G1 THERAPEUTICS, INC.
(Exact Name of Registrant as Specified in Its Charter)

700 Park Offices Drive, Suite 200
Research Triangle Park, NC 27709
(Address of Principal Executive Offices)

Amended and Restated 2017 Employee, Director and Consultant Equity Incentive Plan
(Full Title of the Plan)

Monica Roberts Thomas, Esq.
General Counsel
G1 Therapeutics, Inc.
700 Park Offices Drive, Suite 200
Research Triangle Park, NC 27709
(Name and Address of Agent for Service)
(919) 213-9835
(Telephone Number, Including Area Code, of Agent for Service)

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company,” and “emerging growth company” in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐ Accelerated filer ☐
Non-accelerated filer ☑ Smaller reporting company ☑
Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☐
EXPLANATORY NOTE

This Registration Statement on Form S-8 is filed to register 1,096,553 shares of common stock, par value $0.0001 per share (“Common Stock”), of G1 Therapeutics, Inc. (the “Registrant”) issuable for compensatory purposes under the Registrant’s Amended and Restated 2017 Employee, Director and Consultant Equity Incentive Plan (the “2017 Plan”), which were added to the shares authorized for issuance under the 2017 Plan as of January 1, 2023, pursuant to an “evergreen” provision.

In accordance with the instructional Note to Part I of Form S-8 as promulgated by the Securities and Exchange Commission (the “Commission”), the information specified by Part I of Form S-8 has been omitted from this Registration Statement on Form S-8 for offers of the Registrant’s Common Stock pursuant to the 2017 Plan. The documents containing the information specified in Part I will be delivered to the participants in the 2017 Plan as required by Rule 428(b)(1) under the Securities Act.
PART II
INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.
The following documents filed by the Registrant with the Commission are incorporated herein by reference:

- The Annual Report on Form 10-K for the year ended December 31, 2022, filed with the Commission on March 1, 2023, as amended by the Registrant’s Amendment No.1 on Form 10-K/A, filed with the Commission on April 14, 2023;
- The Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023, June 30, 2023, and September 30, 2023, filed with the Commission on May 3, 2023, August 2, 2023, and November 1, 2023 respectively;
- The Current Reports on Form 8-K filed with the Commission on June 9, 2023, June 16, 2023, and September 21, 2023 (other than any portions thereof deemed furnished and not filed);
- The Definitive Proxy Statement on Schedule 14A, filed with the Commission on April 26, 2023 (excluding those portions that are not incorporated by reference into the Registrant’s Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as amended); and
- The description of the Common Stock contained in the Registrant’s Registration Statement on Form 8-A filed with the Commission on May 16, 2017 (File No. 001-38096), including any amendments or reports filed for the purpose of updating such description.

All reports and other documents filed by the Registrant after the date hereof pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, as amended (other than Current Reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits furnished on such form that relate to such items), prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference herein and to be part hereof from the date of filing of such reports and documents. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for the purposes of this Registration Statement to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Registration Statement.

Item 4. Description of Securities.
Not applicable.

Item 5. Interests of Named Experts and Counsel.
Not applicable.

Item 6. Indemnification of Directors and Officers.
The Registrant’s amended and restated certificate of incorporation and amended and restated bylaws provide that each person who was or is made a party to or is otherwise involved (including, without limitation, as a witness) in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he or she is or was one of the Registrant’s directors or officers or is or was serving at the Registrant’s request as a director, officer or trustee of another corporation, or of a partnership, joint venture, trust or other enterprise, including service with respect to an employee benefit plan, whether the basis of such proceeding is alleged action in an official capacity as a director, officer or trustee or in any other capacity while serving as a director, officer or trustee, shall be indemnified and held harmless by the Registrant to the fullest extent authorized by the Delaware General Corporation Law against all expense, liability and loss (including attorneys’ fees, judgments, fines, ERISA excise taxes or penalties and amounts paid in settlement) reasonably incurred or suffered by such.

Section 145 of the Delaware General Corporation Law permits a corporation to indemnify any director or officer of the corporation against expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with any action, suit or proceeding brought by reason of
the fact that such person is or was a director or officer of the corporation, if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, if he or she had no reasonable cause to believe his or her conduct was unlawful. In a derivative action (i.e., one brought by or on behalf of the corporation), indemnification may be provided only for expenses actually and reasonably incurred by any director or officer in connection with the defense or settlement of such an action or suit if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, except that no indemnification shall be provided if such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the Delaware Chancery Court or the court in which the action or suit was brought shall determine that such person is fairly and reasonably entitled to indemnity for such expenses despite such adjudication of liability.

Pursuant to Section 102(b)(7) of the Delaware General Corporation Law, Article SEVENTH of the Registrant’s amended and restated certificate of incorporation eliminates the liability of a director to the Registrant or its stockholders for monetary damages for such a breach of fiduciary duty as a director, except for liabilities arising:

- from any breach of the director’s duty of loyalty to the Registrant or its stockholders;
- from acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- under Section 174 of the Delaware General Corporation Law; and
- for any transaction from which the director derived an improper personal benefit.

