UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

G1 THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)

2834 (Primary Standard Industrial Classification Code Number) 26-3648180 (I.R.S. Employer Identification Number)

79 T.W. Alexander Drive 4501 Research Commons, Suite 100 Research Triangle Park, NC 27709 (919) 213-9835

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Mark A. Velleca, M.D., Ph.D.
President and Chief Executive Officer
G1 Therapeutics, Inc.
79 T.W. Alexander Drive
4501 Research Commons, Suite 100
Research Triangle Park, NC 27709
(919) 213-9835

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Jonathan L. Kravetz, Esq. Megan N. Gates, Esq. Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, P.C. One Financial Center Boston, MA 02111 (617) 542-6000 Michael D. Maline, Esq. Edwin M. O'Connor, Esq. Goodwin Procter LLP The New York Times Building 620 Eighth Avenue New York, NY 10018 (212) 813-8800

Approximate date of commencement of proposed sale to the public: **As soon as practicable after the effective date of this registration statement.**

| As soon as practicable after the effective date of this registration statement. | | | |
|---|--|--|--|
| If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box. \square | | | |
| If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. Registration No. 333-223445 | | | |
| If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. □ | | | |

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. \Box

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 \square | Accelerated filer \square |
| Non-accelerated filer ⊠ (Do not check if a smaller reporting company) | Smaller reporting company \square |
| | Emerging growth company $oximes$ |

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. \boxtimes

CALCULATION OF REGISTRATION FEE

Amount to be Registered(1) Proposed Maximum Offering Price Per Share Proposed Maximum Aggregate Offering Price

Amount of Registration Fee(2)

| (1) | Represents only the additional number of shares of common stock being registered hereby, which includes up to 60,000 shares that may be purchased |
|-----|---|
| | by the underwriters upon the exercise of their option to purchase additional shares. Does not include 3,450,000 shares of common stock that the |
| | Registrant previously registered on the registration statement on Form S-1 (File No. 333-223445). |

460,000

\$29.50

\$13,570,000

\$1,689.47

Registrant previously registered on the registration statement on Form S-1 (File No. 333-223445).

(2) The registrant previously registered securities at an aggregate offering price not to exceed \$83,248,500 on a Registration Statement on Form S-1 (File No. 333-223445), which was declared effective by the Securities and Exchange Commission on March 7, 2018. In accordance with Rule 462(b) under

the Securities Act of 1933, as amended, an additional amount of securities having a proposed maximum aggregate offering price of \$13,570,000 is

hereby registered.

Common stock, \$0.0001 par value per share

This Registration Statement shall become effective upon filing with the Securities and Exchange Commission in accordance with Rule 462(b) promulgated under the Securities Act.

EXPLANATORY NOTE AND INCORPORATION BY REFERENCE

This registration statement on Form S-1 relates to the public offering of common stock of G1 Therapeutics, Inc. contemplated by the registration statement on Form S-1 (File No. 333-223445), as amended, filed by G1 Therapeutics, Inc. with the Securities and Exchange Commission (the "Commission") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), which was declared effective by the Commission on March 7, 2018 (the "Prior Registration Statement"). This registration statement is filed pursuant to Rule 462(b) promulgated under the Securities Act, solely to increase the number of shares of common stock to be offered in the public offering by 460,000 shares, which includes up to 60,000 shares that may be purchased by the underwriters upon the exercise of their option to purchase additional shares. The contents of the Prior Registration Statement, including all exhibits thereto, are hereby incorporated by reference herein.

The required opinions and consents are listed on an Exhibit Index attached hereto and filed herewith.

EXHIBIT INDEX

| Exhibit Number | Description of Exhibit |
|-------------------|---|
| 5.1 | Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. |
| 23.1 | Consent of PricewaterhouseCoopers LLP. |
| 23.2 | Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in Exhibit 5.1). |
| 24.1* | Power of Attorney. |

^{*} Included on the signature page to the Registrant's registration statement on Form S-1 (File No. 333-223445), filed with the Securities and Exchange Commission on March 5, 2018, and incorporated by reference herein.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this registration statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in Research Triangle Park, North Carolina, on the 7th day of March, 2018.

G1 THERAPEUTICS, INC.

