

Prospectus supplement
(to Prospectus dated February 23, 2022)**7,700,000 Shares****Common Stock**

We are offering 7,700,000 shares of our common stock. Our common stock is listed on The Nasdaq Global Select Market under the symbol “GTHX.” On November 17, 2022, the last reported sale price of our common stock on The Nasdaq Global Select Market was \$8.55 per share.

Investing in our common stock involves a high degree of risk. Please read “[Risk Factors](#)” beginning on page S-9 of this prospectus supplement, page 4 of the accompanying prospectus and under similar headings in the documents that are incorporated by reference into this prospectus supplement and the accompanying 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 supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	<u>Per Share</u>	<u>Total</u>
Public Offering Price	\$ 6.50	\$50,050,000
Underwriting Discounts and Commissions ⁽¹⁾	\$ 0.39	\$ 3,003,000
Proceeds to us, before expenses	\$ 6.11	\$47,047,000

(1) We refer you to “Underwriting” beginning on page S-16 of this prospectus supplement for additional information regarding underwriting compensation.

Fredric N. Eshelman, a former member of our board of directors and a greater than 5% stockholder of our company, has indicated an interest in purchasing an aggregate of up to approximately \$7.0 million of our common stock in this offering at the public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares of common stock to Mr. Eshelman, and Mr. Eshelman could determine to purchase more, fewer or no shares of common stock in this offering.

Delivery of shares of common stock is expected to be made on or about November 22, 2022. We have granted the underwriters an option for a period of 30 days after the date of this prospectus supplement to purchase up to an additional 1,155,000 shares of our common stock, at the public offering price less the underwriting discount. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$3,453,450, and the total proceeds to us, before expenses, will be \$54,104,050.

Joint Book-Running Managers**Cowen****Raymond James****Lead Managers****Needham & Company****Wedbush PacGrow**

Prospectus Supplement dated November 17, 2022

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a “shelf” registration statement on Form S-3 (File No. 333-257640) that we filed with the Securities and Exchange Commission, or SEC, on July 2, 2021, and that was subsequently amended by Post-Effective Amendment No. 1 to the Registration Statement on Form S-3, filed on February 23, 2022, and Post-Effective Amendment No. 2 to the Registration Statement on Form S-3, filed on February 23, 2022 and declared effective by the SEC on May 3, 2022. This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, including the documents incorporated by reference therein, gives more general information, some of which does not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined.

If the description of the offering varies between this prospectus supplement and the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information contained in this prospectus supplement. However, 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 supplement or the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

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 prospectus supplement or 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.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering. Neither we nor the underwriters have authorized anyone to provide you with information different from that contained in this prospectus supplement, the accompanying prospectus or any accompanying free writing prospectus. We are offering to sell, and seeking offers to buy, common stock only in jurisdictions where offers and sales are permitted. If anyone provides you with different or inconsistent information, you should not rely on it. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. The information contained in this prospectus supplement, the accompanying prospectus and any accompanying free writing prospectus is accurate only as of the date of this prospectus supplement, the accompanying prospectus and any such accompanying free writing prospectus, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus, any such accompanying free writing prospectus or of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled “Where You Can Find More Information” and “Incorporation of Documents by Reference.”

No action is being taken in any jurisdiction outside the United States to permit a public offering of the common stock or possession or distribution of this prospectus supplement, the accompanying prospectus or any free writing prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement, the accompanying prospectus or any free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus

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supplement, the accompanying prospectus and any accompanying free writing prospectus applicable to that jurisdiction. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless we have indicated otherwise, or the context otherwise requires, references in this prospectus supplement and the accompanying prospectus to “G1,” “G1 Therapeutics,” “the Company,” “we,” “us” and “our” or similar terms are to G1 Therapeutics, Inc.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the “Risk Factors” section contained in this prospectus supplement, our consolidated financial statements and the related notes thereto and the other documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus and the information included in any free writing prospectus that we have authorized for use in connection with this offering.

Overview

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 product, COSELA[®] (trilaciclib), approved by the U.S. Food and Drug Administration, or FDA, on February 12, 2021, 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 myeloprotection in decades. In July 2022, COSELA (trilaciclib hydrochloride for injection) was conditionally approved by the China National Medical Products Administration (NMPA) for marketing in China. We are exploring the use of trilaciclib in a variety of trials across multiple tumor types and treatment combinations to optimize these potential benefits of proactive multi-lineage myeloprotection and survival in combination with leading and emerging treatments for patients globally.

