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

**POST-EFFECTIVE AMENDMENT NO. 2
TO
FORM S-3
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)

26-3648180
(I.R.S. Employer
Identification No.)

**700 Park Offices Drive, Suite 200
Research Triangle Park, NC 27709
(919) 213-9835**

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

**James Stillman Hanson, Esq.
General Counsel and Secretary
G1 Therapeutics, Inc.
700 Park Offices Drive, Suite 200
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:

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Approximate date of commencement of proposed sale to the public: **From time to time after the effective date of this registration statement as determined by the registrant.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

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, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

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.

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 registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following 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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 Securities Act.

EXPLANATORY NOTE

G1 Therapeutics, Inc. (the “Registrant”) filed Post-Effective Amendment No. 1 (“Amendment No. 1”) to the Registration Statement on Form S-3 (Commission File No. 333- 257640) (the “Automatic Shelf Registration Statement”) of the Registrant because the Registrant was no longer a well-known seasoned issuer (as such term is defined in Rule 405 of the Securities Act of 1933, as amended (the “Securities Act”)) upon the filing of its Annual Report on Form 10-K for the fiscal year ended December 31, 2021. Amendment No. 1 was filed using EDGAR submission type POSASR and added disclosure to the Automatic Shelf Registration Statement required for a registrant other than a well-known seasoned issuer and made certain other amendments as set forth therein. This Post-Effective Amendment No. 2 is being filed using EDGAR submission type POS AM in order to convert the Automatic Shelf Registration Statement, as amended, to the proper EDGAR submission type for a non-automatic shelf registration statement.

This registration statement contains:

- a base prospectus which covers the offering, issuance and sale by us of up to \$300,000,000 in the aggregate of the securities identified above from time to time in one or more offerings; and
- a sales agreement prospectus covering the offering, issuance and sale by us of up to a maximum aggregate offering price of \$100,000,000 of our common stock that may be issued and sold from time to time under a sales agreement with Cowen and Company, LLC.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The sales agreement prospectus immediately follows the base prospectus. The \$100,000,000 of shares of common stock that may be offered, issued and sold under the sales agreement prospectus is included in the \$300,000,000 of securities that may be offered, issued and sold by us under the base prospectus. As of February 23, 2022, the Registrant has not sold any shares of common stock under the sales agreement prospectus pursuant to the Automatic Shelf Registration Statement.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED FEBRUARY 23, 2022

PROSPECTUS

G1 Therapeutics, Inc.

\$300,000,000
COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
RIGHTS
UNITS

We may offer and sell securities from time to time in one or more offerings. This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to \$300,000,000, any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock upon conversion of or exchange for the debt securities; common stock upon conversion of or exchange for the preferred stock; or common stock, preferred stock or debt securities upon the exercise of warrants or rights.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our securities may be sold directly by us to you, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. If any underwriters or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "GTHX." On February 22, 2022, the last reported sale price of our common stock was \$9.64 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The Nasdaq Global Select Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our securities, where applicable.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 4 of this prospectus under the caption "Risk Factors." We may include specific risk factors in supplements to this prospectus under the caption "[Risk Factors](#)." This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is _____, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process. Under this shelf registration process, we may from time to time offer shares of our common stock and preferred stock, various series of debt securities and/or warrants or rights to purchase any of such securities, either individually or in units, in one or more offerings, at prices and on terms to be set forth in one or more supplements to this prospectus at the time of an offering, with a total value of up to \$300,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits and the prospectus supplement, as applicable. The prospectus supplement may also add, update or change information contained or incorporated by reference in this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to the offering of securities under this prospectus. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated herein by reference and the additional information under the headings “Where You Can Find More Information” and “Incorporation of Documents by Reference” before making an investment decision.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus or any prospectus supplement. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated herein by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus or any prospectus supplement were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus may not be used to consummate sales of our securities unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

Unless the context otherwise requires, “G1,” “G1 Therapeutics,” “GTHX,” “the Company,” “we,” “us,” “our” and similar terms refer to G1 Therapeutics, Inc.

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC or included in any applicable prospectus supplement. Investing in our securities involves risks. Therefore, carefully consider the risk factors set forth in any prospectus supplements and in our most recent annual and quarterly filings with the SEC, as well as other information in this prospectus and any prospectus supplements and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

About G1 Therapeutics, Inc.

We are a commercial-stage biopharmaceutical company focused on the development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. Our first FDA-approved product, COSELA™ (trilaciclib) is the first and only therapy indicated to proactively help protect bone marrow from the damage of chemotherapy (myeloprotection) and is the first innovation in managing myelosuppression in decades. Trilaciclib was developed from a technology platform that targets key cellular pathways including transient arrest of the cell cycle at the G1 phase, prior to the beginning of DNA replication. Controlled administration and clean G1 arrest reduce hematologic adverse events (AEs) caused by cytotoxic therapy and may increase the ability to receive longer treatment durations. Transient CDK4/6 inhibition also modulates multiple immune functions while allowing beneficial T cell proliferation which may improve patients' anti-tumor immune responses. We are exploring the use of trilaciclib in a variety of trials across multiple tumors and treatment combinations to optimize the dual benefits of myeloprotection and improved anti-tumor efficacy for patients globally.

Additional Information

For additional information related to our business and operations, please refer to the reports incorporated herein by reference, as described under the caption "Incorporation of Documents by Reference" on page 26 of this prospectus.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in May 2008 under the name "G-Zero Therapeutics, Inc." In September 2012, we changed our name to "G1 Therapeutics, Inc." Our principal executive offices are located at 700 Park Offices Drive, Suite 200, Research Triangle Park, NC 27709, and our telephone number is (919) 213-9835. Our website address is www.g1therapeutics.com. The information contained on, or that can be accessed through, our website is not and shall not be deemed to be part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference. Investors should not rely on any such information in deciding whether to purchase our securities.

"G1 Therapeutics," "COSELA" and our logo are our trademarks. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

Offerings Under This Prospectus

Under this prospectus, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants or rights to purchase any of such securities, either individually or in units, from time to time at prices and on terms to be determined by market conditions at the time of the offering, with a total value of up to \$300,000,000. This prospectus provides you with a general description of the securities we may offer. Each

time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion or sinking fund terms, if any;
- voting or other rights, if any; and
- conversion or exercise prices, if any, and the various factors considered in determining such price.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

This prospectus may not be used to consummate a sale of any securities unless it is accompanied by a prospectus supplement.

