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

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**SCHEDULE 13G**  
Under the Securities Exchange Act of 1934  
(Amendment No. 2)\*

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**Denali Therapeutics Inc.**

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(Name of Issuer)

**Common Stock par value \$0.01 per share**

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(Title of Class of Securities)

**24823R105**

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(CUSIP Number)

**December 31, 2020**

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(Date of Event Which Requires Filing of This Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

- Rule 13d-1(b)  
 Rule 13d-1(c)  
 Rule 13d-1(d)

\* 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 in 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  | NAMES OF REPORTING PERSON(S)<br><br><b>ARCH Venture Fund VIII, L.P.</b>   |   |
| 2  | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/></span><br><span style="float: right;">(b) <input type="checkbox"/></span> |   |
| 3  | SEC USE ONLY  |   |
| 4  | CITIZENSHIP OR PLACE OF ORGANIZATION<br><br><b>Delaware</b>   |   |
| NUMBER OF<br>SHARES<br>BENEFICIALLY<br>OWNED BY EACH<br>REPORTING<br>PERSON WITH | 5   | SOLE VOTING POWER<br><br><b>0</b>                 |
|  | 6   | SHARED VOTING POWER<br><br><b>10,668,749</b>      |
|  | 7   | SOLE DISPOSITIVE POWER<br><br><b>0</b>            |
|  | 8   | SHARED DISPOSITIVE POWER<br><br><b>10,668,749</b> |
| 9  | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON<br><br><b>10,668,749</b>   |   |
| 10   | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <span style="float: right;"><input type="checkbox"/></span>  |   |
| 11   | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)<br><br><b>8.9%</b>  |   |
| 12   | TYPE OF REPORTING PERSON<br><br><b>PN</b>   |   |

|  |   |   |  |
|--|---|---|--|
| <b>1</b>   | NAMES OF REPORTING PERSON(S)<br><b>ARCH Venture Partners VIII, L.P.</b>                                       |   |  |
| <b>2</b>   | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/><br>(b) <input type="checkbox"/> |   |  |
| <b>3</b>   | SEC USE ONLY  |   |  |
| <b>4</b>   | CITIZENSHIP OR PLACE OF ORGANIZATION<br><b>Delaware</b>   |   |  |
| <b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b> | <b>5</b>  | SOLE VOTING POWER<br><b>0</b>                 |  |
|  | <b>6</b>  | SHARED VOTING POWER<br><b>10,668,749</b>      |  |
|  | <b>7</b>  | SOLE DISPOSITIVE POWER<br><b>0</b>            |  |
|  | <b>8</b>  | SHARED DISPOSITIVE POWER<br><b>10,668,749</b> |  |
| <b>9</b>   | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON<br><b>10,668,749</b>                             |   |  |
| <b>10</b>  | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>                 |   |  |
| <b>11</b>  | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)<br><b>8.9%</b>  |   |  |
| <b>12</b>  | TYPE OF REPORTING PERSON<br><b>PN</b>   |   |  |

|  |   |   |  |
|--|---|---|--|
| 1  | NAMES OF REPORTING PERSON(S)<br><b>ARCH Venture Partners VIII, LLC</b>  |   |  |
| 2  | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/></span><br><span style="float: right;">(b) <input type="checkbox"/></span> |   |  |
| 3  | SEC USE ONLY  |   |  |
| 4  | CITIZENSHIP OR PLACE OF ORGANIZATION<br><b>Delaware</b>   |   |  |
| NUMBER OF<br>SHARES<br>BENEFICIALLY<br>OWNED BY EACH<br>REPORTING<br>PERSON WITH | 5   | SOLE VOTING POWER<br><br><b>0</b>                 |  |
|  | 6   | SHARED VOTING POWER<br><br><b>10,668,749</b>      |  |
|  | 7   | SOLE DISPOSITIVE POWER<br><br><b>0</b>            |  |
|  | 8   | SHARED DISPOSITIVE POWER<br><br><b>10,668,749</b> |  |
| 9  | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON<br><br><b>10,668,749</b>   |   |  |
| 10   | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <span style="float: right;"><input type="checkbox"/></span>  |   |  |
| 11   | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)<br><br><b>8.9%</b>  |   |  |
| 12   | TYPE OF REPORTING PERSON<br><br><b>OO</b>   |   |  |

