Filed Pursuant to Rule 424(b)(5)
Registration No. 333-222268

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED DECEMBER 9, 2020

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated January 5, 2018)

Shares

Common Stock

We are offering shares of our common stock. Our common stock is listed on The Nasdaq Capital Market under the symbol "ONCT." On December 8, 2020, the last reported sale price of our common stock on The Nasdaq Capital Market was $5.08 per share.

The underwriter may offer the shares of common stock from time to time to purchasers directly or through agents, or through brokers in brokerage transactions on The Nasdaq Capital Market, or to dealers in negotiated transactions or in a combination of such methods of sale, or otherwise, at fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to such prevailing market prices.

Investing in our common stock involves risks. See "Risk Factors" beginning on page S-7 of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions (1)	$	$
Proceeds, before expenses, to us	$	$

(1) See the section entitled "Underwriting" for additional disclosure regarding underwriting compensation and estimated offering expenses.

We have granted the underwriter an option for a period of 30 days to purchase up to an additional shares of our common stock on the same terms as set forth above. If the underwriter exercises its option in full, the total underwriting discounts and commissions payable by us will be $, and the total proceeds to us, before estimated offering expenses, will be $.

The underwriter expects to deliver shares of common stock to purchasers on , 2020.

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.

H.C. Wainwright & Co.

The date of this prospectus supplement is , 2020

TABLE OF CONTENTS

Neither we have nor the underwriter has authorized anyone to provide information different from that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus we have authorized for use in connection with this offering. When you make a decision about whether to invest in our common stock, you should not rely upon any information other than the information in this prospectus supplement, the accompanying prospectus or any such free writing prospectus. Neither the delivery of this prospectus supplement nor the sale of shares of our common stock means that information contained in this prospectus supplement is correct after the date of this prospectus supplement. This prospectus supplement is not an offer to sell or solicitation of an offer to buy shares of our common stock in any circumstances under which the offer or solicitation is unlawful.

About This Prospectus Supplement

This prospectus supplement and the accompanying prospectus dated January 5, 2018, are part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. This prospectus supplement and the accompanying prospectus relate to the offer by us of shares of our common stock to certain investors. We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this "prospectus," we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on 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 as our business, financial condition, results of operations and prospects may have changed since the earlier dates. You should read this prospectus supplement, the accompanying prospectus, the documents and information 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 when making your investment decision. You should also read and consider the information in the documents we have referred you to under the heading "Where You Can Find More Information; Information Incorporated by Reference."

You should rely only on information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not, and the underwriter has not, authorized anyone to provide you with information that is different. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement, the accompanying prospectus, the documents and information 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 are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock.

In this prospectus supplement, unless the context otherwise indicates, the terms "Oncternal," the "Company," "we," "our" and "us" or similar terms refer to Oncternal Therapeutics, Inc., including its consolidated subsidiaries.

We use our registered trademarks, Oncternal and the Oncternal logo in this prospectus. All other trademarks, trade names and service marks appearing in this prospectus or the documents incorporated by reference herein are the property of their respective owners. Use or display by us of other parties' trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owner. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

Prospectus Supplement Summary

The items in the following summary are described in more detail later in this prospectus supplement and in the accompanying prospectus. This summary provides an overview of selected information and does not contain all the information you should consider before investing in our common stock. Therefore, you should read the entire prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the "Risk Factors" section, and other documents or information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before making any investment decision.

Oncternal Therapeutics, Inc.