RISK FACTORS

Investing in our securities involves significant risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in G1. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading “Risk Factors” in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading “Risk Factors” included in our most recent annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our subsequent current reports on Form 8-K that we have filed with the SEC, all of which are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Words such as, but not limited to, “believe,” “expect,” “anticipate,” “estimate,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “targets,” “likely,” “will,” “would,” “could,” “should,” “continue,” and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus and incorporated by reference in this prospectus, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by these forward-looking statements, to differ. The sections in our periodic reports, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, entitled “Business,” “Risk Factors,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” as well as other sections in this prospectus and the documents or reports incorporated by reference in this prospectus, discuss some of the factors that could contribute to these differences. These factors include, among other things, statements about:

- our history of losses;
- our dependence on the commercial success of COSELA;
- the nature of our business and our requirements for substantial additional funding;
- our limited operating history;
- the accuracy of our estimates regarding the number of patients, expenses, future revenues, capital requirements and our needs for additional financing;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;

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- our ability to advance product candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to enter into strategic arrangements and/or collaborations and the potential benefits of such arrangements;
- our financial performance;
- developments relating to our competitors and our industry;
- the volatility of our stock price;
- the marketability of our common stock; and
- our broad discretion to invest or spend the proceeds of our financings in ways with which our stockholders may not agree and may have limited ability to influence.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important cautionary statements in this prospectus or in the documents incorporated by reference in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. For a summary of such factors, please refer to the section entitled “Risk Factors” in this prospectus, as updated and supplemented by the discussion of risks and uncertainties under “Risk Factors” contained in any supplements to this prospectus and in our most recent annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference. The information contained in this document is believed to be current as of the date of this document. We do not intend to update any of the forward-looking statements after the date of this document to conform these statements to actual results or to changes in our expectations, except as required by law.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus or in any document incorporated herein by reference might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this prospectus or the date of the document incorporated by reference in this prospectus. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we intend to use any net proceeds from the sale of securities under this prospectus to fund activities related to the commercialization of COSELA, including the expansion of our sales force, the advancement of our drug development programs, and for other general corporate purposes, including, but not limited to, working capital, capital expenditures, investments, acquisitions, should we choose to pursue any, and collaborations. We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus for any purpose. Pending application of the net proceeds as described above, we may initially invest the net proceeds in short-term, investment-grade, interest-bearing securities.

PLAN OF DISTRIBUTION

We may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents or (3) directly to one or more purchasers, or through a combination of such methods. We may distribute the securities from time to time in one or more transactions at:

- a fixed price or prices, which may be changed from time to time;
- market prices prevailing at the time of sale;
- prices related to the prevailing market prices; or
- negotiated prices.

We may directly solicit offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time, and may enter into arrangements for “at-the-market,” equity line or similar transactions. We will name in a prospectus supplement any underwriter or agent involved in the offer or sale of the securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale, and we will provide the name of any underwriter in the prospectus supplement which the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

With respect to underwritten public offerings, negotiated transactions and block trades, we will provide in the applicable prospectus supplement information regarding any compensation we pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

If so indicated in the applicable prospectus supplement, we will authorize underwriters, dealers or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in each applicable prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in each applicable prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

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- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

One or more firms, referred to as “remarketing firms,” may also offer or sell the securities, if a prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as our agents. These remarketing firms will offer or sell the securities in accordance with the terms of the securities. Each prospectus supplement will identify and describe any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm’s compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale. Any underwriters involved in the sale of the securities may qualify as “underwriters” within the meaning of Section 2(a)(11) of the Securities Act. In addition, the underwriters’ commissions, discounts or concessions may qualify as underwriters’ compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority, Inc., or FINRA.

Shares of our common stock sold pursuant to the registration statement of which this prospectus is a part will be authorized for listing and trading on The Nasdaq Global Select Market. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The Nasdaq Global Select Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. Underwriters may make a market in our common stock, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the liquidity of or the existence, development or maintenance of trading markets for any of the securities.

In order to facilitate the offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the applicable security in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

The underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business.

DESCRIPTION OF COMMON STOCK

We are authorized to issue 120,000,000 shares of common stock, par value \$0.0001 per share. As of February 22, 2022, we had 42,705,532 shares of common stock outstanding and approximately 9 stockholders of record. Holders of record are defined as those stockholders whose shares are registered in their names in our stock records and do not include beneficial owners of common stock whose shares are held in the names of brokers, dealers or clearing agencies.

The following summary of certain provisions of our common stock does not purport to be complete. You should refer to the section of this prospectus entitled “Anti-Takeover Effects of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated By-Laws” and our amended and restated certificate of incorporation, as amended, and our amended and restated by-laws, both of which are included as exhibits to the registration statement of which this prospectus is a part. The summary below is also qualified by provisions of applicable law.

General

Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. All shares of common stock outstanding as of the date of this prospectus and, upon issuance and sale, all shares of common stock that we may offer pursuant to this prospectus, will be fully paid and nonassessable.

Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described under the “Anti-Takeover Effects of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated By-Laws” section below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and amended and restated by-laws.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar’s address is 250 Royall Street, Canton, MA 02021.

Stock Exchange Listing

Our common stock is listed for quotation on The Nasdaq Global Select Market under the symbol “GTHX.”

DESCRIPTION OF PREFERRED STOCK

The following description of preferred stock and the description of the terms of any particular series of preferred stock that G1 chooses to issue hereunder are not complete. These descriptions are qualified in their entirety by reference to G1's amended and restated certificate of incorporation and the certificate of designation relating to any series of preferred stock issued by G1. The rights, preferences, privileges and restrictions of the preferred stock of each series will be fixed by the certificate of designation relating to that series.

G1 currently has no shares of preferred stock outstanding and we have no current plans to issue any shares of preferred stock. Our board of directors will make any determination to issue such shares based on its judgment as to our company's best interests and the best interests of our stockholders.

Our board of directors is authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. Our board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Any or all of these rights may be greater than the rights of the G1 common stock. Our board of directors, without stockholder approval, can issue preferred stock with voting, conversion or other rights that could negatively affect the voting power and other rights of the holders of G1 common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a change in control of our company, which might harm the market price of our common stock. See also the "Anti-Takeover Effects of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated By-Laws" section below.

Our board of directors may specify the following characteristics of any preferred stock:

- the maximum number of shares;
- the designation of the shares;
- the annual dividend rate, if any, whether the dividend rate is fixed or variable, the date or dates on which dividends will accrue, the dividend payment dates, and whether dividends will be cumulative;
- the price and the terms and conditions for redemption, if any, including redemption at the option of G1 or at the option of the holders, including the time period for redemption, and any accumulated dividends or premiums;
- the liquidation preference, if any, and any accumulated dividends upon the liquidation, dissolution or winding up of G1's affairs;
- any sinking fund or similar provision, and, if so, the terms and provisions relating to the purpose and operation of the fund;
- the terms and conditions, if any, for conversion or exchange of shares of any other class or classes of G1's capital stock or any series of any other class or classes, or of any other series of the same class, or any other securities or assets, including the price or the rate of conversion or exchange and the method, if any, of adjustment;
- the voting rights;
- any or all other preferences and relative, participating, optional or other special rights, privileges or qualifications, limitations or restrictions; and
- any preferred stock issued will be fully paid and nonassessable upon issuance.

