FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

| Check this box if no longer subject to Section 16. | | | EMENT OF CHANGES IN BENEFICIAL OWNERSHIP | OMB Number: Estimated average bu hours per response: | 3235-0287 rden 0.5 | | |
|--|-------------------|---------------|--|--|--------------------------|---|------------------------------------|
| insudcion 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 | | | | |
| 1. Name and Address of F <u>Watts Ryan J.</u> | Reporting Person* | | 2. Issuer Name and Ticker or Trading Symbol <u>Denali Therapeutics Inc.</u> [DNLI] | (Check all a | | ng Person(s) to Issue | 10% Owner Other (specify below) |
| (Last) C/O DENALI THER 161 OYSTER POINT | | (Middle) | 3. Date of Earliest Transaction (Month/Day/Year) 02/09/2022 | | | President and CEC | |
| (Street) SOUTH SAN FRANCISCO | СА | 94080 | 4. If Amendment, Date of Original Filed (Month/Day/Year) | x | Form filed by | ip Filing (Check Appli One Reporting Perso More than One Repo | n |
| (City) | (State) | (Zip) | | | | | |
| | | Table I - Non | Derivative Securities Acquired, Disposed of, or Beneficially Ov | vned | | | |

| 1. Title of Security (Instr. 3) | 2. Transaction Date (Month/Day/Year) | 2A. Deemed Execution Date, if any | Code (Instr. 8) | | 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5) | | | 5. Amount of Securities Beneficially Owned Following Reported | 6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | Indirect Beneficial |
|---------------------------------|--|---|------------------|---|--|------------|--------------------------|---|--|--------------------------------|
| | | (Month/Day/Year) | Code | v | Amount | (A) or (D) | Price | Transaction(s) (Instr. 3 and 4) | | Ownership (Instr. 4) |
| Common Stock | 02/09/2022 | | S ⁽¹⁾ | | 2,719 | D | \$37.5519 ⁽²⁾ | 2,119,442 ⁽³⁾ | I | See footnote ⁽⁴⁾ |
| Common Stock | 02/10/2022 | | М | | 64,631 | A | \$5.28 | 254,522 | D | |
| Common Stock | 02/10/2022 | | М | | 6,118 | A | \$ <mark>9.6</mark> | 260,640 ⁽³⁾⁽⁵⁾ | D | |

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

| (cigi, puts, cans, warants, 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/Year) | Code (Instr. 8) D A D | | Derivative Securities | | 6. Date Exercisable and Expiration Date (Month/Day/Year) | | 7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) | | 8. Price of Derivative Security (Instr. 5) | 9. Number of derivative Securities Beneficially Owned Following | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) |
| | Security | | | Code | v | (A) | (D) | Date Exercisable | Expiration Date | Title | Amount or Number of Shares | | Reported Transaction(s) (Instr. 4) | l' í | |
| Stock Option (right to buy) | \$5.28 | 02/10/2022 | | М | | | 64,631 | (6) | 03/07/2027 | Common Stock | 64,631 | \$0 | 0 | D | |
| Stock Option (right to buy) | \$9.6 | 02/10/2022 | | М | | | 6,118 | (6) | 08/21/2027 | Common Stock | 6,118 | \$0 | 0 | D | |

Explanation of Responses:

1. Shares sold to satisfy the tax obligations by the reporting person in connection with the settlement of previously vested restricted stock units.

2. The sale price reported in column 4 of Table I represents the weighted average sale price of the shares ranging from \$37.51 to \$37.745 per share. Upon request by the Commission staff, the Issuer, or a security holder of the Issuer, the Reporting Person will provide full information regarding the number of shares sold at each separate price. 3. Reflects the issuance of shares to the Watts Family 2015 Trust in connection with the vesting of 8800 restricted stock units held by the Reporting Person.

4. The shares are held of record by the Watts Family 2015 Trust dated July 7, 2015, for which the Reporting Person serves as trustee.

5. Includes 189,891 restricted stock units.

6. The shares subject to the option were fully vested and exercisable.

Remarks:

/s/ Tyler Nielsen, by power of attorney 02/11/2022

** Signature of Reporting Person

Date

OMB APPROVAL

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.

POWER OF ATTORNEY

The undersigned, as a Section 16 reporting person of Denali Therapeutics Inc. (the "Company"), hereby constitutes and appoints Ryan J. Watts, 5

1. complete and execute Forms 3, 4 and 5 and other forms and all amendments thereto as such attorneys-in-fact shall in their discretion det

2. do all acts necessary in order to file such forms with the Securities and Exchange Commission, any securities exchange or national assoc: The undersigned hereby ratifies and confirms all that said attorneys-in-fact and agents shall do or cause to be done by virtue hereof. The under 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

IN WITNESS WHEREOF, the undersigned has caused this Power of Attorney to be executed as of this 7th day of February, 2022.

Signature, Print Name: =Erik Harris