|  |   |   |  |
|--|---|---|--|
| <b>1</b>   | NAMES OF REPORTING PERSON(S)<br><b>Keith Crandell</b>   |   |  |
| <b>2</b>   | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (a) <input type="checkbox"/><br>(b) <input type="checkbox"/> |   |  |
| <b>3</b>   | SEC USE ONLY  |   |  |
| <b>4</b>   | CITIZENSHIP OR PLACE OF ORGANIZATION<br><b>United States of America</b>                                       |   |  |
| <b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b> | <b>5</b>  | SOLE VOTING POWER<br><b>2,030</b>             |  |
|  | <b>6</b>  | SHARED VOTING POWER<br><b>10,668,749</b>      |  |
|  | <b>7</b>  | SOLE DISPOSITIVE POWER<br><b>2,030</b>        |  |
|  | <b>8</b>  | SHARED DISPOSITIVE POWER<br><b>10,668,749</b> |  |
| <b>9</b>   | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON<br><b>10,670,779</b>                             |   |  |
| <b>10</b>  | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <input type="checkbox"/>                 |   |  |
| <b>11</b>  | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)<br><b>8.9%</b>  |   |  |
| <b>12</b>  | TYPE OF REPORTING PERSON<br><b>IN</b>   |   |  |

|  |   |   |  |
|--|---|---|--|
| <b>1</b>   | NAMES OF REPORTING PERSON(S)<br><br><b>Clinton Bybee</b>  |   |  |
| <b>2</b>   | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/></span><br><span style="float: right;">(b) <input type="checkbox"/></span> |   |  |
| <b>3</b>   | SEC USE ONLY  |   |  |
| <b>4</b>   | CITIZENSHIP OR PLACE OF ORGANIZATION<br><br><b>United States of America</b>   |   |  |
| NUMBER OF<br>SHARES<br>BENEFICIALLY<br>OWNED BY EACH<br>REPORTING<br>PERSON WITH | <b>5</b>  | SOLE VOTING POWER<br><br><b>1,955</b>             |  |
|  | <b>6</b>  | SHARED VOTING POWER<br><br><b>10,668,749</b>      |  |
|  | <b>7</b>  | SOLE DISPOSITIVE POWER<br><br><b>1,955</b>        |  |
|  | <b>8</b>  | SHARED DISPOSITIVE POWER<br><br><b>10,668,749</b> |  |
| <b>9</b>   | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON<br><br><b>10,670,704</b>   |   |  |
| <b>10</b>  | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <span style="float: right;"><input type="checkbox"/></span>  |   |  |
| <b>11</b>  | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)<br><br><b>8.9%</b>  |   |  |
| <b>12</b>  | TYPE OF REPORTING PERSON<br><br><b>IN</b>   |   |  |

|  |   |   |  |
|--|---|---|--|
| <b>1</b>   | NAMES OF REPORTING PERSON(S)<br><br><b>Robert Nelsen</b>  |   |  |
| <b>2</b>   | CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/></span><br><span style="float: right;">(b) <input type="checkbox"/></span> |   |  |
| <b>3</b>   | SEC USE ONLY  |   |  |
| <b>4</b>   | CITIZENSHIP OR PLACE OF ORGANIZATION<br><br><b>United States of America</b>   |   |  |
| NUMBER OF<br>SHARES<br>BENEFICIALLY<br>OWNED BY EACH<br>REPORTING<br>PERSON WITH | <b>5</b>  | SOLE VOTING POWER<br><br><b>67,199</b>            |  |
|  | <b>6</b>  | SHARED VOTING POWER<br><br><b>10,668,749</b>      |  |
|  | <b>7</b>  | SOLE DISPOSITIVE POWER<br><br><b>67,199</b>       |  |
|  | <b>8</b>  | SHARED DISPOSITIVE POWER<br><br><b>10,668,749</b> |  |
| <b>9</b>   | AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON<br><br><b>10,735,948</b>   |   |  |
| <b>10</b>  | CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES <span style="float: right;"><input type="checkbox"/></span>  |   |  |
| <b>11</b>  | PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)<br><br><b>9.0%</b>  |   |  |
| <b>12</b>  | TYPE OF REPORTING PERSON<br><br><b>IN</b>   |   |  |

**Item 1(a). Name of Issuer:**

Denali Therapeutics Inc. (the "Issuer").