Transfer Agent and Registrar

The transfer agent and registrar for our preferred stock will be set forth in the applicable prospectus supplement.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer pursuant to this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any debt securities offered under such prospectus supplement may differ from the terms we describe below, and to the extent the terms set forth in a prospectus supplement differ from the terms described below, the terms set forth in the prospectus supplement shall control.

We may sell from time to time, in one or more offerings under this prospectus, debt securities, which may be senior or subordinated. We will issue any such senior debt securities under a senior indenture that we will enter into with a trustee to be named in the senior indenture. We will issue any such subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement of which this prospectus is a part. We use the term “indentures” to refer to either the senior indenture or the subordinated indenture, as applicable. The indentures will be qualified under the Trust Indenture Act of 1939, as in effect on the date of the indenture. We use the term “debenture trustee” to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities.

General

Each indenture provides that debt securities may be issued from time to time in one or more series and may be denominated and payable in foreign currencies or units based on or relating to foreign currencies. Neither the senior indenture nor any subordinated indenture limits the amount of debt securities that may be issued thereunder, and each indenture provides that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

- the title or designation;
- the aggregate principal amount and any limit on the amount that may be issued;
- the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;
- whether we will issue the series of debt securities in global form, the terms of any global securities and who the depositary will be;
- the maturity date and the date or dates on which principal will be payable;
- the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

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- the terms of the subordination of any series of subordinated debt;
- the place or places where payments will be payable;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities;
- whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;
- whether we will be restricted from incurring any additional indebtedness;
- a discussion of any material or special U.S. federal income tax considerations applicable to a series of debt securities;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate.

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change of control or in the event of a highly leveraged transaction (whether or not such transaction results in a change of control), which could adversely affect holders of debt securities.

Events of Default Under the Indenture

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and our failure continues for 90 days and the time for payment has not been extended or deferred;

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- if we fail to pay the principal, or premium, if any, when due and the time for payment has not been extended or delayed;
- if we fail to observe or perform any other covenant set forth in the debt securities of such series or the applicable indentures, other than a covenant specifically relating to and for the benefit of holders of another series of debt securities, and our failure continues for 90 days after we receive written notice from the debenture trustee or holders of not less than a majority in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur as to us.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time, if any.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of and premium and accrued and unpaid interest, if any, on all debt securities of that series. Before a judgment or decree for payment of the money due has been obtained with respect to debt securities of any series, the holders of a majority in principal amount of the outstanding debt securities of that series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the applicable indenture (including payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration). We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;

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- the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
- the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series (or at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) other conflicting directions within 60 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the applicable debenture trustee regarding our compliance with specified covenants in the applicable indenture.

Modification of Indenture; Waiver

The debenture trustee and we may change the applicable indenture without the consent of any holders with respect to specific matters, including:

- to fix any ambiguity, defect or inconsistency in the indenture; and
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series issued pursuant to such indenture.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) that is affected. However, the debenture trustee and we may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon the redemption of any debt securities;
- reducing the principal amount of discount securities payable upon acceleration of maturity;
- making the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series or in respect of a covenant or provision, which cannot be modified or amended without the consent of the holder of each outstanding debt security of the series affected; *provided, however*, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for obligations to:

- the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged with respect to a series, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, the premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange, and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange or in the applicable indenture, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under the applicable indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee under such indenture must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check which we will mail to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Debt Securities

Our obligations pursuant to any subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness, if any, to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of senior indebtedness we may incur. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

General

We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in the applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the warrant agreements and the prospectus supplement relating to the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of debt securities to be received upon exercise, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants may be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

As of February 22, 2022, we had no warrants outstanding.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

DESCRIPTION OF RIGHTS

General

We may issue rights to our stockholders to purchase shares of our common stock, preferred stock or the other securities described in this prospectus. We may offer rights separately or together with one or more additional rights, debt securities, preferred stock, common stock, or warrants, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights. We will provide in a prospectus supplement the following terms of the rights being issued:

- the date of determining the stockholders entitled to the rights distribution;
- the aggregate number of shares of common stock, preferred stock or other securities purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- whether the rights are transferrable and the date, if any, on and after which the rights may be separately transferred;
- the date on which the right to exercise the rights will commence, and the date on which the right to exercise the rights will expire;
- the method by which holders of rights will be entitled to exercise;
- the conditions to the completion of the offering, if any;
- the withdrawal, termination and cancellation rights, if any;
- whether there are any backstop or standby purchaser or purchasers and the terms of their commitment, if any;
- whether stockholders are entitled to oversubscription rights, if any;
- any applicable material U.S. federal income tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights, as applicable.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock, preferred stock or other securities at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or

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any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock, preferred stock or other securities, as applicable, purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Rights Agent

The rights agent for any rights we offer will be set forth in the applicable prospectus supplement.

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of common stock, preferred stock, one or more debt securities, warrants or rights for the purchase of common stock, preferred stock and/or debt securities in one or more series, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under “Description of Common Stock,” “Description of Preferred Stock,” “Description of Debt Securities,” “Description of Warrants,” and “Description of Rights” will apply to each unit, as applicable, and to any common stock, preferred stock, debt security, warrant, or right included in each unit, as applicable.

Unit Agent

The name and address of the unit agent, if any, for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act

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as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

ANTI-TAKEOVER EFFECTS OF DELAWARE LAW, OUR AMENDED AND RESTATED CERTIFICATE OF INCORPORATION AND OUR AMENDED AND RESTATED BY-LAWS

Our amended and restated certificate of incorporation and amended and restated by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies

In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes serving three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board of directors, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

No written consent of stockholders

Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of stockholders

Our amended and restated by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements

Our amended and restated by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the amended and restated by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Amendment to by-laws and certificate of incorporation

As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors and, if required by law or our amended and restated certificate of incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability, exclusive jurisdiction of Delaware Courts and the amendment of our amended and restated by-laws and amended and restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the amended and restated by-laws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Blank check preferred stock

Our amended and restated certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in our best interests or those of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A “business combination” includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An “interested stockholder” is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation’s voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or

- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

A Delaware corporation may “opt out” of these provisions with an express provision in its original certificate of incorporation or an express provision in its amended and restated certificate of incorporation or by-laws resulting from a stockholders’ amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Exclusive jurisdiction of certain actions

Our amended and restated certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought in our name, actions against our directors, officers and employees for breach of fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware, unless we otherwise consent. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

LIMITATION OF LIABILITY AND INDEMNIFICATION

Our amended and restated certificate of incorporation provides that no director of our company shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, except for liability (1) for any breach of the director’s duty of loyalty to us or our stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) in respect of unlawful dividend payments or stock redemptions or repurchases, or (4) for any transaction from which the director derived an improper personal benefit. In addition, our amended and restated certificate of incorporation provides that if the Delaware General Corporation Law is amended to authorize the further elimination or limitation of the liability of directors, then the liability of a director of our company shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

The amended and restated certificate of incorporation further provides that any repeal or modification of such article by our stockholders or amendment to the Delaware General Corporation Law will not adversely affect any right or protection existing at the time of such repeal or modification with respect to any acts or omissions occurring before such repeal or modification of a director serving at the time of such repeal or modification.