We use “COSELA” when referring to our FDA approved drug and “trilaciclib” when referring to our development of COSELA for additional indications.

COSELA is a prescription medicine used to help reduce the occurrence of low blood cell counts caused by damage to bone marrow from chemotherapy. COSELA is used to treat adults taking certain chemotherapies (platinum/etoposide or topotecan) for extensive-stage small cell lung cancer (ES-SCLC).

COSELA is an injection for intravenous (IV) use given within four hours before chemotherapy.

Commercial Product



On February 12, 2021, COSELA was approved by the FDA to decrease the incidence of chemotherapy-induced myelosuppression in adult patients treated with a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC. COSELA became commercially available through our specialty distributor network on March 2, 2021.

We announced on March 25, 2021 that COSELA had been included in two updated National Comprehensive Cancer Network[®], or NCCN, Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]): The Treatment Guidelines for Small Cell Lung Cancer and the Supportive Care Guidelines for Hematopoietic Growth Factors. These guidelines document evidence-based, consensus-driven management to ensure that all patients receive preventive, diagnostic, treatment, and supportive services that are most likely to lead to optimal outcomes. The permanent J-code for COSELA that was issued in July 2021 by the Centers for Medicare & Medicaid Services (CMS) is now effective for provider billing for all sites of care. Our new technology add-on payment (NTAP) for

COSELA provides additional payment to inpatient hospitals above the standard Medicare Severity Diagnosis-Related Group (MS-DRG) payment amount.

We are also exploring potential use of trilaciclib in a variety of tumors, including colorectal cancer, or CRC, breast cancer, bladder cancer, and in trials designed to inform the design of future additional pivotal studies across multiple tumor types and treatment combinations including certain chemotherapies, checkpoint inhibitors, and targeted chemotherapy medicines called antibody-drug conjugates, or ADCs.

In December 2021, we announced that we would hire and deploy our own oncology sales team and we and Boehringer Ingelheim Pharmaceuticals, Inc. mutually agreed to end the co-promotion agreement for COSELA. As of February 2022, our sales team was hired, trained, and deployed.

On August 3, 2020, we entered into an exclusive license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd, or Simcere, for the development and commercialization of trilaciclib in all indications in Greater China (mainland China, Hong Kong, Macau and Taiwan). On July 13, 2022, the NMPA conditionally approved COSELA for marketing in China. As a result of receiving approval in China, Simcere paid the Company a \$13.0 million milestone (less applicable withholding taxes of \$1.3 million) payment in the third quarter of 2022. In total, we may receive up to \$156.0 million in milestone payments. We will also receive double-digit royalties on annual net sales of COSELA in China.

Product Portfolio

Trilaciclib is a first-in-class therapy designed to help protect against chemotherapy-induced myelosuppression. It is a novel transient IV CDK4/6 inhibitor has unique attributes including rapid onset from IV administration, potent and selective CDK4 and CDK6 inhibition and a short half-life. Controlled administration and clean G1-phase arrest reduce hematologic AEs caused by cytotoxic therapy and may increase patients' abilities to receive longer treatment durations. Transient CDK4/6 inhibition also modulates multiple immune functions, or immunomodulation, while allowing beneficial T cell proliferation which may improve patients' anti-tumor immune responses.

We are pursuing trilaciclib across key growth platforms. First, trilaciclib provides proactive multi-lineage myeloprotection by transiently arresting hematopoietic stem and progenitor cells, or HSPCs, helping to protect them from damage caused by cytotoxic therapy thereby minimizing cytopenias across neutrophils, erythrocytes, and platelets. These proactive multi-lineage myeloprotection benefits were seen in our three double-blind, placebo-controlled clinical trials in ES-SCLC, where highly myelosuppressive chemotherapy regimens are administered multiple days in a row. This myeloprotection benefit is being explored as the primary endpoint in our ongoing PRESERVE 1 pivotal Phase 3 trial in 1L CRC which is exploring the use of trilaciclib in combination with FOLFOXIRI, the most efficacious chemotherapy regimen in CRC but also the most myelosuppressive. If the myeloprotection data are positive, we will meet with regulatory authorities to discuss filing for approval in this indication.