The Registrant has entered into indemnification agreements with its non-employee directors and with certain officers, in addition to the indemnification provided for in the Registrant’s amended and restated certificate of incorporation and restated bylaws, and intends to enter into indemnification agreements with any new directors and executive officers in the future. The Registrant has purchased and intends to maintain insurance on behalf of any person who is or was a director or officer against any loss arising from any claim asserted against him or her and incurred by him or her in any such capacity, subject to certain exclusions.

The foregoing discussion of the Registrant’s amended and restated certificate of incorporation, restated bylaws, indemnification agreements and Delaware law is not intended to be exhaustive and is qualified in its entirety by such amended and restated certificate of incorporation, restated bylaws, indemnification agreements or law.

Item 7. Exemption from Registration Claimed.

Not applicable.

Item 8. Exhibits.

The following exhibits are filed as part of this Registration Statement:

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>Amended and Restated Certificate of Incorporation, as amended, of the Registrant (incorporated herein by reference from Exhibit 3.1 to the Registrant’s Form 8-K filed on May 26, 2017)</td>
</tr>
<tr>
<td>4.2</td>
<td>Certificate of Correction to the Amended and Restated Certificate of Incorporation, as amended, of the Registrant (incorporated herein by reference from Exhibit 3.1 to the Registrant’s Form 8-K filed on July 2, 2021)</td>
</tr>
<tr>
<td>4.3</td>
<td>Amended and Restated Bylaws of the Registrant (incorporated herein by reference from Exhibit 3.2 to the Registrant’s Form 8-K, filed on May 26, 2017)</td>
</tr>
<tr>
<td>4.4</td>
<td>Form of common stock certificate of the Registrant (incorporated herein by reference from Exhibit 4.1 to the Registrant’s Form S-1 filed May 8, 2017)</td>
</tr>
<tr>
<td>5.1</td>
<td>Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., counsel to the Registrant</td>
</tr>
<tr>
<td>23.1</td>
<td>Consent of PricewaterhouseCoopers LLP</td>
</tr>
<tr>
<td>23.2</td>
<td>Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in Exhibit 5.1)</td>
</tr>
<tr>
<td>24.1</td>
<td>Powers of Attorney (included on signature page to this registration statement)</td>
</tr>
</tbody>
</table>
Item 9. Undertakings.

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of this Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the “Calculation of Filing Fee Table” in the effective Registration Statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement;

provided, however, that paragraphs (a)(1)(i) and (a)(1)(ii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the Registration Statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering; and

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant’s annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan’s annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in such Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in such Act and will be governed by the final adjudication of such issue.
Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Research Triangle Park, North Carolina on this 1st day of November, 2023.

G1 THERAPEUTICS, INC.

By: /s/ John W. Umstead V
John W. Umstead V
Chief Financial Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of G1 Therapeutics, Inc., hereby severally constitute and appoint John E. Bailey, Jr. and John W. Umstead V, and each of them singly, our true and lawful attorneys with full power to them, and each of them singly, to sign for us and in our names in the capacities indicated below, the registration statement on Form S-8 filed herewith and any and all subsequent amendments to said registration statement, and generally to do all such things in our names and on our behalf in our capacities as officers and directors to enable G1 Therapeutics, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said registration statement and any and all amendments thereto.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>/s/ John E. Bailey, Jr.</td>
<td>President, Chief Executive Officer and Director</td>
<td>November 1, 2023</td>
</tr>
<tr>
<td>John E. Bailey, Jr.</td>
<td>(Principal Executive Officer)</td>
<td></td>
</tr>
<tr>
<td>/s/ John W. Umstead V</td>
<td>Chief Financial Officer</td>
<td>November 1, 2023</td>
</tr>
<tr>
<td>John W. Umstead V</td>
<td>(Principal Financial and Accounting Officer)</td>
<td></td>
</tr>
<tr>
<td>/s/ Jacks Lee</td>
<td>Director</td>
<td>November 1, 2023</td>
</tr>
<tr>
<td>Jacks Lee</td>
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</tr>
<tr>
<td>/s/ Cynthia L. Flowers</td>
<td>Director</td>
<td>November 1, 2023</td>
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<tr>
<td>Cynthia L. Flowers</td>
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</tr>
<tr>
<td>/s/ Glenn P. Muir</td>
<td>Director</td>
<td>November 1, 2023</td>
</tr>
<tr>
<td>Glenn P. Muir</td>
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<tr>
<td>/s/ Garry A. Nicholson</td>
<td>Director</td>
<td>November 1, 2023</td>
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<tr>
<td>Garry A. Nicholson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/s/ Alicia Secor</td>
<td>Director</td>
<td>November 1, 2023</td>
</tr>
<tr>
<td>Alicia Secor</td>
<td></td>
<td></td>
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<tr>
<td>/s/ Norman E. Sharpless, M.D.</td>
<td>Director</td>
<td>November 1, 2023</td>
</tr>
<tr>
<td>Norman E. Sharpless, M.D.</td>
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</tbody>
</table>
November 1, 2023