Our amended and restated by-laws provide that we will indemnify each of our directors and officers and, in the discretion of our board of directors, certain employees, to the fullest extent permitted by the Delaware General Corporation Law as the same may be amended (except that in the case of amendment, only to the extent that the amendment permits us to provide broader indemnification rights than the Delaware General Corporation Law permitted us to provide prior to such the amendment) against any and all expenses, judgments, penalties, fines and amounts reasonably paid in settlement that are incurred by the director, officer or such employee or on the director’s, officer’s or employee’s behalf in connection with any threatened, pending or completed proceeding or any claim, issue or matter therein, to which he or she is or is threatened to be made a party because he or she is or was serving as a director, officer or employee of our company, or at our request as a director, partner, trustee, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of our company and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. Article V, Section 5 of the amended and restated by-laws further provides for the advancement of expenses to each of our directors and, in the discretion of the board of directors, to certain officers and employees.

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In addition, the amended and restated by-laws provide that the right of each of our directors and officers to indemnification and advancement of expenses shall be a contract right and shall not be exclusive of any other right now possessed or hereafter acquired under any statute, provision of the amended and restated certificate of incorporation or amended and restated by-laws, agreement, vote of stockholders or otherwise. Furthermore, Article V, Section 10 of the amended and restated by-laws authorizes us to provide insurance for our directors, officers and employees, against any liability, whether or not we would have the power to indemnify such person against such liability under the Delaware General Corporation Law or the provisions of Article V of the amended and restated by-laws.

We have also entered into indemnification agreements with each of our directors and our executive officers and plan to enter into indemnification agreements with any newly elected or appointed director or executive officer. These agreements provide that we will indemnify each of our directors and such officers to the fullest extent permitted by law and the amended and restated certificate of incorporation and amended and restated by-laws.

We also maintain a general liability insurance policy, which covers certain liabilities of directors and officers of our company arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of securities being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, against certain liabilities.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will pass upon the validity of the issuance of the securities to be offered by this prospectus.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available at the SEC's web site at <http://www.sec.gov>. This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933, as amended, and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document.

We also maintain a website at www.g1therapeutics.com, through which you can access our SEC filings. The information set forth on our website is not part of this prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities we may offer pursuant to this prospectus. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in “Where You Can Find More Information.” The documents we are incorporating by reference are:

- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021 that we filed with the SEC on February 23, 2022;
- the description of our common stock contained in our Registration Statement on [Form 8-A](#) initially filed on May 16, 2017, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

The SEC file number for each of the documents listed above is 001-38096.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of the post-effective amendment to the registration statement of which this prospectus is a part and prior to effectiveness of the post-effective amendment shall be deemed to be incorporated by reference into this prospectus.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting:

G1 Therapeutics, Inc.
Attn: Investor Relations
700 Park Offices Drive, Suite 200
Research Triangle Park, NC 27709
Telephone: (919) 213-9835

You may also access these documents on our website, www.g1therapeutics.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

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You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

G1 THERAPEUTICS, INC.

**\$300,000,000
Common Stock
Preferred Stock
Debt Securities
Warrants
Rights
Units**

PROSPECTUS

, 2022

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED FEBRUARY 23, 2022

PROSPECTUS

Up to \$100,000,000

G1 Therapeutics, Inc.

Common Stock

We have entered into a Sales Agreement, or sales agreement, with Cowen and Company, LLC, or Cowen, dated February 23, 2022, relating to the sale of shares of our common stock, \$0.0001 par value per share, offered by this prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$100,000,000 from time to time through Cowen, acting as our sales agent.

Sales of our common stock, if any, under this prospectus will be made by any method permitted that is deemed an “at the market offering” as defined in Rule 415 under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through The Nasdaq Global Select Market or any other existing trading market for our common stock. Cowen is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Cowen will be entitled to compensation at a commission rate of up to 3.0% of the gross sales price per share sold under the sales agreement. See “Plan of Distribution” beginning on page SA-16 for additional information regarding the compensation to be paid to Cowen. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Our common stock is listed on The Nasdaq Global Select Market under the symbol “GTHX.” On February 22, 2022, the last reported sale price of our common stock was \$9.64 per share.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page SA-4 of this prospectus under the caption “[Risk Factors](#)” and in the documents incorporated by reference in this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

Cowen

The date of this prospectus is _____, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the “SEC”), utilizing a “shelf” registration process. Under this shelf registration process, we may from time to time sell shares of our common stock having an aggregate offering price of up to \$100,000,000 under this prospectus at prices and on terms to be determined by market conditions at the time of the offering. In connection with such offers and when accompanied by the base prospectus included in the registration statement of which this prospectus forms a part, this prospectus will be deemed a prospectus supplement to such base prospectus.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus and all of the information incorporated by reference herein and therein, as well as the additional information described under the headings “Where You Can Find More Information” and “Incorporation of Documents by Reference.” These documents contain important information that you should consider when making your investment decision.

To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference in this prospectus, on the other hand, you should rely on the information in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in or incorporated by reference in this prospectus and any related free writing prospectus filed by us with the SEC. We have not, and Cowen has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless the context otherwise requires, “G1,” “GTHX,” “the Company,” “we,” “us,” “our” and similar terms refer to G1 Therapeutics, Inc.

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC. Investing in our securities involves risks. Therefore, carefully consider the risk factors set forth in our most recent annual and quarterly filings with the SEC, as well as other information in this prospectus and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

About G1 Therapeutics, Inc.

We are a commercial-stage biopharmaceutical company focused on the development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. Our first FDA-approved product, COSELA™ (trilaciclib) is the first and only therapy indicated to proactively help protect bone marrow from the damage of chemotherapy (myeloprotection) and is the first innovation in managing myelosuppression in decades. Trilaciclib was developed from a technology platform that targets key cellular pathways including transient arrest of the cell cycle at the G1 phase, prior to the beginning of DNA replication. Controlled administration and clean G1 arrest reduce hematologic adverse events (AEs) caused by cytotoxic therapy and may increase the ability to receive longer treatment durations. Transient CDK4/6 inhibition also modulates multiple immune functions while allowing beneficial T cell proliferation which may improve patients' anti-tumor immune responses. We are exploring the use of trilaciclib in a variety of trials across multiple tumors and treatment combinations to optimize the dual benefits of myeloprotection and improved anti-tumor efficacy for patients globally.