**Item 1(b). Address of Issuer's Principal Executive Offices:**

161 Oyster Point Blvd., 2nd Floor, South San Francisco, CA 94080

**Item 2(a). Name of Person Filing:**

ARCH Venture Fund VIII, L.P. ("ARCH Venture Fund VIII"); ARCH Venture Partners VIII, L.P. ("AVP VIII LP"); ARCH Venture Partners VIII, LLC ("AVP VIII LLC") (collectively, the "Reporting Entities" and individually, each a "Reporting Entity"); and Keith Crandell ("Crandell"), Robert Nelsen ("Nelsen") and Clinton Bybee ("Bybee") (collectively, the "Managing Directors" and individually, each a "Managing Director"). The Reporting Entities and the Managing Directors collectively are referred to as the "Reporting Persons".

**Item 2(b). Address of Principal Business Office or, if none, Residence:**

8755 W. Higgins Avenue, Suite 1025, Chicago, IL 60631

**Item 2(c). Citizenship:**

ARCH Venture Fund VIII and AVP VIII LP are limited partnerships organized under the laws of the State of Delaware. AVP VIII LLC is a limited liability company organized under the laws of the State of Delaware. Each Managing Director is a US citizen.

**Item 2(d). Title of Class of Securities.**

Common stock, par value \$0.01 per share.

**Item 2(e). CUSIP Number.**

24823R105

**Item 3. If this statement is filed pursuant to Rule 13d-1(b), or 13d-2(b) or (c), Check Whether the Person Filing is a:**

Not Applicable.

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**Item 4. Ownership:**

(a) Amount beneficially owned:

ARCH Venture Fund VIII is the record owner of 10,668,749 shares of Common Stock (the "Record Shares") as of December 31, 2020. AVP VIII LP, as the sole general partner of ARCH Venture Fund VIII, may be deemed to beneficially own the Record Shares. AVP VIII LLC, as the sole general partner of AVP VIII LP, may be deemed to beneficially own the Record Shares. As managing directors of AVP VIII LLC, each Managing Director may also be deemed to share the power to direct the disposition and vote of the Record Shares. In addition, as of December 31, 2020, Crandell is a holder of 2,030 Shares of Common Stock, Bybee is the holder of 1,955 shares of Common Stock, and Nelsen is a holder of 2,030 shares of Common Stock and vested options to 67,199 shares of Common Stock (the "Vested Option Shares").

(b) Percent of class:

See line 11 of the cover sheets. The percentages set forth on the cover sheet for each Reporting Person (other than Nelsen) is based upon 119,918,496 shares of common stock outstanding as of October 28, 2020 as reported on the Issuer's Form 10Q filed on November 5, 2020 with Securities and Exchange Commission. For Nelsen, the Vested Option Shares were included in the number of shares of Common Stock outstanding.

(c) Number of shares as to which such person has:

(i) Sole power to vote or to direct the vote:

See line 5 of the cover sheets.

(ii) Shared power to vote or to direct the vote:

See line 6 of the cover sheets.

(iii) Sole power to dispose or to direct the disposition:

See line 7 of the cover sheets.

(iv) Shared power to dispose or to direct the disposition:

See line 8 of the cover sheets.

Each Reporting Person disclaims beneficial ownership of such shares of Common Stock except for the shares, if any, such Reporting Person holds of record.

**Item 5. Ownership of Five Percent or Less of a Class.**

Not applicable.

**Item 6. Ownership of More than Five Percent on Behalf of Another Person.**

Not applicable.

**Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company.**

Not applicable.

**Item 8. Identification and Classification of Members of the Group.**

Not applicable.

**Item 9. Notice of Dissolution of Group.**

Not applicable.

**Item 10. Certifications.**

Not applicable.

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**SIGNATURE**

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

Dated: February 2, 2021

ARCH VENTURE FUND VIII, L.P.

By: ARCH Venture Partners VIII, L.P.  
its General Partner

By: ARCH Venture Partners VIII, LLC  
its General Partner

By: \_\_\_\_\_  
\*  
Keith Crandell  
Managing Director

ARCH VENTURE PARTNERS VIII, L.P.