We are a clinical-stage biopharmaceutical company focused on the development of novel oncology therapies for cancers with critical unmet medical need. Our development efforts are focused on promising, yet untapped, biological pathways implicated in cancer generation or progression. Our pipeline includes cirmtuzumab, an investigational monoclonal antibody that is designed to inhibit Receptor tyrosine kinase-like Orphan Receptor 1, or ROR1, a growth factor receptor that is widely expressed on many tumors and that activates pathways leading to increased tumor proliferation, invasiveness and drug resistance. Cirmtuzumab is being evaluated in a Phase 1/2 clinical trial in combination with ibrutinib (Imbruvica®) (Cirmtuzumab and Ibrutinib targeting ROR1 for Leukemia and Lymphoma, or CIRLL) for the treatment of patients with B-cell lymphoid malignancies, including mantle cell lymphoma, or MCL, and chronic lymphocytic leukemia, or CLL, and in an investigator-sponsored, Phase 1b clinical trial in combination with paclitaxel for the treatment of women with HER2-negative metastatic or locally advanced, unresectable breast cancer. We are also developing TK216, an investigational small molecule that is designed to inhibit the ETS, or E26 Transformation Specific, family of oncoproteins. ETS alterations have been shown in preclinical studies to alter gene transcription and RNA processing and lead to increased cell proliferation and invasion. TK216 is being evaluated in a Phase 1 clinical trial as a single agent and in combination with vincristine in patients with relapsed or refractory Ewing sarcoma, a rare pediatric cancer. In addition, we are developing a chimeric antigen receptor T cell, or CAR-T, therapy candidate that targets ROR1, which is currently in preclinical development as a potential treatment for hematologic cancers and solid tumors. The U.S Food and Drug Administration, or FDA, has granted orphan drug designations for cirmtuzumab for the treatment of MCL and for the treatment of CLL/small lymphocytic lymphoma, and has granted rare pediatric disease designation, orphan drug designation and fast track status for TK216 for the treatment of Ewing sarcoma.

Cirmtuzumab is an investigational, humanized, potentially first-in-class, anti-ROR1 monoclonal antibody that is designed to bind to a specific functionally important epitope of ROR1. ROR1, which is a protein expressed on many tumors, is a potentially attractive target for cancer therapy because it is an onco-embryonic antigen, which is a protein typically expressed only during embryogenesis that may confer a survival and fitness advantage when reactivated and expressed by tumor cells. ROR1 overexpression in various tumor types, including MCL, CLL and breast cancer, has been associated with more aggressive disease, resistance to therapy and shorter progression-free and overall survival. In preclinical models, inhibition of ROR1 has shown anti-tumor activity, and we believe may have additive or synergistic effects when combined with either targeted therapy or chemotherapy. Preclinical data indicated that when cirmtuzumab bound to ROR1, it blocked growth factor Wnt5a signaling, inhibited tumor cell proliferation, migration and survival, and induced differentiation of CLL tumor cells. Cirmtuzumab was developed in the laboratory of one of our scientific advisors, Professor Thomas Kipps, M.D., Ph.D., Professor of Medicine and Evelyn and Edwin Tasch Chair in Cancer Research at the University of California San Diego, or UC San Diego, with support from the California Institute for Regenerative Medicine, or CIRM. We have an exclusive license to cirmtuzumab for therapeutic uses from UC San Diego.

On June 30, 2020, we announced an updated clinical strategy for cirmtuzumab that prioritizes development in MCL, based on encouraging interim clinical results from the CIRLL Phase 1/2 clinical trial that were presented

at the American Society of Clinical Oncology 2020 Virtual Annual Meeting, or ASCO, in May 2020. As a result, we are amending the CIRLL study to increase the number of patients with relapsed/refractory MCL to be enrolled in the Phase 2 expansion cohort to at least 20 patients and to allow the enrollment of patients with a broader range of prior Bruton's tyrosine kinase inhibitor treatments. In addition, we have limited the total enrollment of CLL patients in the CIRLL study to approximately 30 patients, in order to focus resources on the MCL portion of the study. In September 2020, we met with the FDA and are in a dialogue with the FDA regarding potential accelerated approval pathways for cirmtuzumab plus ibrutinib in patients with relapsed/refractory MCL.