Second, trilaciclib has the potential to improve survival in combination with leading and emerging treatments, as a result of (1) myeloprotection, thus enabling increased cytotoxic exposure while protecting the immune system, and/or (2) immunomodulation, thus improving overall immune response. Its ability to enhance the cancer immune cycle occurs through multiple factors, including (1) enhancing T cell activation, (2) favorably altering the tumor microenvironment, and (3) improving long-term immune surveillance. We are exploring this potential survival benefit in a variety of ongoing Phase 2 and Phase 3 clinical trials. A meaningful anti-tumor efficacy benefit was observed in our Phase 2 mTNBC study in which trilaciclib led to a significant improvement in overall survival when administered in combination with chemotherapy (gemcitabine/carboplatin) compared to chemotherapy alone. These are the foundational data for our ongoing PRESERVE 2 pivotal Phase 3 trial in 1L mTNBC.

We are executing on our tumor-agnostic strategy to evaluate the potential benefits of trilaciclib to patients with other tumors to continuously develop new data with trilaciclib in a variety of chemotherapeutic settings and in

combination with other agents to maximize the applicability of the drug to potential future treatment paradigms. We currently have five ongoing clinical trials: (i) a pivotal Phase 3 trial in 1L CRC, (ii) a pivotal Phase 3 trial in 1L mTNBC, (iii) a Phase 2 trial in 1L bladder cancer with chemotherapy induction and a checkpoint inhibitor maintenance, (iv) a Phase 2 trial in combination with an ADC in 2L/3L mTNBC, and (v) a Phase 2 trial in neoadjuvant TNBC designed to validate trilaciclib’s immune-based mechanism of action, or MOA. We are also conducting significant preclinical work to assess the additive/synergistic potential of trilaciclib with a variety of novel and emerging therapeutic agents to identify synergies to evaluate in future clinical trials. New non-clinical data presented in September 2022 showed consistent synergistic potential of trilaciclib to enhance the cancer immune cycle by enhancing T cell activation, favorably altering the tumor microenvironment, and improving long-term surveillance. Our overall development approach includes monitoring and anticipating the evolving future standards of care across tumor types to maximize future usage of trilaciclib across relevant treatment settings.

In November 2022, we provided encouraging initial data from our ongoing Phase 2 trial of trilaciclib in combination with the ADC, sacituzumab govitecan-hziy. Initial data demonstrate the potential for an on-target effect of trilaciclib to reduce (>50%) the rates of adverse events associated with sacituzumab govitecan-hziy, including myelosuppression, diarrhea, and potentially alopecia, due to the presence of CDK4/6-expressing cells in the intestinal crypt and hair follicles, compared to the previously published sacituzumab govitecan-hziy single agent safety profile. We expect to release a more comprehensive data set including safety and initial efficacy results at a medical meeting in the first half of 2023.

Trilaciclib Product Portfolio

<u>Candidate</u>	<u>Indication</u>	<u>Phase (Current Status)</u>	<u>Timing of Initial Results</u>	<u>Endpoints</u>	<u>Development & Commercialization Rights (all indications)</u>
trilaciclib	1L metastatic Colorectal cancer (CRC)	Phase 3 trial (Enrollment Completed)	1Q 2023	Primary: myeloprotection* Secondary: ORR, PFS/OS, PRO	G1 Therapeutics owns all global development and commercial rights across all indications, with the exception of Greater China (Simcere)
	1L metastatic Triple negative breast cancer (mTNBC)	Phase 3 trial (Enrollment Completed)	2H 2023	Primary: OS* Secondary: PRO, myeloprotection, PFS/ORR	
	1L Bladder cancer (mUC)	Phase 2 trial (Enrollment Completed)	4Q 2022	Primary: PFS Secondary: ORR, OS, safety*, others	
	Antibody-drug conjugate (ADC) combination trial in mTNBC	Phase 2 trial (Enrolling)	4Q 2022 - milestone achieved	Primary: PFS Secondary: ORR, OS, safety*, myeloprotection*, others	
	Mechanism of action trial in early stage neoadjuvant TNBC	Phase 2 trial (Enrollment Completed)	4Q 2022	Primary: Immune-based MOA* Secondary: pCR, immune response, others	

PFS=progression-free survival; OS=overall survival; PRO=patient reported outcome; ORR=overall response rate; pCR=pathological complete response; MOA=mechanism of action.