By: ARCH Venture Partners VIII, LLC  
its General Partner

By: \_\_\_\_\_  
\*  
Keith Crandell  
Managing Director

ARCH VENTURE PARTNERS VIII, LLC

By: \_\_\_\_\_  
\*  
Keith Crandell  
Managing Director

\_\_\_\_\_  
\*  
Keith Crandell

\_\_\_\_\_  
\*  
Robert Nelsen

\_\_\_\_\_  
\*  
Clinton Bybee

\* By: /s/ Mark McDonnell  
Mark McDonnell as  
Attorney-in-Fact

This Amendment No. 2 to Schedule 13G was executed by Mark McDonnell pursuant to Powers of Attorney attached hereto as Exhibit 2 and incorporated herein by reference.

**AGREEMENT**

Pursuant to Rule 13d-1-(k)(1) under the Securities Exchange Act of 1934, the undersigned hereby agree that only one statement containing the information required by Schedule 13G need be filed with respect to the ownership by each of the undersigned of shares of stock of Denali Therapeutics Inc.

This Agreement may be executed in any number of counterparts, each of which shall be deemed an original.

Dated: February 2, 2021

ARCH VENTURE FUND VIII, L.P.

By: ARCH Venture Partners VIII, L.P.  
its General Partner

By: ARCH Venture Partners VIII, LLC  
its General Partner

By: \_\_\_\_\_  
\*  
Keith Crandell  
Managing Director

ARCH VENTURE PARTNERS VIII, L.P.

By: ARCH Venture Partners VIII, LLC  
its General Partner

By: \_\_\_\_\_  
\*  
Keith Crandell  
Managing Director

ARCH VENTURE PARTNERS VIII, LLC

By: \_\_\_\_\_  
\*  
Keith Crandell  
Managing Director

\_\_\_\_\_  
\*  
Keith Crandell

\_\_\_\_\_  
\*  
Robert Nelsen

\_\_\_\_\_  
\*  
Clinton Bybee

\* By: /s/ Mark McDonnell  
Mark McDonnell as  
Attorney-in-Fact

**POWERS OF ATTORNEY**

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Mark McDonnell his true and lawful attorney-in-fact, with full power of substitution, to sign any and all instruments, certificates and documents that may be necessary, desirable or appropriate to be executed on behalf of himself as an individual or in his capacity as a direct or indirect general partner, member, director, officer or manager of any partnership, corporation or limited liability company, pursuant to section 13 or 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and any and all regulations promulgated thereunder, and to file the same, with all exhibits thereto, and any other documents in connection therewith, with the Securities and Exchange Commission, and with any other entity when and if such is mandated by the Exchange Act or by the Financial Industry Regulatory Authority, granting unto said attorney-in-fact full power and authority to do and perform each and every act and thing necessary, desirable or appropriate, fully to all intents and purposes as he might or could do in person, thereby ratifying and confirming all that said attorney-in-fact, or his substitutes, may lawfully do or cause to be done by virtue hereof. This Power of Attorney shall remain in full force and effect with respect to each undersigned person unless and until six months after such person is both no longer a Managing Director of ARCH Venture Partners and no longer serving on the board of directors of any portfolio company of any ARCH Venture Partners fund.

IN WITNESS WHEREOF, this Power of Attorney has been signed as of the 9<sup>th</sup> day of March, 2015.

ARCH VENTURE FUND VIII, L.P.

By: ARCH Venture Partners VIII, L.P.  
its General Partner

By: ARCH Venture Partners VIII, LLC  
its General Partner

By: /s/ Keith Crandell  
Managing Director

ARCH VENTURE PARTNERS VIII, L.P.

By: ARCH Venture Partners VIII, LLC  
its General Partner

By: /s/ Keith Crandell  
Managing Director

ARCH VENTURE PARTNERS VIII, LLC

By: /s/ Keith Crandell  
Managing Director

/s/ Keith Crandell  
Keith Crandell

/s/ Robert Nelsen  
Robert Nelsen

/s/ Clinton Bybee  
Clinton Bybee

/s/ Kristina Burow  
Kristina Burow

/s/ Paul Thurk  
Paul Thurk