On December 7, 2020, we presented updated interim data from the CIRLL trial in patients with MCL and CLL at the American Society for Hematology 2020 Virtual Meeting. As of the data cut-off date of October 30, 2020, 15 patients with relapsed/refractory MCL enrolled in the dose-finding and dose-expansion cohorts of this clinical trial were evaluable for efficacy. The overall best objective response rate, or ORR, was 87% (13 of 15 evaluable patients), improved over the 83% ORR reported at the ASCO annual meeting. The complete response, CR, rate, determined by Cheson criteria, remains 57% (7 of 12 evaluable patients) for Part 1 of the study, and is 47% (7 of 15 evaluable patients) for Part 1 + Part 2, including the three patients from Part 2 who have shorter follow up. One of the seven patients had a complete metabolic response as assessed by PET scan, with an indeterminate bone marrow biopsy on blinded review. All complete responses remained durable, ranging from 5-25 months as of the cutoff date, with no progressions reported after achieving a CR. Six patients (40%) achieved a partial response, or PR. In addition, two patients had stable disease, or SD, for a total best clinical benefit rate (CR, PR and SD) of 100%. Median progression-free survival, or PFS, was not reached, with the 95% confidence interval above 17.5 months, after a median follow-up of 12.1 months. Patients had received a median of two prior therapies (range 1-5) before participating in this clinical trial, with 73% of patients with two or more prior lines of therapy. Four patients had received prior treatment with ibrutinib and all four achieved clinical responses in this clinical trial, with two CRs and two PRs. Fourteen of the 15 evaluable patients (93%) had high or intermediate MCL International Prognostic Index (MIPI-b) risk score at study entry. Historical data published for single-agent ibrutinib for 370 patients with relapsed/refractory MCL, who had received a median of two prior therapies, reported an ORR of 66%, CR rate of 20%, PR rate of 46%, and median PFS of 12.8 months (Rule et al., 2017, *British Journal of Haematology*).

Additionally, as of the data cut-off date on October 30, 2020, 56 evaluable patients with CLL were enrolled in the dose-finding, dose-confirming and randomized cohorts of this clinical trial, 49 of whom were treated with the combination of cirmtuzumab and ibrutinib. Forty-five of the 49 patients achieved a clinical response, for an overall best objective response rate of 92%, including one patient who achieved a CR. In addition, four patients had stable disease, for a total clinical benefit rate (CR, PR, and SD) of 100%. The median PFS was not reached for patients with treatment-naïve CLL (n=19) after a median follow-up of 16.6 months, and median PFS was 29.5 months for patients with relapsed/refractory CLL (n=30) after a median follow-up of 17.1 months. The combination of cirmtuzumab plus ibrutinib has been well tolerated, with adverse events consistent with those reported for ibrutinib alone. There have been no dose-limiting toxicities and no serious adverse events attributed to cirmtuzumab alone.

Cirmtuzumab is also being evaluated in an investigator-sponsored, Phase 1b clinical trial in combination with paclitaxel in patients with HER2 negative breast cancer. We expect to announce data from this Phase 1b clinical trial at a scientific conference in the first half of 2021. Additionally, we plan to further explore clinical combination strategies for cirmtuzumab for patients with hematologic malignancies. For example, we are supporting a new investigator-sponsored Phase 2 clinical trial of cirmtuzumab in combination with venetoclax, a Bcl-2 inhibitor, in patients with relapsed/refractory CLL in collaboration with UC San Diego. We also continue to evaluate the use of cirmtuzumab in additional ROR1-expressing tumors and expect to complete additional preclinical studies by the first half of 2021.

TK216 is an investigational, potentially first-in-class, targeted small molecule that is designed to specifically inhibit the biological activity of the ETS family of oncoproteins. Tumorigenic gene fusions involving ETS factors are frequently found in tumors such as Ewing sarcoma and prostate cancer, and ETS factors are often overexpressed in other tumors, such as acute myeloid leukemia, or AML, and diffuse large B cell lymphoma, or DLBCL. Researchers in the laboratory of Professor Jeffrey Toretsky, M.D., at Georgetown Lombardi Comprehensive Cancer Center, identified the precursor to TK216 using a novel chemical screening assay they developed based on a deep understanding of the underlying biological mechanism of ETS factors. Following this early work, TK216, which is designed to be a specific inhibitor of ETS factors, was created by us through the rational design and screening of novel small molecule inhibitors of a critical protein-protein interaction. In preclinical models, TK216 inhibited the interaction between ETS family members and RNA helicase A, or RHA, and by doing so, shut down excessive cell proliferation. We own intellectual property related to TK216 and have an exclusive license to product candidates targeting ETS oncoproteins for therapeutic, diagnostic or research tool purposes from Georgetown University.