Additional Information

For additional information related to our business and operations, please refer to the reports incorporated herein by reference, as described under the caption "Incorporation of Documents by Reference" on page SA-18 of this prospectus.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in May 2008 under the name "G-Zero Therapeutics, Inc." In September 2012, we changed our name to "G1 Therapeutics, Inc." Our principal executive offices are located at 700 Park Offices Drive, Suite 200, Research Triangle Park, NC 27709, and our telephone number is (919) 213-9835. Our website address is www.g1therapeutics.com. The information contained on, or that can be accessed through, our website is not and shall not be deemed to be part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference. Investors should not rely on any such information in deciding whether to purchase our common stock.

"G1 Therapeutics," "COSELA" and our logo are our trademarks. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$100,000,000.
Manner of offering	“At the market” offering that may be made from time to time through our sales agent, Cowen and Company, LLC, or Cowen. See “Plan of Distribution” on page SA-16 of this prospectus.
Use of proceeds	We currently intend to use any net proceeds from this offering to fund activities related to the commercialization of COSELA, including the expansion of our sales force, the advancement of our drug development programs, and for other general corporate purposes, including, but not limited to, working capital, capital expenditures, investments, acquisitions, should we choose to pursue any, and collaborations. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds. See the section entitled “Use of Proceeds” on page SA-8 of this prospectus.
Risk factors	See “Risk Factors” beginning on page SA-4 of this prospectus and the other information included in, or incorporated by reference into, this prospectus for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	“GTHX”

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the sections captioned “Risk Factors” contained in our most recent Annual Report on Form 10-K, as well as in any of our subsequent Quarterly Reports on Form 10-Q or our Current Reports on Form 8-K, which are incorporated by reference herein in their entirety, together with other information in this prospectus, the information and documents incorporated by reference in this prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose part or all of your investment. This prospectus and the incorporated documents also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned below. Forward-looking statements included in this prospectus are based on information available to us on the date hereof, and all forward-looking statements in documents incorporated by reference are based on information available to us as of the date of such documents. We disclaim any obligation to update any forward-looking statements.

Risks Related to This Offering

Our management will have broad discretion over the use of the net proceeds from this offering, and you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

Our management will have broad discretion as to the use of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you are relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds will be used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for G1.

Purchasers will experience immediate dilution in the book value per share of the common stock purchased in the offering.

The shares sold in this offering, if any, will be sold from time to time at various prices. However, we expect that the offering price of our common stock will be substantially higher than the net tangible book value per share of our outstanding common stock. After giving effect to the sale of shares of our common stock in the aggregate amount of \$100,000,000 at an assumed offering price of \$9.64 per share, the last reported sale price of our common stock on February 22, 2022 on The Nasdaq Global Select Market, and after deducting commissions and estimated offering expenses, our as adjusted net tangible book value as of December 31, 2021 would have been approximately \$241.3 million or approximately \$4.56 per share. This represents an immediate increase in net tangible book value of approximately \$1.19 per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of approximately \$5.08 per share to purchasers of our common stock in this offering. Because the sales of the shares offered under this prospectus will be made directly into the market, the prices at which we sell these shares will vary and these variations may be significant. Any purchaser of the shares we sell, as well as any existing stockholder, will experience significant dilution if we sell shares at prices significantly below the price at which the purchaser or existing stockholder invested.

In addition to this offering, subject to market conditions and other factors, we may pursue additional equity financings in the future, including future public offerings or future private placements of equity securities or securities convertible into or exchangeable for equity securities. Further, the exercise of outstanding options or

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the vesting of restricted stock units could result in further dilution to investors and any additional shares issued in connection with acquisitions, should we choose to pursue any, will result in dilution to investors. In addition, the market price of our common stock could fall as a result of resales of any of these shares of common stock due to an increased number of shares available for sale in the market.

As of December 31, 2021, we had 6,701,727 shares of our common stock issuable upon the exercise of stock options outstanding, of which 3,660,578 shares were vested as of such date, 414,991 shares issuable upon the vesting of restricted stock units outstanding, 68,900 shares of common stock reserved for future issuance under our G1 Therapeutics, Inc. 2021 Inducement Equity Incentive Plan, 395,000 shares of common stock reserved for future issuance under our G1 Therapeutics, Inc. 2021 Sales Force Inducement Equity Incentive Plan, or the 2021 Inducement Plan, and 1,307,735 shares of common stock reserved for future issuance under our 2017 Employee, Director and Consultant Equity Incentive Plan, or the 2017 Plan.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

The actual number of shares we will issue under the sales agreement with Cowen, at any one time or in total, is uncertain.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Cowen at any time throughout the term of the sales agreement. The number of shares that are sold by Cowen after we deliver a placement notice will fluctuate based on the market price of the common stock during the sales period and limits we set with Cowen. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares, if any, that will ultimately be issued.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Words such as, but not limited to, “believe,” “expect,” “anticipate,” “estimate,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “targets,” “likely,” “will,” “would,” “could,” “should,” “continue,” and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus and incorporated by reference in this prospectus, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by these forward-looking statements, to differ. The sections in our periodic reports, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, entitled “Business,” “Risk Factors,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” as well as other sections in this prospectus and the documents or reports incorporated by reference in this prospectus, discuss some of the factors that could contribute to these differences. These factors include, among other things, statements about:

- our history of losses;
- our dependence on the commercial success of COSELA;
- the nature of our business and our requirements for substantial additional funding;
- our limited operating history;
- the accuracy of our estimates regarding the number of patients, expenses, future revenues, capital requirements and our needs for additional financing;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to enter into strategic arrangements and/or collaborations and the potential benefits of such arrangements;
- our financial performance;
- developments relating to our competitors and our industry;
- the volatility of our stock price;

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- the marketability of our common stock; and
- our broad discretion to invest or spend the proceeds of our financings in ways with which our stockholders may not agree and may have limited ability to influence.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important cautionary statements in this prospectus or in the documents incorporated by reference in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. For a summary of such factors, please refer to the section entitled “Risk Factors” in this prospectus, as updated and supplemented by the discussion of risks and uncertainties under “Risk Factors” contained in any supplements to this prospectus and in our most recent annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference. The information contained in this document is believed to be current as of the date of this document. We do not intend to update any of the forward-looking statements after the date of this document to conform these statements to actual results or to changes in our expectations, except as required by law.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus or in any document incorporated herein by reference might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this prospectus or the date of the document incorporated by reference in this prospectus. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sale proceeds of up to \$100,000,000 from time to time (before deducting sales agent commissions and expenses). Because there is no minimum offering amount required to be sold in connection with this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We currently intend to use any net proceeds from this offering to fund activities related to the commercialization of COSELA, including the expansion of our sales force, the advancement of our drug development programs, and for other general corporate purposes, including, but not limited to, working capital, capital expenditures, investments, acquisitions, should we choose to pursue any, and collaborations. The amounts and timing of our actual expenditures will depend on numerous factors, including the progress of our clinical trials and other development efforts and other factors described under “Risk Factors” in this prospectus and the documents incorporated by reference herein, as well as the amount of cash used in our operations. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with shares of our common stock offered pursuant to this prospectus for any purpose. Pending use of the proceeds as described above, we intend to invest the proceeds in short-term, interest-bearing, investment-grade securities, U.S. Treasuries and government agency securities.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future.

