Instruction 1(b)

FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

| Vashington,  | D.C. | 20549 |
|--------------|------|-------|
| vasilliyton, | D.C. | 20343 |

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

|     | OMB APPROVAL             |           |  |  |  |  |  |  |  |  |
|-----|--------------------------|-----------|--|--|--|--|--|--|--|--|
| - 1 |                          |           |  |  |  |  |  |  |  |  |
|     | 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 Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

| 1. Name and Address of Reporting Person*  Ryan Jason   |  |  |   |                 | 2. I:<br>Se                             | 2. Issuer Name and Ticker or Trading Symbol Sema4 Holdings Corp. [ SMFR ] |  |     |   |   |   | (Ch  | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable)  X Director 10% Owner |   |                                       |                    |            |  |
|--|--|--|---|-----------------|---|---|--|-----|---|---|---|--|---|---|---------------------------------------|--------------------|------------|--|
| (Last) (First) (Middle) C/O SEMA4 HOLDINGS CORP.   |  |  |   |                 |   | 3. Date of Earliest Transaction (Month/Day/Year) 10/15/2021               |  |     |   |   |   |  | Officer<br>below)   | (give title   |                                       | Other (s<br>below) | pecify     |  |
| 333 LUDLOW ST, NORTH TOWER, 8TH FL.  |  |  |   |                 | 4. 1                                    | If Amendment, Date of Original Filed (Month/Day/Year)                     |  |     |   |   |   |  | 6. Individual or Joint/Group Filing (Check Applicable   |   |                                       |                    |            |  |
| (Street)   |  |  |   |                 |   |   |  |     |   |   |   | Line)  X Form filed by One Reporting Person  |   |   |                                       |                    |            |  |
| STAMFO   | ORD C'   | O CT 06902                                 |   |                 |   |   |  |     |   |   |   |  | Form filed by More than One Reporting<br>Person   |   |                                       |                    |            |  |
| (City)   | (S   | tate)                                      | (Zip)   |                 |   |   |  |     |   |   |   |  |   |   |                                       |                    |            |  |
|  | Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned |  |   |                 |   |   |  |     |   |   |   |  |   |   |                                       |                    |            |  |
| 1. Title of Security (Instr. 3)  2. Transar Date (Month/D.   |  |  |   | Execution Date, |   | Code (Ins   |  |     |   | 5. Amount Securities Beneficial Owned F | s<br>ally<br>ollowing                               | Form: Dir  | rm: Direct<br>) or Indirect<br>(Instr. 4)   | 7. Nature<br>of Indirect<br>Beneficial<br>Ownership |                                       |                    |            |  |
|  |  |  |   |                 |   |   |  |     | Code V  | Amount                                  | (A) or<br>(D)                                       | Price  | Transact<br>(Instr. 3 a   | ion(s)  |                                       |                    | (Instr. 4) |  |
| Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) |  |  |   |                 |   |   |  |     |   |   |   |  |   |   |                                       |                    |            |  |
| 1. Title of<br>Derivative<br>Security<br>(Instr. 3)  | 2.<br>Conversion<br>or Exercise<br>Price of<br>Derivative<br>Security            | 3. Transaction<br>Date<br>(Month/Day/Year) | 3A. Deemed<br>Execution I<br>if any<br>(Month/Day | ate, T          | ransaction of Eode (Instr. Derivative ( |   | Expiration Date of (Month/Day/Year) Un |     | 7. Title and Amount<br>of Securities<br>Underlying<br>Derivative Security<br>(Instr. 3 and 4) |   | 8. Price of<br>Derivative<br>Security<br>(Instr. 5) | 9. Number<br>derivative<br>Securities<br>Beneficially<br>Owned<br>Following<br>Reported<br>Transaction<br>(Instr. 4) | Ow<br>For<br>Dir<br>or I<br>(I) (   | nership   | Beneficial<br>Ownership<br>(Instr. 4) |                    |            |  |
|  |  |  |   |                 |   |   |  |     |   |   |   | Amount   | ]   |   |                                       |                    |            |  |
|  |  |  |   |                 | Code                                    | v   | (A)                                    | (D) | Date<br>Exercisable   | Expiration<br>Date                      | Title   | Number<br>of<br>Shares   |   |   |                                       |                    |            |  |
| Employee<br>Stock<br>Option<br>(Right to<br>Buy)   | \$7.79   | 10/15/2021                                 |   |                 | A                                       |   | 22,286                                 |     | (1)   | 10/14/2031                              | Class A<br>Common<br>Stock                          | 22,286   | \$0.00  | 22,286  |                                       | D                  |            |  |
| Employee<br>Stock<br>Option<br>(Right to<br>Buy)   | \$7.79   | 10/15/2021                                 |   |                 | A                                       |   | 22,286                                 |     | (2)   | 10/14/2031                              | Class A<br>Common<br>Stock                          | 22,286   | \$0.00  | 22,286  |                                       | D                  |            |  |
| Restricted<br>Stock Unit   | (3)  | 10/15/2021                                 |   |                 | A                                       |   | 12,836                                 |     | (1)   | (1)                                     | Class A<br>Common<br>Stock                          | 12,836   | \$0.00  | 12,836  |                                       | D                  |            |  |
| Restricted<br>Stock Unit   | (3)  | 10/15/2021                                 |   |                 | A                                       |   | 12,836                                 |     | (4)   | (4)                                     | Class A<br>Common<br>Stock                          | 12,836   | \$0.00  | 12,836  |                                       | D                  |            |  |

## **Explanation of Responses:**

- 1. The stock options and restricted stock units ("RSUs") will vest on the earlier of (i) the date of the next annual meeting of the Issuer's shareholders following the grant date and (i) the first anniversary of the grant date, in each case so long as the Reporting Person continues to provide services to the Issuer through such vesting date.
- 2. The stock option shall vest as of 1/36 of the total shares monthly beginning on November 15, 2021 until fully vested, subject to the Reporting Person continuing to provide services to the Issuer through each
- 3. Each RSU represents a contingent right to receive 1 share of the Issuer's Class A Common Stock upon settlement for no consideration.
- 4. The RSUs will vest in equal annual installments over the three-year period following the grant date, subject to the Reporting Person continuing to provide services to the Issuer through each vesting date.

## Remarks:

/s/ Daniel Clark, Attorney-in-Fact \*\* Signature of Reporting Person

10/19/2021

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.