We are evaluating TK216 as a single agent and in combination with vincristine in an open-label, multicenter Phase 1 clinical trial in patients with relapsed/refractory Ewing sarcoma. The dose-finding portion of the study was completed in 2019, and we continue to enroll patients in an expansion cohort to evaluate the clinical response of treatment with TK216 in combination with vincristine using the recommended Phase 2 dosing, or RP2D, regimen. The RP2D has been established to be 200 mg/m2/day of TK216 for 14 days, with vincristine dosed at 0.75 mg/m2 on the first day of each treatment cycle. In November 2020, we announced updated interim clinical data from our ongoing open-label, multicenter Phase 1 clinical trial evaluating TK216 in patients with relapsed or refractory Ewing sarcoma. The objectives of the clinical trial include the evaluation of safety, tolerability, pharmacokinetics, and tumor response. Patients entering the trial had previously been treated with a median of three, and as many as eight prior lines of systemic therapy. The presentation included interim data for 50 evaluable patients, including 23 evaluable patients treated at the RP2D as of the October 16, 2020 efficacy cut-off date. Two of the 23 patients treated at the RP2D (9%) achieved a CR, including one surgical CR. Both patients achieving CRs remain on treatment, with no evidence of disease. The first patient has been on treatment in this clinical trial for over 1.5 years and the second patient for over 8 months. The best ORR was 9%. Eight additional patients treated at the RP2D had SD, for a disease control rate (CR, partial response or SD) of 43%. The median progression-free survival for patients treated at the RP2D was 1.8 months.

TK216 has been generally well tolerated in this trial. As of the October 2, 2020 safety cutoff date, the most common drug-related adverse events included myelosuppression, fatigue, alopecia, nausea, pyrexia, and decreased appetite. Dose limiting toxicities consisted of transient and manageable myelosuppression, primarily neutropenia. No unexpected off-target toxicities have been observed.

Pharmacokinetic data from the clinical trial showed that TK216 drug levels at the RP2D exceeded plasma levels associated with anti-tumor activity in preclinical models.

We are also developing a ROR1-targeted CAR-T therapy utilizing the binding domain of cirmtuzumab as a single-chain variable fragment, or scFv, as a potential treatment for patients with aggressive hematological malignancies or solid tumors. Because cirmtuzumab has been shown to bind to multiple cancers but not to normal adult tissues in preclinical studies, we believe that a cirmtuzumab-based CAR-T may be selective in distinguishing cancer from normal tissues. Our ROR1-targeted CAR-T therapy candidate is in preclinical development in collaboration with UC San Diego, supported by funding from CIRM, and with Shanghai Pharmaceuticals Holding Co., Ltd., or SPH, in China. We expect the first-in-human dosing of our ROR1-targeted CAR-T therapy in China in 2021.

Pipeline

The following figure summarizes our current programs:

Business Update Regarding COVID-19

The COVID-19 worldwide pandemic has presented substantial public health and economic challenges and is affecting economies, financial markets and business operations around the world. International and U.S. governmental authorities in impacted regions are taking action in an effort to slow the spread of COVID-19, including issuing and modifying varying forms of "stay-at-home" orders, and restricting business functions outside of one's home. In response, we have put restrictions on employee travel and working from our executive offices, with many employees continuing their work remotely. To date, we have been able to continue to supply cirmtuzumab and TK216 clinical trial sites for patients enrolled in our ongoing clinical trials and do not currently anticipate any interruptions in the supply of cirmtuzumab or TK216. While we are continuing the clinical trials we have underway in sites across the U.S., we expect that COVID-19 precautions may directly or indirectly impact the timeline for some of our clinical trials. For example, some of our clinical trial sites, including those located in areas severely impacted by the pandemic, have placed new patient enrollment into clinical trials on hold or, for patients travelling from out-of-state, have implemented a 14-day self-quarantine before appointments. Patients with MCL or CLL may be at increased risk of severe disease if they develop COVID-19 because of advanced age and/or immunosuppression, and so may be unwilling to travel to our study centers to enroll in our clinical trials. For our existing patients, we are actively working with all of our clinical trial sites to minimize disruptions and address concerns on an individual site or patient basis in order to allow participating patients to continue to receive treatment at home or in alternative healthcare settings while minimizing their potential exposure to the virus that causes COVID-19. If restrictions related to the COVID-19 pandemic continue for a prolonged period of time or if additional clinical trial sites pause patient enrollment or treatments, our clinical trial milestones would be negatively impacted. Additionally, our expectations for the timing of first-in-human dosing of our ROR1 CAR-T therapy in China has been delayed. Any delays in the completion of our clinical trials and any disruption in our supply chain could have a material adverse effect on our business, results of operations and financial condition. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition, will depend on future developments

that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain or treat it, as well as the economic impact on local, regional, national and international markets.