* Additional initial results expected: (i) Phase 3 colorectal cancer trial: myeloprotection and ORR endpoints; (ii) Phase 3 1L mTNBC trial: interim OS analysis; if the trial meets the interim analysis stopping rule, it will terminate and we will report the topline results. If it does not, the trial will continue to the final analysis; (iii) Phase 2 bladder cancer trial: ORR and preliminary safety data; (iv) Phase 2 trial to confirm the immune-based mechanism of action (MOA) of trilaciclib in early-stage neoadjuvant TNBC: immune endpoints (e.g., CD8+ / Treg ratio).

Lerociclib

Lerociclib is a differentiated clinical-stage oral CDK4/6 inhibitor being developed for use in combination with other targeted therapies in multiple oncology indications. In 2020, we entered into separate, exclusive agreements with EQRx, Inc. (rights for U.S., Europe, Japan and all markets outside Asia-Pacific) and Genor Biopharma Co. Inc. (rights for Asia-Pacific, excluding Japan) for the development and commercialization of lerociclib in all indications. Combined, these agreements provide \$26.0 million in upfront payments, along with sales-based royalties, and the opportunity for up to \$330.0 million in potential milestone payments. EQRx, Inc. and Genor Biopharma Co. Inc. are responsible for all costs related to the development and commercialization of lerociclib in their respective territories.

CDK2 Inhibitor

In 2020, we entered into a global license agreement with Incyclix Bio, LLC, or Incyclix, formerly ARC Therapeutics, LLC, for the development and commercialization of an internally discovered cyclin-dependent kinase 2, or CDK2, inhibitor for all human and veterinary uses. Incyclix is currently granted an exclusive, royalty-bearing, license with the right to grant sublicenses to one of our solely owned patent families.

Going Concern

In our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 as filed with the SEC on November 2, 2022, we disclosed that we had concluded that substantial doubt exists about our ability to continue as a going concern for a period of at least 12 months from the date of the filing of such Form 10-Q as our cash and cash equivalents and marketable securities at September 30, 2022 were not sufficient to fund our planned operations and remain in compliance with our financial covenants. In addition, until such time, if ever, we can generate substantial revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. There can be no assurances that we will be able to secure such additional financing if at all, or on terms that are satisfactory to us, and that it will be sufficient to meet our needs. In the event we are not successful in obtaining sufficient funding, this could force us to delay, limit, or reduce our product development, commercialization efforts or other operations, and could result in the default on our loan payable.

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,” our logo, “COSELA” and the COSELA 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 pursuant to this prospectus supplement	7,700,000 shares
Option to purchase additional shares	We have granted the underwriters an option, exercisable for a period of up to 30 days from the date of this prospectus supplement, to purchase up to 1,155,000 additional shares of our common stock at the offering price less the underwriting discount.
Common stock to be outstanding immediately after this offering	50,597,081 shares (or 51,752,081 shares if the underwriters elect to exercise in full their option to purchase additional shares from us).
Use of proceeds	<p>The net proceeds from this offering will be approximately \$46.75 million, or approximately \$53.80 million if the underwriters exercise their option to purchase additional shares in full, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.</p> <p>We intend to use the net proceeds from this offering to fund activities related to the commercialization of COSELA, 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. See “Use of Proceeds” on page S-13 of this prospectus supplement for a more complete description of the intended use of proceeds from this offering.</p>
Risk factors	Investing in our common stock involves a high degree of risk. See the information contained in or incorporated by reference under “Risk Factors” on page S-9 of this prospectus supplement, as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors that you should consider before buying shares of our common stock.
Nasdaq Global Select Market symbol	GTHX

The number of shares of our common stock to be outstanding after this offering is based on an aggregate of 42,897,081 shares of our common stock outstanding as of September 30, 2022. The number of shares outstanding as of September 30, 2022 excludes:

- 7,484,758 shares of our common stock issuable upon exercise of outstanding options as of September 30, 2022, at a weighted average exercise price of \$16.19 per share, of which 4,377,489 shares were vested as of such date;

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- 633,206 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2022;
- 1,630,159 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; and
- 651,850 shares of common stock reserved for future issuance under our G1 Therapeutics, Inc. Amended and Restated 2021 Inducement Equity Incentive Plan.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding stock options, no vesting of outstanding restricted stock units, and no new stock options or other types of awards are issued under our equity incentive plans, as described above, and no exercise by the underwriters of their option to purchase additional shares of our common stock.