G1 Therapeutics, Inc.
700 Park Offices Drive, Suite 200
Research Triangle Park, NC 27709

Ladies and Gentlemen:

We have acted as legal counsel to G1 Therapeutics, Inc., a Delaware corporation (the “Company”), in connection with the preparation and filing with the Securities and Exchange Commission (the “Commission”) of a Registration Statement on Form S-8 (the “Registration Statement”), pursuant to which the Company is registering the issuance under the Securities Act of 1933, as amended (the “Securities Act”), of 1,096,553 shares (the “Shares”) of the Company’s common stock, $0.0001 par value per share, that may be issued pursuant to the Company’s Amended and Restated 2017 Employee, Director and Consultant Equity Plan, as amended (the “2017 Plan”). This opinion is being rendered in connection with the filing of the Registration Statement with the Commission. All capitalized terms used herein and not otherwise defined shall have the respective meanings given to them in the Registration Statement.

In connection with this opinion, we have examined the Company’s Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws, each as currently in effect; the 2017 Plan; such other records of the corporate proceedings of the Company and certificates of the Company’s officers as we have deemed relevant; and the Registration Statement and the exhibits thereto.

Our opinion expressed herein is limited to the General Corporation Law of the State of Delaware and we express no opinion with respect to the laws of any other jurisdiction. No opinion is expressed herein with respect to the qualification of the Shares under the securities or blue sky laws of any state or any foreign jurisdiction.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

Based upon the foregoing, we are of the opinion that the Shares, when issued and delivered in accordance with the terms of the 2017 Plan will be validly issued, fully paid and non-assessable.

We understand that you wish to file this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K promulgated under the Securities Act, and we hereby consent thereto. In giving this consent, we do not admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

BOSTON LOS ANGELES NEW YORK SAN DIEGO SAN FRANCISCO TORONTO WASHINGTON

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.
CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-8 of G1 Therapeutics, Inc. of our report dated March 1, 2023 relating to the financial statements, which appears in G1 Therapeutics, Inc.’s Annual Report on Form 10-K for the year ended December 31, 2022.

/s/ PricewaterhouseCoopers LLP

Raleigh, North Carolina
November 1, 2023

PricewaterhouseCoopers LLP, 4208 Six Forks Road, Captrust Tower, Suite 1200, Raleigh, NC 27609
T: (919) 791 4000, www.pwc.com/us
Calculation of Filing Fee Table

Form S-8
(Form Type)

G1 Therapeutics, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered

<table>
<thead>
<tr>
<th>Security Type</th>
<th>Security Class Title</th>
<th>Fee Calculation Rule</th>
<th>Amount Registered(1)</th>
<th>Proposed Minimum Offering Price Per Unit</th>
<th>Maximum Aggregate Offering Price</th>
<th>Fee Rate</th>
<th>Amount of Registration Fee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equity</td>
<td>Common Stock, par value $0.0001 per share</td>
<td>457(c) and 457(h)</td>
<td>1,096,553 (2)</td>
<td>$1.38(3)</td>
<td>$1,513,243.14</td>
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<td>Total Offering Amount</td>
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<td>$1,513,243.14</td>
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<td>$223.35</td>
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<tr>
<td>Total Fees Previously Paid</td>
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<tr>
<td>Total Fee Offsets</td>
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<tr>
<td>Net Fee Due</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>$223.35</td>
</tr>
</tbody>
</table>

(1) Pursuant to Rule 416(a) under the Securities Act of 1933, as amended (the “Securities Act”), this Registration Statement also covers an indeterminate number of additional shares of common stock, par value $0.0001 per share (“Common Stock”), of G1 Therapeutics, Inc. (the “Registrant”), which may be subject to grant or otherwise issuable after the operation of any anti-dilution and other provisions of the Registrant’s Amended and Restated 2017 Employee, Director and Consultant Equity Incentive Plan, as amended (the “2017 Plan”).

(2) Represents an increase of 1,096,553 shares of Common Stock of the Registrant reserved for issuance for compensatory purposes only, as previously authorized under the 2017 Plan as of January 1, 2023, in connection with an “evergreen” provision in the 2017 Plan.

(3) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) and Rule 457(h) promulgated under the Securities Act. The offering price per share and the aggregate offering price are based on the average of the high and the low price of the Registrant’s Common Stock as reported on The Nasdaq Global Select Market as of a date (October 25, 2023) within five business days prior to filing this Registration Statement.