Corporate Information

We were incorporated under the name Genotherapeutics, Inc. in Tennessee in September 1997. We changed our name to GTx, Inc. in 2001 and reincorporated in Delaware in 2003. On March 6, 2019, we, then operating as GTx, Inc., entered into an Agreement and Plan of Merger and Reorganization, as amended, or the Merger Agreement, with privately-held Oncternal Therapeutics, Inc., or Private Oncternal, and Grizzly Merger Sub, Inc., our wholly-owned subsidiary, or Merger Sub. Under the Merger Agreement, Merger Sub merged with and into Private Oncternal, with Private Oncternal surviving as our wholly-owned subsidiary, or the Merger. On June 7, 2019, the Merger was completed and GTx, Inc. changed its name to Oncternal Therapeutics, Inc. Private Oncternal, which remains as our wholly-owned subsidiary, changed its name to Oncternal Oncology, Inc. On June 10, 2019, the combined company's common stock began trading on The Nasdaq Capital Market under the ticker symbol "ONCT."

Our principal executive offices are located at 12230 El Camino Real, Suite 300, San Diego, CA 92130, and our telephone number is (858) 434-1113. Our website address is www.oncternal.com. The information on, or accessible through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

The Offering

Common stock offered by us	shares.
Common stock to be outstanding after this offering	shares (or shares if the underwriter exercises in full its option to purchase additional shares).
Option to purchase additional shares	We have granted the underwriter an option to purchase up to an additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes, including expenses related to the clinical and preclinical development of cirmtuzumab and TK216, preclinical development of our ROR1 CAR-T program, and for working capital. See "Use of Proceeds."
Risk factors	You should read the "Risk Factors" section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to invest in our common stock.
Nasdaq Capital Market symbol	ONCT

The number of shares of common stock to be outstanding after this offering is based on 22,346,766 shares outstanding as of September 30, 2020, and excludes as of that date:

- 3,521,438 shares of common stock issuable upon the exercise of outstanding warrants with a weighted average exercise price of $10.96 per share;
- 2,340,939 shares of common stock issuable upon the exercise of outstanding stock options with a weighted average exercise price of $7.73 per share; and
- 842,837 shares of common stock reserved for future issuance under our 2019 Incentive Award Plan.

In addition, the number of shares of our common stock to be outstanding after this offering excludes the following securities issued subsequent to September 30, 2020:

- 7,258,065 shares of common stock issued on November 20, 2020, at a price per share of $3.10; and
- 435,484 shares of our common stock issuable upon exercise of warrants issued on November 20, 2020.

In addition, the number of shares of our common stock to be outstanding after this offering excludes shares (or if the underwriter exercises its option to purchase additional shares in full) of common stock issuable upon exercise of warrants to be issued to the underwriter with an exercise price of $ per share, as described in "Underwriting."

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriter of its option to purchase up to an additional shares of our common stock or the warrants to be issued to the underwriter as compensation in connection with this offering.

Risk Factors

You should consider carefully the risks described below and discussed under the section captioned "Risk Factors" contained in our annual report on Form 10-K for the year ended December 31, 2019, as supplemented by our subsequent Quarterly Reports on Form 10-Q as filed under the Securities Exchange Act of 1934, as amended, or the Exchange Act, 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 and the information and 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 before you make a decision to invest in our common stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Relating to This Offering

If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to investors.

The offering price per share of common stock in this offering exceeds the net tangible book value per share of our outstanding common stock. As a result, investors purchasing shares of common stock in this offering may experience immediate and substantial dilution in the net tangible book value of the shares they purchase. For a more detailed discussion of the foregoing, see the section entitled "Dilution" below. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors. In addition, to the extent we need to raise additional capital in the future and we issue additional equity or convertible debt securities, our then existing stockholders may experience dilution and the new securities may have rights senior to those of our common stock offered in this offering.

