FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

| Washington | D.C. | 20549 | |
|------------|------|-------|--|

| STATEMENT | OF CHANGES | IN BENEFICIAL | OWNERSHIP |
|------------------|-------------------|---------------|------------------|

| OMB APPROVAL | | | | | | | | |
|--------------------------|-----------|--|--|--|--|--|--|--|
| OMB Number: | 3235-0287 | | | | | | | |
| Estimated average burden | | | | | | | | |
| hours per response: | 0.5 | | | | | | | |

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

| Name and Address of Reporting Person* O'Donnell Niall | | | | | 2. Issuer Name and Ticker or Trading Symbol SPRUCE BIOSCIENCES, INC. [SPRB] | | | | | | | | 5. Relationship of (Check all applica X Director | | ole) | Perso | 10% Ov | ner | | |
|--|--|--|---|-----|---|-------|---|------------------------|--|-------------------|---------------------------------|------------|---|----------------------------|--|--|---|-----------|--|---|
| | ERVEST V | irst) ENTURE FUN D., STE. 1850 | (Middle) DS | | 3. Date of Earliest Transaction (Month/Day/Year) 10/14/2020 | | | | | | | | Officer (g below) | | | Other (s below) | | | | |
| (Street) ST. LOU | TIS M | 10 | 63105 | | 4. If Ar | mendr | nent, Date c | of Or | riginal F | iled (| Month/Da | y/Year] |) | | i. Indivine) | | d by One | Report | Check Appl ing Person One Report | |
| (City) | (5 | state) | (Zip) | | | | | | | | | | | | | | | | | |
| | Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned | | | | | | | | | | | | | | | | | | | |
| Date | | | Execution Date, Day/Year) if any | | Transaction Disposed Of Code (Instr. | | ties Acquired (A) or d Of (D) (Instr. 3, 4 and 5 | | | d 5) | Beneficially Owned Following | | Form: Direct (D) or Indirect (I) (Instr. 4) | | 7. Nature of Indirect Beneficial Ownership | | | | | |
| | | | | | | | - | Code | v | Amount (A) or (D) | | r Price | Reported Transactio (Instr. 3 ar | | n(s) id 4) | | " | Instr. 4) | | |
| Common Stock 10/14/ | | 3/2020 | | | С | | 445,905 | | A | (1 | 1) | 445,905 | | | I | By RiverVest Venture Fund IV, L.P. ⁽²⁾ | | | | |
| Common Stock 10/14. | | | 4/2020 | | | p(3) | | 250,000 ⁽³⁾ | | A | \$1 | 15 | 695,905 | | | I | By RiverVest Venture Fund IV, L.P. ⁽²⁾ | | | |
| Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) | | | | | | | | | | | | | | | | | | | | |
| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deemed Execution Date if any (Month/Day/Ye | Cod | ransaction ode (Instr. | | n Derivative E | | 6. Date Exercisable Expiration Date (Month/Day/Year) | | Securities Under | | Underlyin Security | rlying Derivat | | 9. Number derivative Securities Beneficial Owned Following Reported Transact | or Ownersh Form: Direct (D or Indirect (I) (Instr. | Ownership | Beneficial Ownership (Instr. 4) | |
| | | | | Cod | e V | (A) | (D) | Dat Exe | te ercisabl | | xpiration ate | Title | - 1 | Amount Number Shares | | (Instr | | | | |
| Series B Preferred Stock | (1) | 10/14/2020 | | С | | | 2,916,664 | | (1) | | (1) | Comm | | 445,90 | 5(1) | \$0.00 | 0 | | I | By RiverVest Venture Fund IV, L.P. ⁽²⁾ |

Explanation of Responses:

- 1. Each share of Series B Preferred Stock automatically converted into 0.152881822351322 shares of the Issuer's common stock upon the closing of the Issuer's initial public offering on October 14, 2020 (on an adjusted basis, after giving effect to the 1-for-6.541 reverse stock split of the common stock effected by the Issuer on October 2, 2020). The shares have no expiration date.
- 2. RiverVest Venture Partners IV, L.P. is the general partner of RiverVest Venture Fund IV, L.P. The Reporting Person is a manager of RiverVest Venture Partners IV, L.P., the sole general partner of RiverVest Venture Partners IV, L.P., and as a result may be deemed to share dispositive voting and investment power with respect to the shares held by RiverVest Venture Partners IV, L.P. The Reporting Person disclaims beneficial ownership of all shares held by RiverVest Venture Partners IV, L.P. except to the extent of his pecuniary interests therein.
- 3. The shares were purchased in the Issuer's initial public offering.

Remarks:

/s/ Samir Gharib, Attorney-in-

10/16/2020

Fact

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

Know all by these presents, that the undersigned hereby constitutes and appoints each of Richard $\,$

King and Samir Gharib, or any of them signing singly, and with full power of substitution, the undersigneds

true and lawful attorney-in-fact to:

execute for and on behalf of the undersigned, in the undersigneds capacity as an officer,

director and/or more than 10% stockholder of Spruce Biosciences, Inc. (the Company),

Forms 3, 4, and 5 in accordance with Section 16(a) of the Securities Exchange Act of 1934

and the rules thereunder;

(2) do and perform any and all acts for and on behalf of the undersigned which may be necessary

or desirable to complete and execute any such Form 3, 4, or 5, complete and execute any

amendment or amendments thereto, and timely file such form with the SEC and any stock

exchange or similar authority; and

(3) take any other action of any type whatsoever in connection with the foregoing which, in the

opinion of such attorney-in-fact, may be of benefit to, in the best interest of, or legally $\ensuremath{\mathsf{G}}$

required by, the undersigned, it being understood that the documents executed by such

attorney-in-fact on behalf of the undersigned pursuant to this Power of Attorney shall be in

such form and shall contain such terms and conditions as such attorney-in-fact may approve

in such attorney-in-facts discretion.

The undersigned hereby grants to each such attorney-in-fact full power and authority to do and

perform any and every act and thing whatsoever requisite, necessary, or proper to be done in the exercise of

any of the rights and powers herein granted, as fully to all intents and purposes as the undersigned might or

could do if personally present, with full power of substitution or revocation, hereby ratifying and confirming

all that such attorney-in-fact, or such attorney-in-facts substitute or substitutes, shall lawfully do or cause to

be done by virtue of this power of attorney and the rights and powers herein granted. The undersigned

acknowledges that the foregoing attorneys-in-fact, in serving in such capacity at the request of the

undersigned, are not assuming, nor is the Company assuming, any of the undersigneds responsibilities to $\,$

comply with Section 16 of the Securities Exchange Act of 1934.

This Power of Attorney shall remain in full force and effect until the undersigned is no longer required

to file Forms 3, 4, and 5 with respect to the undersigneds holdings of and transactions in securities issued by

the Company, unless earlier revoked by the undersigned in a signed writing delivered to the foregoing attorneys-in-fact.

IN WITNESS WHEREOF, the undersigned has caused this Power of Attorney to be executed as of September 25, 2020.

/s/ Niall O Donnell