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 section 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 and Current Reports on Form 8-K, which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference, 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 operation 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. The risks below and incorporated by reference in this prospectus supplement and the accompanying prospectus are not the only ones we face. Additional risks not currently known to us or that we currently deem immaterial may also affect our business operations. Please also read carefully the section below titled “Special Note Regarding 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 us.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered is substantially higher than the book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. After giving effect to the sale by us of shares of common stock in this offering, and based on the public offering price of \$6.50 per share in this offering, and less the estimated underwriting discounts and commissions and estimated offering expenses payable by us, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$4.67 per share in the net tangible book value of our common stock. If the underwriters exercise their option to purchase additional shares you will also experience dilution. See the “Dilution” section on page S-14 for a more detailed discussion of the dilution you will incur in connection with this offering.

In addition, we have a significant number of stock options. To the extent that outstanding stock options have been or may be exercised, or other securities are issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders or result in downward pressure on the price of our common stock.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We,

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our directors and our executive officers have agreed not to sell, dispose of or hedge any common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through and including the date 90 days after the date of this prospectus supplement, subject to certain exceptions. The underwriters may, in their discretion, release the restrictions on any such shares at any time without notice. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents we have filed with the SEC that are incorporated by reference include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act of 1934, as amended, or the Exchanges 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 supplement, the accompanying prospectus and the documents incorporated by reference, 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 supplement, the accompanying prospectus and the documents or reports incorporated by reference, discuss some of the factors that could contribute to these differences. These forward-looking statements include, among other things, statements about:

- our history of losses;
- our ability to continue as a going concern;
- our dependence on the commercial success of COSELA;
- the therapeutic potential of COSELA;
- our ability to generate data to maximize trilaciclib’s applicability to future treatment paradigms;
- 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;

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- 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;
- the potential impacts of the COVID-19 pandemic, inflation and increased interest rates on our business operations or financial condition; 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 supplement, the accompanying prospectus and the documents incorporated by reference, 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 supplement, as updated and supplemented by the discussion of risks and uncertainties under “Risk Factors” contained in the accompanying 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 supplement, the accompanying prospectus and the documents 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 supplement, the accompanying prospectus or the documents incorporated by reference. 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

The net proceeds we will receive from this offering will be approximately \$46.75 million, or approximately \$53.80 million if the underwriters exercise their option to purchase additional shares in full, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to fund activities related to the commercialization of COSELA, 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 supplement 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.

DILUTION

If you invest in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share after giving effect to this offering. We calculate net tangible book value per share by dividing the net tangible book value, which is tangible assets less total liabilities, by 42,897,081, the number of outstanding shares of our common stock as of September 30, 2022. Dilution represents the difference between the amount per share paid by purchasers of shares in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. Our net tangible book value as of September 30, 2022 was approximately \$46.0 million, or \$1.07 per share.

After giving effect to the sale of 7,700,000 shares of common stock by us at the public offering price of \$6.50 per share, less the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of September 30, 2022 would have been \$92.7 million, or \$1.83 per share of common stock. This amount represents an immediate increase in the as adjusted net tangible book value of \$0.76 per share of common stock to our existing shareholders and an immediate dilution in net tangible book value of \$4.67 per share of common stock to new investors. We determine dilution by subtracting the net tangible book value per share after the offering from the amount of cash that a new investor paid for a share of common stock.

The following table illustrates this dilution on a per share basis:

Public offering price per share		\$6.50
Net tangible book value per share as of September 30, 2022	\$1.07	
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering	\$0.76	
As adjusted net tangible book value per share as of September 30, 2022 after this offering		\$1.83
Dilution per share to new investors purchasing shares in this offering		\$4.67

If the underwriters exercise their option to purchase 1,155,000 additional shares of our common stock in full at the public offering price of \$6.50 per share, the as adjusted net tangible book value would increase to approximately \$99.8 million, or \$1.93 per share, representing an increase in net tangible book value per share to existing shareholders of approximately \$0.86 per share, and there would be an immediate dilution in net tangible book value of approximately \$4.57 per share to new investors.