DILUTION

If you invest in our common stock, your interest will be diluted to the extent of the difference between the price per share of our common stock you pay in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

As of December 31, 2021, our historical net tangible book value was \$143.5 million, or \$3.37 per share of common stock. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by 42,562,148, the number of shares of common stock outstanding as of December 31, 2021.

After giving effect to the assumed sale of our common stock in the aggregate amount of \$100,000,000 at an assumed offering price of \$9.64 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on February 22, 2022, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2021, would have been \$241.3 million, or \$4.56 per share of common stock. This amount represents an immediate increase in net tangible book value of \$1.19 per share to our existing stockholders and an immediate dilution in net tangible book value of approximately \$5.08 per share to new investors in this offering.

The following table illustrates this calculation on a per share basis. The as adjusted information is illustrative only and will adjust based on the actual price to the public, the actual number of shares sold and other terms of the offering determined at the time shares of our common stock are sold pursuant to this prospectus. The shares sold in this offering, if any, will be sold from time to time at various prices.

Assumed offering price per share		\$9.64
Historical net tangible book value per share as of December 31, 2021	\$3.37	
Increase in net tangible book value per share attributable to this offering	<u>1.19</u>	
As adjusted net tangible book value per share after giving effect to this offering		<u>4.56</u>
Dilution per share to new investors participating in this offering		\$5.08

The table above assumes for illustrative purposes that an aggregate of 10,373,443 shares of our common stock are sold during the term of the sales agreement with Cowen at a price of \$9.64 per share, the last reported sale price of our common stock on The NASDAQ Global Select Market on February 22, 2022, for aggregate gross proceeds of \$100.0 million. The shares subject to the sales agreement with Cowen are being sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$9.64 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$100,000,000 during the term of the sales agreement with Cowen is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$4.64 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$6.00 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$9.64 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$100,000,000 during the term of the sales agreement with Cowen is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$4.46 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$4.18 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

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The number of shares of our common stock to be outstanding immediately after this offering is based on 42,562,148 shares of our common stock outstanding as of December 31, 2021. The number of shares outstanding as of December 31, 2021 excludes:

- 6,701,727 shares of common stock issuable upon exercise of outstanding options as of December 31, 2021, at a weighted average exercise price of \$17.88 per share, of which 3,660,578 shares were vested as of such date;
- 414,991 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2021;
- 1,307,735 shares of common stock reserved for future issuance under the 2017 Employee, Director and Consultant Equity Incentive Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan;
- 68,900 shares of common stock reserved for future issuance under our G1 Therapeutics, Inc. 2021 Inducement Equity Incentive Plan; and
- 395,000 shares of common stock reserved for future issuance under our G1 Therapeutics, Inc. 2021 Sales Force Inducement Equity Incentive Plan.

To the extent that any shares are issued upon the exercise of outstanding options, the vesting of outstanding restricted stock units or otherwise pursuant to any grants made in the future under our 2021 Inducement Plan and 2017 Plan, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of such securities could result in further dilution to our stockholders.

DESCRIPTION OF CAPITAL STOCK

We are authorized to issue 120,000,000 shares of common stock, par value \$0.0001 per share, and 5,000,000 shares of preferred stock, par value \$0.0001 per share. As of February 22, 2022, we had 42,705,532 shares of common stock outstanding and approximately 9 stockholders of record. Holders of record are defined as those stockholders whose shares are registered in their names in our stock records and do not include beneficial owners of common stock whose shares are held in the names of brokers, dealers or clearing agencies.

The following summary of certain provisions of our common stock does not purport to be complete. You should refer to the section of this prospectus entitled “Anti-Takeover Effects of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated By-Laws” and our amended and restated certificate of incorporation, as amended, or the restated certificate of incorporation, and our amended and restated by-laws, both of which are included as exhibits to the registration statement of which this prospectus is a part. The summary below is also qualified by provisions of applicable law.

General

Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. All shares of common stock outstanding as of the date of this prospectus and, upon issuance and sale, all shares of common stock that we may offer pursuant to this prospectus, will be fully paid and nonassessable.

Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described under the “Anti-Takeover Effects of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated By-Laws” section below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and amended and restated by-laws.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar’s address is 250 Royall Street, Canton, MA 02021.

Stock Exchange Listing

Our common stock is listed for quotation on The Nasdaq Global Select Market under the symbol “GTHX.”

Anti-takeover effects of Delaware law, our amended and restated certificate of incorporation and our amended and restated by-laws

Our amended and restated certificate of incorporation and amended and restated by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies

In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes serving three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board of directors, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

No written consent of stockholders

Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of stockholders

Our amended and restated by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements

Our amended and restated by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the amended and restated by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Amendment to by-laws and certificate of incorporation

As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors and, if required by law or our amended and restated certificate of incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability, exclusive jurisdiction of Delaware Courts and the amendment of our amended and restated by-laws and amended and restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the amended and restated by-laws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Blank check preferred stock

Our amended and restated certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in our best interests or those of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A “business combination” includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An “interested stockholder” is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation’s voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

A Delaware corporation may “opt out” of these provisions with an express provision in its original certificate of incorporation or an express provision in its amended and restated certificate of incorporation or by-laws resulting from a stockholders’ amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Exclusive jurisdiction of certain actions

Our amended and restated certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought in our name, actions against our directors, officers and employees for breach of

fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware, unless we otherwise consent. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

Limitation of Liability and Indemnification

Our amended and restated certificate of incorporation provides that no director of our company shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, except for liability (1) for any breach of the director's duty of loyalty to us or our stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) in respect of unlawful dividend payments or stock redemptions or repurchases, or (4) for any transaction from which the director derived an improper personal benefit. In addition, our amended and restated certificate of incorporation provides that if the Delaware General Corporation Law is amended to authorize the further elimination or limitation of the liability of directors, then the liability of a director of our company shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

The amended and restated certificate of incorporation further provides that any repeal or modification of such article by our stockholders or amendment to the Delaware General Corporation Law will not adversely affect any right or protection existing at the time of such repeal or modification with respect to any acts or omissions occurring before such repeal or modification of a director serving at the time of such repeal or modification.

