrants to purchase the Common Stock in a private placement transaction. Pursuant to the Securities Purchase Agreement RiverVest III, RiverVest III (Ohio) and RiverVest IV purchased the securities set forth in Item 3 of this Amendment No. 1.



Under the Securities Purchase Agreement, the Issuer is required to file one or more registration statements (the “Registration Statements”) covering the resale of the Common Stock and the shares of Common Stock issuable upon conversion of the Warrants issued under the Securities Purchase Agreement as soon as reasonably practicable, but in no event later than 30 days after the closing of the transaction (the “Filing Deadline”) and to cause the applicable Registration Statements to become effective within a specified period after the Filing Deadline. The Issuer is required to use its best efforts to keep the Registration Statements continuously effective until the earlier of: February 16, 2026 or the date the covered shares and warrant shares held by or issuable to such Holder may be sold under Rule 144 without being subject to any volume, manner of sale or publicly available information requirements. Certain cash penalties will apply to the Issuer in the event of registration failures, as described in the Securities Purchase Agreement. All registration expenses incurred shall be borne by the Issuer. From February 8, 2023 and until 90 days following the effectiveness of the Registration Statements, the Issuer may not issue shares of Common Stock or file a registration statement with the SEC for equity other than the Registration Statements, unless all securities sold under the Securities Purchase Agreement are sold or may be sold under Rule 144 during the 90 day period. The foregoing description is qualified in its entirety by the Securities Purchase Agreement incorporated by reference in this filing.

Pursuant to the Common Stock Purchase Warrant, dated February 16, 2023, the Warrants are currently exercisable, with an exercise price of \$3.96 per share, subject to adjustment, and expire February 16, 2028. The Common Stock Purchase Warrant permits cashless exercises in certain circumstances, and contains certain anti-dilution adjustments and an obligation of the Issuer, at the election of the holder in the event of a Fundamental Transaction (as defined), to purchase the warrants from the holder.

Pursuant to the Securities Purchase Agreement and the Common Stock Purchase Warrant, certain exercise limitations apply. RiverVest III, RiverVest III (Ohio) and RiverVest IV may not exercise any portion of its Warrants if after the exercise RiverVest III, RiverVest III (Ohio) or RiverVest IV, respectively, would beneficially own more than 19.99% of the Common Stock, unless shareholder approval from the stockholders of the Issuer is obtained prior to issuance. The foregoing description is qualified in its entirety by the Form of Common Stock Purchase Warrant incorporated by reference in this filing.

**Item 7. Material to be Filed as Exhibits.**

Exhibit A: Securities Purchase Agreement, dated February 8, 2023, by and among Spruce Biosciences, Inc. and Purchasers (incorporated by reference to Exhibit 10.1 of the Issuer’s Current Report on Form 8-K, filed with the Securities and Exchange Commission on February 9, 2023).

Exhibit B: Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.2 of the Issuer’s Current Report on Form 8-K, filed with the Securities and Exchange Commission on February 9, 2023).

**SIGNATURES**

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

May 30, 2023

**RiverVest Venture Fund III, L.P.**

By: RiverVest Venture Partners III, L.P.,  
its general partner

By: RiverVest Venture Partners III, LLC,  
its general partner

By: /s/ Jay Schmelter  
Name: Jay Schmelter  
Title: Member

**RiverVest Venture Partners III (Ohio), LLC**

By: RiverVest Venture Partners III, L.P.,  
its sole member

By: RiverVest Venture Partners III, LLC,  
its general partner

By: /s/ Jay Schmelter  
Name: Jay Schmelter  
Title: Member

**RiverVest Venture Partners III, LLC**

By: /s/ Jay Schmelter  
Name: Jay Schmelter  
Title: Member

**RiverVest Venture Partners IV, L.P.**

By: RiverVest Venture Partners IV, LLC,  
its general partner

By: /s/ Jay Schmelter  
Name: Jay Schmelter  
Title: Member

/s/ John P. McKearn, Ph.D.  
John P. McKearn, Ph.D.

/s/ Thomas C. Melzer  
Thomas C. Melzer

**RiverVest Venture Fund III (Ohio), L.P.**

By: RiverVest Venture Partners III (Ohio), LLC,  
its general partner

By: RiverVest Venture Partners III, L.P.,  
its sole member

By: RiverVest Venture Partners III, LLC,  
its general partner

By: /s/ Jay Schmelter  
Name: Jay Schmelter  
Title: Member

**RiverVest Venture Partners III, L.P.**

By: RiverVest Venture Partners III, LLC,  
its general partner

By: /s/ Jay Schmelter  
Name: Jay Schmelter  
Title: Member

**RiverVest Venture Fund IV, L.P.**

By: RiverVest Venture Partners IV, L.P.,  
its general partner

By: RiverVest Venture Partners IV, LLC,  
its general partner

By: /s/ Jay Schmelter  
Name: Jay Schmelter  
Title: Member

**RiverVest Venture Partners IV, LLC**

By: /s/ Jay Schmelter  
Name: Jay Schmelter  
Title: Member

/s/ Jay Schmelter  
Jay Schmelter

/s/ Niall O'Donnell, Ph.D.  
Niall O'Donnell, Ph.D.