The number of shares of our common stock to be outstanding after this offering is based on an aggregate 42,897,081 shares of our common stock outstanding as of September 30, 2022. The number of shares outstanding as of September 30, 2022 excludes:

- 7,484,758 shares of our common stock issuable upon exercise of outstanding options as of September 30, 2022, at a weighted average exercise price of \$16.19 per share, of which 4,377,489 shares were vested as of such date;
- 633,206 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2022;
- 1,630,159 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; and
- 651,805 shares of common stock reserved for future issuance under our G1 Therapeutics, Inc. Amended and Restated 2021 Inducement Equity Incentive Plan.

To the extent that any options are exercised, new options are issued or we otherwise issue additional shares of common stock in the future at a price less than the public offering price, there may be further dilution to purchasers of our common stock in this offering.

DIVIDEND POLICY

We have never paid or declared 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 and we do not anticipate paying any cash dividends in the foreseeable future. In addition, the terms of our loan and security agreement with Hercules Capital, Inc. prohibit us from paying cash dividends. Any future determination to pay cash dividends will be at the discretion of our Board of Directors and will depend on our financial condition, operating results, restrictions in the agreements governing any indebtedness we may enter into, capital requirements and such other factors as our Board of Directors deems relevant.

UNDERWRITING

We are offering the shares of common stock described in this prospectus supplement through a number of underwriters. Cowen and Company, LLC and Raymond James & Associates, Inc. are acting as representatives of the underwriters named below. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

<u>Name</u>	<u>Number of shares</u>
Cowen and Company, LLC	3,850,000
Raymond James & Associates, Inc.	2,310,000
Needham & Company, LLC	770,000
Wedbush Securities Inc.	770,000
Total	7,700,000

Fredric N. Eshelman, a former member of our board of directors and a greater than 5% stockholder of our company, has indicated an interest in purchasing an aggregate of up to approximately \$7.0 million of our common stock in this offering at the public offering price per share and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares of common stock to Mr. Eshelman, and Mr. Eshelman could determine to purchase more, fewer or no shares of common stock in this offering.

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the option to purchase additional shares described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares

We have granted to the underwriters an option to purchase up to 1,155,000 additional shares of common stock at the public offering price, less the underwriting discounts and commissions. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and Commissions.

The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	<u>Without option to purchase additional shares exercise</u>	<u>With full option to purchase additional shares exercise</u>
Per Share	\$ 0.39	\$ 0.39
Total	\$ 3,003,000	\$ 3,453,450

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We estimate that our total expenses of this offering, including filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$300,000. We have agreed to reimburse the underwriters for certain of their expenses, as set forth in the underwriting agreement, including an amount of up to \$50,000, that may be incurred in connection with the review by the Financial Industry Regulatory Authority of the terms of the offering.

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus supplement. The underwriters may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of \$0.234 per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Discretionary Accounts

The underwriters do not intend to confirm sales of the shares to any accounts over which they have discretionary authority.

Stabilization

In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in the option to purchase additional shares. The underwriters may close out any short position by exercising their option to purchase additional shares and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the option to purchase additional shares. If the underwriters sell more shares than could be covered by exercise of the option to purchase additional shares and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.

Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock.

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These transactions may be effected on the Nasdaq Stock Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making.

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934, as amended, during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements

We have agreed that we will not, directly or indirectly, (i) offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of, or announce the intention to otherwise dispose of, any shares of our common stock (including, without limitation, common stock which may be deemed to be beneficially owned by us in accordance with the rules and regulations promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act) or securities convertible into or exercisable or exchangeable for our common stock, or (ii) enter into any swap, hedge, or similar agreement or other arrangement that transfers in whole or in part, the economic risk of ownership of any shares of common stock or any such other securities, or (iii) engage in any short selling of our common stock or securities convertible into or exercisable or exchangeable for our common stock, in each case without the prior written consent of the Representatives for a period of 90 days, or 30 days, in the case of our existing at-the-market offering program, after the date of this prospectus supplement.