Our amended and restated by-laws provide that we will indemnify each of our directors and officers and, in the discretion of our board of directors, certain employees, to the fullest extent permitted by the Delaware General Corporation Law as the same may be amended (except that in the case of amendment, only to the extent that the amendment permits us to provide broader indemnification rights than the Delaware General Corporation Law permitted us to provide prior to such the amendment) against any and all expenses, judgments, penalties, fines and amounts reasonably paid in settlement that are incurred by the director, officer or such employee or on the director's, officer's or employee's behalf in connection with any threatened, pending or completed proceeding or any claim, issue or matter therein, to which he or she is or is threatened to be made a party because he or she is or was serving as a director, officer or employee of our company, or at our request as a director, partner, trustee, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of our company and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. Article V, Section 5 of the amended and restated by-laws further provides for the advancement of expenses to each of our directors and, in the discretion of the board of directors, to certain officers and employees.

In addition, the amended and restated by-laws provide that the right of each of our directors and officers to indemnification and advancement of expenses shall be a contract right and shall not be exclusive of any other right now possessed or hereafter acquired under any statute, provision of the amended and restated certificate of incorporation or amended and restated by-laws, agreement, vote of stockholders or otherwise. Furthermore, Article V, Section 10 of the amended and restated by-laws authorizes us to provide insurance for our directors, officers and employees, against any liability, whether or not we would have the power to indemnify such person against such liability under the Delaware General Corporation Law or the provisions of Article V of the amended and restated by-laws.

We have also entered into indemnification agreements with each of our directors and our executive officers and plan to enter into indemnification agreements with any newly elected or appointed director or executive officer. These agreements provide that we will indemnify each of our directors and such officers to the fullest extent permitted by law and the amended and restated certificate of incorporation and amended and restated by-laws.

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We also maintain a general liability insurance policy, which covers certain liabilities of directors and officers of our company arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, against certain liabilities.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen, dated February 23, 2022, under which we may issue and sell from time to time up to \$100,000,000 of our common stock through Cowen as our sales agent. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an “at the market” offering as defined in Rule 415 under the Securities Act, including sales made directly on The NASDAQ Global Select Market or any other trading market for our common stock. If authorized by us in writing, Cowen may purchase shares of our common stock as principal.

Cowen will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party’s sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent equals up to 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. We may also reimburse Cowen up to \$50,000 of Cowen’s actual outside legal expenses incurred by Cowen in connection with this offering, and for certain other expenses, including Cowen’s FINRA counsel fees in an amount up to \$10,000, if any. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$190,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The NASDAQ Global Select Market on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act or the Exchange Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on The NASDAQ Global Select Market and trades under the symbol “GTHX.” The transfer agent of our common stock is Computershare Trust Company, N.A.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will pass upon the validity of the issuance of the securities to be offered by this prospectus. Cowen and Company, LLC is being represented by DLA Piper LLP (US), New York, NY in connection with this offering.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. SEC filings are available at the SEC's web site at <http://www.sec.gov>.

This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933, as amended, and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document.

We also maintain a website at www.g1therapeutics.com through which you can access our SEC filings. The information set forth on our website is not part of this prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities we may offer pursuant to this prospectus. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in “Where You Can Find More Information.” The documents we are incorporating by reference are:

- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021 that we filed with the SEC on February 23, 2022;
- the description of our common stock contained in our Registration Statement on [Form 8-A](#) initially filed on May 16, 2017, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

The SEC file number for each of the documents listed above is 001-38096.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of the post-effective amendment to the registration statement of which this prospectus is a part and prior to effectiveness of the post-effective amendment shall be deemed to be incorporated by reference into this prospectus.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting:

G1 Therapeutics, Inc.
Attn: Investor Relations
700 Park Offices Drive, Suite 200
Research Triangle Park, NC 27709
Telephone: (919) 213-9835

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You may also access these documents on our website, www.g1therapeutics.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

You should rely only on information contained in, or incorporated by reference into, this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

G1 THERAPEUTICS, INC.

Up to \$100,000,000

Common Stock

PROSPECTUS

Cowen

, 2022

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth an itemization of the various expenses, all of which we will pay, in connection with the issuance and distribution of the securities being registered. All of the amounts shown are estimated except the SEC Registration Fee.

SEC Registration Fee	\$27,810.00(1)
Printing and Engraving Expenses	(2)(3)
Legal Fees and Expenses	(2)(3)
Accounting Fees and Expenses	(2)(3)
Transfer Agent and Registrar Fees	(2)(3)
Miscellaneous	(2)(3)
Total	(2)(3)

- (1) We previously paid a fee of \$16,365 related to the at the market offering, issuance and sale of up to \$150,000,000 of our common stock pursuant to a sales agreement with Cowen and Company, LLC, dated July 2, 2021. Of such shares of common stock, \$150,000,000 remain unsold (the "Unsold Shelf Securities"). \$100,000,000 of the Unsold Shelf Securities are being included in this registration statement and the registration fee in the amount of \$10,910.00 related thereto is applied to the registrant's total registration fee hereunder.
- (2) These fees will be calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.
- (3) Estimates of total fees paid at this time related to the at the market offering of our common stock pursuant to a sales agreement with Cowen and Company, LLC, dated February 23, 2022, consist of approximately \$25,000 in printing and engraving fees, \$40,000 in accounting services fees, \$100,000 in legal fees, and \$25,000 in miscellaneous fees, for total fees related to the at the market offering of \$190,000, other than the registration fee.

Item 15. Indemnification of Directors and Officers

Section 145(a) of the Delaware General Corporation Law provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation), because he or she is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding, if he or she acted in good faith and in a manner 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, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the Delaware General Corporation Law provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor because the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, except that no

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indemnification shall be made with respect to any claim, issue or matter as to which he or she shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, he or she is fairly and reasonably entitled to indemnity for such expenses that the Court of Chancery or other adjudicating court shall deem proper.

Section 145(g) of the Delaware General Corporation Law provides, in general, that a corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his or her status as such, whether or not the corporation would have the power to indemnify the person against such liability under Section 145 of the Delaware General Corporation Law.

Our amended and restated certificate of incorporation provides that no director of our company shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, except for liability (1) for any breach of the director's duty of loyalty to us or our stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) in respect of unlawful dividend payments or stock redemptions or repurchases, or (4) for any transaction from which the director derived an improper personal benefit. In addition, our amended and restated certificate of incorporation provides that if the Delaware General Corporation Law is amended to authorize the further elimination or limitation of the liability of directors, then the liability of a director of our company shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

The amended and restated certificate of incorporation further provides that any repeal or modification of such article by our stockholders or amendment to the Delaware General Corporation Law will not adversely affect any right or protection existing at the time of such repeal or modification with respect to any acts or omissions occurring before such repeal or modification of a director serving at the time of such repeal or modification.

