FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

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| <i>N</i> ashington,   | 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*     Watts Ryan J.  |        |            |           |   |             |   | 2. Issuer Name <b>and</b> Ticker or Trading Symbol  Denali Therapeutics Inc. [ DNLI ] |                              |   |        |  |                 |   | . Relationship of Report<br>Check all applicable)  X Director  |   | 10% Owner |   | wner                                      |  |
|--|--------|------------|-----------|---|-------------|---|---|------------------------------|---|--------|--|-----------------|---|--|---|-----------|---|---|--|
| (Last) (First) (Middle) C/O DENALI THERAPEUTICS INC.   |        |            |           |   |             | 3. Date of Earliest Transaction (Month/Day/Year) 06/16/2023   |   |                              |   |        |  |                 |   | helow)   | Officer (give title below)  Other (specify below)  President and CEO              |           |   |   |  |
| 161 OYSTER POINT BLVD.   |        |            |           |   |             | 4. If Amendment, Date of Original Filed (Month/Day/Year)  |   |                              |   |        |  |                 |   | 6. Individual or Joint/Group Filing (Check Applicable Line)  |   |           |   |   |  |
| (Street)<br>SOUTH<br>FRANC   | ( C    | A          | 94080     |   |             |   |   |                              |   |        |  |                 |   |  | X Form filed by One Reporting Person Form filed by More than One Reporting Person |           |   |   |  |
| (City)   | (S     | tate)      | (Zip)     |   | $ $ $ $ $ $ | Rule 10b5-1(c) Transaction Indication  Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan that is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10. |   |                              |   |        |  |                 |   |  |   |           |   |   |  |
|  |        | Tab        | le I - No | n-Deriv                                 | ative       | Sec   | urit  | ies Ac                       | quired,                                 | Dis    | posed o  | of, or Be       | neficia   | lly Owne   | t   |           |   |   |  |
| Date   |        |            |           | 2. Transa<br>Date<br>(Month/Da          | Day/Year) i |   | 2A. Deemed<br>Execution Date,<br>if any<br>(Month/Day/Year)                           |                              | 3.<br>Transaction<br>Code (Instr.<br>8) |        | 4. Securities Acquired (A)<br>Disposed Of (D) (Instr. 3, 4<br>5)             |                 |   | Beneficially<br>Owned Follow   |   | Form:     | Direct<br>Indirect<br>str. 4)             | 7. Nature of ndirect Beneficial Ownership |  |
|  |        |            |           |   |             |   |   |                              | Code                                    | v      | Amount   | (A) or<br>(D)   | Price   | Reported<br>Transacti<br>(Instr. 3 a   | tion(s)   |           |   | (Instr. 4)                                |  |
| Common Stock 06/16/  |        |            |           | 2023                                    |             |   |   | М                            |   | 50,000 | 0 A  | \$0.68          | 3 2,289   | 9,913  |   |           | See<br>footnote <sup>(1)</sup>            |   |  |
| Common Stock 06  |        |            |           | 06/16/                                  | /2023       |   |   |                              | S <sup>(2)</sup>                        |        | 50,000   | 0 D             | \$31.4  | 2,239,913  |   |           |   | See<br>footnote <sup>(1)</sup>            |  |
| Common Stock   |        |            |           |   |             |   |   |                              |   |        |  | 188,437(3)      |   | D  |   |           |   |   |  |
|  |        | Т          | able II - |   |             |   |   | -                            |   | -      | osed of  | -               |   | y Owned  |   |           |   |   |  |
| 1. Title of Derivative Security (Instr. 3)  2. Conversion or Exercise Price of Derivative Security  2. Conversion Date (Month/Day/Year)  (Month/Day/Year)  3. Transaction Date Execution Date, if any (Month/Day/Year) |        |            | n Date,   | I.<br>Fransaction<br>Code (Instr.<br>3) |             | n of  |   | 6. Date Expiration (Month/Da | Date                                    | е      | Amount of<br>Securities<br>Underlying<br>Derivative Secu<br>(Instr. 3 and 4) |                 | 8. Price of<br>Derivative<br>Security<br>(Instr. 5) | 9. Numb<br>derivativ<br>Securitie<br>Benefici<br>Owned<br>Followin<br>Reporter<br>Transact<br>(Instr. 4) | e Owners s Form: ally Direct (i) or Indirect (i) (Insti                           | Ownership | Beneficial<br>Ownership<br>ect (Instr. 4) |   |  |
|  |        |            |           |   | Code        | v   | (A)   | (D)                          | Date<br>Exercisal:                      |        | Expiration<br>Date   | Title           | Amount<br>or<br>Number<br>of<br>Shares              |  |   |           |   |   |  |
| Stock<br>Option<br>(right to   | \$0.68 | 06/16/2023 |           |   | М           |   |   | 50,000                       | (4)                                     | (      | 08/20/2025   | Common<br>Stock | 50,000  | \$0  | 1,120,  | 617       | D   |   |  |

## **Explanation of Responses:**

- 1. The shares are held of record by the Watts Family 2015 Trust dated July 7, 2015, for which the Reporting Person serves as trustee.
- 2. The sales reported by the Reporting Person were affected pursuant to a Rule 10b5-1 trading plan adopted February 10, 2023.
- 3. Includes 188,437 RSUs.
- 4. The vesting of the shares subject to the option are contingent upon the achievement of certain performance metrics. 50% of the shares subject to the option vested on March 3, 2021, and 50% of the shares subject to the option will vest on the date the closing price of Issuer's Common Stock equals or exceeds \$80.00 per share on NASDAQ for 90 consecutive trading days.

## Remarks:

/s/ Tyler Nielsen, by power of <u>attorney</u>

06/20/2023

\*\* 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.