We have agreed that, subject to certain conditions, the foregoing restrictions shall not apply to:

(i) the shares of our common stock to be sold in this offering;

(ii) any shares of our common stock and options to purchase our common stock, shares of common stock underlying options granted and other securities, each issued pursuant to any director or employee stock option plan, stock ownership plan or dividend reinvestment plan of the Company;

(i) any shares of our common stock issued pursuant to the conversion of securities or the exercise of warrants;

(ii) adoption of a new equity incentive plan, and filing a registration statement on Form S-8 under the Securities Act to register the offer and sale of securities to be issued pursuant to such new equity incentive plan, subject to certain limitations;

(iii) any options and awards granted under an equity incentive plan described in this prospectus supplement, provided that the recipient executes a lock-up agreement for the remainder of the 90-day period referred to above; or

(iv) issuances of our common stock or securities convertible or exchangeable for shares of common stock in connection with any acquisition, collaboration, licensing or other strategic transaction (but excluding transactions principally of a financing nature); subject to certain limitations.

Our directors and executive officers have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 90 days after the date of this prospectus supplement, may not, without the prior written consent of the Representatives, directly or indirectly, (i) offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of, or announce the intention to otherwise dispose of, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock which may be deemed to be beneficially owned by each such director, executive officer and stockholder in

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accordance with the rules and regulations promulgated under the Exchange Act) or securities convertible into or exercisable or exchangeable for our common stock or (ii) enter into any swap, hedge or similar agreement or arrangement that transfers in whole or in part, the economic risk of ownership of the common stock or securities convertible into or exercisable or exchangeable for our common stock, or (iii) engage in any short selling of our common stock or securities convertible into or exercisable or exchangeable for our common stock.

Each such director and executive officer has agreed that, subject to certain conditions, the foregoing restrictions shall not apply to any shares of our common stock purchased in this offering or in the public market following this offering, or in the case of the following exceptions:

- (i) transfers made as a bona fide gift to an immediate family member, to a trust the beneficiaries of which are exclusively the locked-up party or the locked-up party's immediate family member, or to a charity or educational institution; each of which is subject to certain conditions set forth in the lock-up agreement;
- (ii) transfers made by will or intestate succession upon the death of the locked-up party; each of which is subject to certain conditions set forth in the lock-up agreement;
- (iv) if the locked-up party is a corporation, partnership, limited liability company or other business entity, transfers made by the locked-up party in connection with the sale of all or substantially all of its assets or equity interests;
- (v) if the locked-up party is a corporation, partnership, limited liability company or other business entity, transfers not for value to an affiliate of the locked-up party; each of which is subject to certain conditions set forth in the lock-up agreement;
- (vi) the locked-up party's net exercise or cashless exercise of our options or warrants;
- (vii) transfers or sales of shares made by a locked-up party to satisfy tax withholding obligations in connection with our equity incentive plans or other arrangements disclosed in this prospectus supplement;
- (viii) the establishment of a trading plan in accordance with Rule 10b5-1(c) under the Exchange Act;
- (ix) transactions made pursuant to a trading plan in effect as of the date of the lock-up agreement in accordance with Rule 10b5-1(c) under the Exchange Act;
- (x) sales of shares acquired in this offering or in open market transactions after this offering so long as no public announcement or filing under Section 16(a) of the Exchange Act shall be required or voluntarily made;
- (xi) transfers made through the operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement; or
- (xii) transfers, sales, tenders or other dispositions of our common stock pursuant to a tender offer for our securities or any other transaction, including, without limitation, consolidation or other business combination, involving a change of control that has been approved by our board of directors.

Electronic Offer, Sale and Distribution of Shares.

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Selling restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement and the accompanying prospectus may not be offered or sold, directly or indirectly, nor may this prospectus supplement and the accompanying prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction.

Persons into whose possession this prospectus supplement and the accompanying prospectus come are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Notice to prospective investors in Canada

The common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to prospective investors in the European Economic Area

In relation to each Member State of the European Economic Area, each, a "Member State," no shares have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the competent authority in that Member State, all in accordance with the Prospectus Regulation, except that shares may be offered to the public in that Member State at any time:

- A. to any legal entity which is a qualified investor as defined under Article 2 the Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 the Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- C. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

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provided that no such offer of the shares shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an “offer to the public” in relation to shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Notice to prospective investors in the United Kingdom

No shares have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the shares which has been approved by the Financial Conduct Authority, except that the shares may be offered to the public in the United Kingdom at any time:

- A. to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- C. in any other circumstances falling within Section 86 of the FSMA,

provided that no such offer of the shares shall require the Issuer or any Manager to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an “offer to the public” in relation to the shares in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Notice to prospective investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (the “SFO”) of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong) (the “CO”), or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Notice to prospective investors in Singapore

Each underwriter has acknowledged that this prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each underwriter has represented and agreed that it has not offered or sold any shares or caused the shares to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares or cause the shares to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus or

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any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares, whether directly or indirectly, to any person in Singapore other than:

- A. to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the “SFA”)) pursuant to Section 274 of the SFA;
- B. to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or
- C. otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- A. a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- B. a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries’ rights and interest (however described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- (i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- (ii) where no consideration is or will be given for the transfer;
- (iii) where the transfer is by operation of law;
- (iv) as specified in Section 276(7) of the SFA; or
- (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of shares, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the shares are “prescribed capital markets products” (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Notice to prospective investors in United Arab Emirates

This document has not been reviewed, approved or licensed by the Central Bank of the United Arab Emirates, or UAE, Emirates Securities and Commodities Authority or any other relevant licensing authority in the UAE including any licensing authority incorporated under the laws and regulations of any of the free zones established and operating in the territory of the UAE, in particular the Dubai International Financial Services Authority, or DFSA, a regulatory authority of the Dubai International Financial Centre, or DIFC. The issue of shares of common stock does not constitute a public offer of securities in the UAE, DIFC and/or any other free zone in accordance with the Commercial Companies law, Federal Law No. 8 of 1984 (as amended), DFSA Offered Securities Rules and the Dubai International Financial Exchange Listing Rules, accordingly or otherwise.

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The shares may not be offered to the public in the UAE and/or any of the free zones including, in particular, the DIFC. The shares may be offered and this document may be issued, only to a limited number of investors in the UAE or any of its free zones (including, in particular, the DIFC) who qualify as sophisticated investors under the relevant laws and regulations of the UAE or the free zone concerned. Management of the company and the representatives of the underwriters represent and warrant the shares will not be offered, sold, transferred or delivered to the public in the UAE or any of its free zones.

Notice to prospective investors in Israel

In the State of Israel this prospectus supplement shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 – 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728–1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the “Addressed Investors”); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 – 1968, subject to certain conditions (the “Qualified Investors”). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 – 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 – 1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 – 1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 – 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 – 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor’s name, address and passport number or Israeli identification number.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of shares on our behalf or on behalf of the underwriters.

Other relationships

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

LEGAL MATTERS

The validity of the issuance of the shares of common stock offered by us in this offering will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts. DLA Piper LLP (US), Raleigh, North Carolina, will act as counsel to the underwriters 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 Supplement 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 also available at the SEC's website at <http://www.sec.gov>.

This prospectus supplement and the accompanying prospectus are 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 omit certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus supplement, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You can obtain a copy of the registration statement from the SEC's website.

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 supplement, 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 supplement. This prospectus supplement 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 supplement. Statements in this prospectus supplement 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, are available at the SEC's web site at <http://www.sec.gov>. The documents we are incorporating by reference are:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021 filed on February 23, 2022;
- our Quarterly Reports on Form 10-Q (i) for the quarter ended [March 31, 2022](#) filed on May 4, 2022, (ii) for the quarter ended [June 30, 2022](#) filed on August 3, 2022, and (iii) for the quarter ended [September 30, 2022](#) filed on November 2, 2022;
- our Current Reports on Form 8-K filed on [June 24, 2022](#), [June 28, 2022](#), [July 27, 2022](#), and [November 2, 2022](#) (with respect to Item 8.01 and Exhibit 99.2 of Item 9.01 only);

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- the portions of our [Proxy Statement](#) for the annual meeting of shareholders held on June 23, 2022, as filed on April 28, 2022, that are considered to be filed and not furnished;
- 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.

Any statement contained in this prospectus supplement or the accompanying prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement or in the accompanying prospectus will be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement or the accompanying prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus supplement or the accompanying 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 supplement or the accompanying 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 supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

You should rely only on information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus supplement or the accompanying prospectus or incorporated by reference in this prospectus supplement or the accompanying 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.

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 May 3, 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.

7,700,000 Shares



Common stock

Prospectus supplement

Joint Book-Running Managers

Cowen

Raymond James

Lead Managers

Needham & Company

Wedbush PacGrow

November 17, 2022