Our amended and restated by-laws provide that we will indemnify each of our directors and officers and, in the discretion of our board of directors, certain employees, to the fullest extent permitted by the Delaware General Corporation Law as the same may be amended (except that in the case of amendment, only to the extent that the amendment permits us to provide broader indemnification rights than the Delaware General Corporation Law permitted us to provide prior to such amendment) against any and all expenses, judgments, penalties, fines and amounts reasonably paid in settlement that are incurred by the director, officer or such employee or on the director's, officer's or employee's behalf in connection with any threatened, pending or completed proceeding or any claim, issue or matter therein, to which he or she is or is threatened to be made a party because he or she is or was serving as a director, officer or employee of our company, or at our request as a director, partner, trustee, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of our company and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. Article V, Section 5 of the amended and restated by-laws further provides for the advancement of expenses to each of our directors and, in the discretion of the board of directors, to certain officers and employees.

In addition, the amended and restated by-laws provide that the right of each of our directors and officers to indemnification and advancement of expenses shall be a contract right and shall not be exclusive of any other right now possessed or hereafter acquired under any statute, provision of the amended and restated certificate of incorporation or amended and restated by-laws, agreement, vote of stockholders or otherwise. Furthermore, Article V, Section 10 of the amended and restated by-laws authorizes us to provide insurance for our directors, officers and employees, against any liability, whether or not we would have the power to indemnify such person

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against such liability under the Delaware General Corporation Law or the provisions of Article V of the amended and restated by-laws.

We have also entered into indemnification agreements with each of our directors and our executive officers. These agreements provide that we will indemnify each of our directors and such officers to the fullest extent permitted by law and the amended and restated certificate of incorporation and amended and restated by-laws.

We also maintain a general liability insurance policy, which covers certain liabilities of directors and officers of our company arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, against certain liabilities.

Item 16. Exhibits

The exhibits to this registration statement are listed in the Exhibit Index to this registration statement, which immediately precedes the Signature Page and which Exhibit Index is hereby incorporated by reference.

Item 17. 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 the 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 a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(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), (a)(1)(ii) and (a)(1)(iii) 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, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of 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.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) That, for purposes of determining any liability under the Securities Act:

(1) the information omitted from the form of prospectus filed as part of the registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of the registration statement as of the time it was declared effective; and

(2) each post-effective amendment that contains a form of prospectus 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.

(c) 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

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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.

(d) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the 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 the Act and will be governed by the final adjudication of such issue.

(e) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act ("Act") in accordance with the rules and regulations prescribed by the Commission under section 305(b)(2) of the Act.

EXHIBIT INDEX

<u>Exhibit Number</u>	<u>Exhibit Description</u>	<u>Filed Herewith</u>	<u>Incorporated by Reference herein from Form or Schedule</u>	<u>Filing Date</u>	<u>SEC File/Reg. Number</u>
1.1*	Form of Underwriting Agreement.				
1.2	Sales Agreement, dated as of February 23, 2022 by and between the Registrant and Cowen and Company, LLC		10-K (Exhibit 10.29)	2/23/2022	001-38096
4.1	Amended and Restated Certificate of Incorporation of the Registrant		8-K (Exhibit 3.1)	5/26/2017	001-38096
4.2	Amended and Restated By-laws of the Registrant		8-K (Exhibit 3.2)	5/26/2017	001-38096
4.3	Specimen Stock Certificate evidencing the shares of Common Stock		S-1 (Exhibit 4.1)	5/8/2017	333-217285
4.4*	Form of Certificate of Amendment or Designation with respect to Preferred Stock				
4.5*	Form of Senior Debt Security				
4.6*	Form of Subordinated Debt Security				
4.7**	Form of Senior Indenture				
4.8**	Form of Subordinated Indenture				
4.9*	Form of Warrant Agreement and Warrant Certificate				
4.10*	Form of Rights Agreement and Right Certificate				
4.11*	Form of Unit Agreement and Unit				
5.1***	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. with respect to the legality of the securities being registered				
5.2**	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.				
23.1	Consent of PricewaterhouseCoopers LLP	X			
23.2	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in the opinion filed as Exhibit 5.1)				
23.3	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in the opinion filed as Exhibit 5.2)				
24.1**	Powers of Attorney (included on the signature page of the initial registration statement).				

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Exhibit Number	Exhibit Description	Filed Herewith	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File/Reg. Number
25.1*	The Statement of Eligibility on Form T-1 under the Trust Indenture Act of 1939, as amended, of the Trustee under the Senior Indenture will be incorporated herein by reference from a subsequent filing in accordance with Section 305(b)(2) of the Trust Indenture Act of 1939.				
25.2*	The Statement of Eligibility on Form T-1 under the Trust Indenture Act of 1939, as amended, of the Trustee under the Subordinated Indenture will be incorporated herein by reference from a subsequent filing in accordance with Section 305(b)(2) of the Trust Indenture Act of 1939.				

* To be subsequently filed, if applicable, by an amendment to this registration statement or as an exhibit to a report on Form 10-K, Form 10-Q or Form 8-K and incorporated herein by reference.

** Previously filed as an exhibit to the initial registration statement filed with the Securities and Exchange Commission on July 2, 2021.

*** Previously filed as an exhibit to post-effective amendment no. 1 to the registration statement filed with the Securities and Exchange Commission on February 23, 2022.

SIGNATURES

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-3 and has duly caused this Post-Effective Amendment No. 2 to Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in Research Triangle Park in the State of North Carolina, on February 23, 2022.

G1 THERAPEUTICS, INC.

By: /s/ John E. Bailey, Jr.
John E. Bailey, Jr.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this Post-Effective Amendment No. 2 to Form S-3 has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ John E. Bailey, Jr.</u> John E. Bailey, Jr.	Chief Executive Officer, President and Director <i>(principal executive officer)</i>	February 23, 2022
<u>/s/ Jennifer K. Moses</u> Jennifer K. Moses	Chief Financial Officer <i>(principal financial and accounting officer)</i>	February 23, 2022
* <u>Willie A. Deese</u>	Director	February 23, 2022
* <u>Glenn P. Muir</u>	Director	February 23, 2022
* <u>Garry A. Nicholson</u>	Director	February 23, 2022
* <u>Cynthia L. Schwalm</u>	Director	February 23, 2022
* <u>Alicia Secor</u>	Director	February 23, 2022
* <u>Mark A. Velleca, M.D., Ph.D.</u>	Director	February 23, 2022
*By <u>/s/ John E. Bailey, Jr.</u> John E. Bailey, Jr. <i>Attorney-in-fact</i>		February 23, 2022

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of G1 Therapeutics, Inc. of our report dated February 23, 2022 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in G1 Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2021. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
February 23, 2022