/s/ Mark A. Velleca, M.D., Ph.D.

Mark A. Velleca, M.D., Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement on Form S-1 has been signed by the following persons in the capacities and on the dates indicated.

| <u>Name</u> | <u>Title</u> | <u>Date</u> |
|---|---|----------------|
| /s/ Mark A. Velleca, M.D., Ph.D. Mark A. Velleca, M.D., Ph.D. | Chief Executive Officer, President and Director (principal executive officer) | March 7, 2018 |
| Mark A. Veneca, M.D., 1 n.D. | (principal executive officer) | |
| /s/ Barclay A. Phillips | Chief Financial Officer | March 7, 2018 |
| Barclay A. Phillips | (principal financial officer) | |
| /s/ Jennifer K. Moses | Vice President of Finance and Administration | March 7, 2018 |
| Jennifer K. Moses | (principal accounting officer) | |
| * | Chairman of the Board | March 7, 2018 |
| Seth A. Rudnick, M.D. | | |
| * | Director | March 7, 2018 |
| Fredric N. Eshelman, Pharm.D. | _ | , |
| * | Director | March 7, 2018 |
| Glenn P. Muir | Zaccio. | |
| * | Director | March 7, 2018 |
| Tyrell J. Rivers, Ph.D. | Director | Warei 7, 2010 |
| * | Director | March 7, 2018 |
| Christy L. Shaffer, Ph.D. | Director | Walcii 7, 2010 |
| * | 5 1 | M 1 7 2010 |
| Sir Andrew P. Witty | Director | March 7, 2018 |
| | | |
| | | |
| *By: /s/ Barclay A. Phillips | <u></u> | March 7, 2018 |
| Barclay A. Phillips, Attorney-in-fact | | |

MINTZ LEVIN

One Financial Center Boston, MA 02111 617-542-6000 617-542-2241 fax www.mintz.com

March 7, 2018

G1 Therapeutics, Inc. 79 T.W. Alexander Drive 4501 Research Commons, Suite 100 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 (i) a Registration Statement (No. 333-223445) on Form S-1 (the "Initial Registration Statement"), and (ii) a second Registration Statement on Form S-1 filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the "Securities Act") (the "462(b) Registration Statement"), pursuant to which the Company is registering the offering for sale under the Securities Act of up to an aggregate of 460,000 additional shares (the "Shares") of the Company's common stock, par value \$0.0001 per share (the "Common Stock").

The Shares are to be sold by the Company pursuant to an underwriting agreement (the "Underwriting Agreement") to be entered into by and among the Company and J.P. Morgan Securities LLC and Cowen and Company, LLC, as representatives of the several underwriters to be named therein. The form of the Underwriting Agreement has been filed as Exhibit 1.1 to the Initial Registration Statement. This opinion is being rendered in connection with the filing of the 462(b) Registration Statement with the Commission.

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, and the form of the Underwriting Agreement; such other records of the corporate proceedings of the Company and certificates of the Company's officers as we have deemed relevant; the Initial Registration Statement and the exhibits thereto; and the 462(b) Registration Statement and the exhibits thereto.

In our examination, we have assumed the genuineness of all signatures, the legal capacity of natural persons, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as certified or photostatic copies and the authenticity of the originals of such copies.

Our opinion 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.

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

Boston | London | Los Angeles | New York | San Diego | San Francisco | Stamford | Washington

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

G1 Therapeutics, Inc. March 7, 2018 Page 2

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 sold in accordance with the form of the Underwriting Agreement most recently filed as an exhibit to the Initial Registration Statement and the prospectus that forms a part of the Initial Registration Statement, 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 462(b) Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K promulgated under the Securities Act and to reference the firm's name under the caption "Legal Matters" in the prospectus which is incorporated by reference in the 462(b) Registration Statement, 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.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-1 of our report dated February 21, 2018 relating to the financial statements of G1 Therapeutics, Inc., which appears in the Registration Statement on Form S-1 (No. 333-223445). We also consent to the reference to us under the heading "Experts" in the Registration Statement on Form S-1 (No. 333-223445).

/s/ PricewaterhouseCoopers LLP Raleigh, North Carolina March 7, 2018