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering. We intend to use the net proceeds from this offering for general corporate purposes, including expenses related to the clinical and preclinical development of cirmtuzumab and TK216, preclinical development of our ROR1 CAR-T program, and for working capital. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock.

Risks Related to Our Limited Operating History, Financial Position and Capital Requirements

Our independent registered public accounting firm has included an explanatory paragraph relating to our ability to continue as a going concern in its report on our audited financial statements included in this prospectus.

The report of our independent registered public accounting firm on our consolidated financial statements as of and for the year ended December 31, 2019 includes an explanatory paragraph indicating that there is substantial doubt about our ability to continue as a going concern. If we are unable to raise sufficient capital when needed, our business, financial condition and results of operations will be materially and adversely affected, and we will need to significantly modify our operational plans to continue as a going concern. If we are unable to continue as

a going concern, we might have to liquidate our assets and the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our consolidated financial statements. The inclusion of a going concern explanatory paragraph by our auditors, our lack of cash resources and our potential inability to continue as a going concern may materially adversely affect our share price and our ability to raise new capital or to enter into critical contractual relations with third parties.

The COVID-19 outbreak may adversely impact our business.

The current COVID-19 worldwide pandemic has presented substantial public health and economic challenges and is affecting economies, financial markets and business operations around the world. International and U.S. governmental authorities in impacted regions are taking action in an effort to slow the spread of COVID-19, including issuing varying forms of "stay-at-home" orders, and restricting business functions outside of one's home. In response, we have put restrictions on employee travel and working from our executive offices with many employees continuing their work remotely. In addition, while we are currently continuing the clinical trials we have underway in sites across the U.S., we expect that COVID-19 precautions may directly or indirectly impact the timeline for some of our clinical trials. For example, some of our clinical trial sites, including those located in areas severely impacted by the pandemic, have placed new patient enrollment into clinical trials on hold or, for patients traveling from out of state, have implemented a 14-day self-quarantine before appointments. Patients with MCL or CLL may be at increased risk of severe disease if they develop COVID-19 because of advanced age and/or immunosuppression, and so may be unwilling to travel to our study centers to enroll in our clinical trials. For our existing patients, we are actively working with all of our clinical trial sites to minimize disruptions and address concerns on an individual site or patient basis in order to allow participating patients to continue to receive treatment at home or in alternate healthcare settings while minimizing their potential exposure to the virus that causes COVID-19. If restrictions related to the COVID-19 outbreak continue for a prolonged period of time or if additional clinical trial sites pause patient enrollment or treatments, our clinical trial milestones would be negatively impacted. Additionally, our expectations for the timing of first-in-human dosing of our ROR1 CAR-T therapy in China has been delayed, due primarily to impacts resulting from the COVID-19 outbreak in China.

At the present time, we believe we have sufficient quantities of our cirmtuzumab and TK216 clinical trial materials to continue to treat patients in our clinical trials through at least the end of 2020. However, if our third-party manufacturers, including those located in China, experience additional manufacturing difficulties due to the COVID-19 outbreak or as a result of natural disasters, labor disputes, unstable political environments, or other public health emergencies, our ability to provide our product candidates to patients in clinical trials, or to provide product for treatment of patients if approved, would be jeopardized.

As the COVID-19 pandemic continues to spread around the globe, we may experience disruptions that could severely impact our business, clinical trials and manufacturing and supply chains, including:

- interruptions or delays in the operations of the FDA or other regulatory authorities, which may delay receiving feedback or approvals from the FDA or other regulatory authorities with respect to future clinical trials or regulatory submissions;
- further delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;

- limiting our ability to interact with our clinical trial investigators, present our data in person at scientific and investor conferences, develop and renew contracts due to travel limitations or cancellations of scientific or investor conferences;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems, including interruption of supply cirmtuzumab or TK216;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials and interruption in global shipping that may affect the transport of clinical trial materials;
- limitations on employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- changes in local regulations as part of a response to COVID-19 which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees; and
- difficulties launching or commercializing products, including due to reduced access to doctors as a result of social distancing protocols.

In addition, the spread of COVID-19 may have impacted, and may continue to impact, the trading price of shares of our common stock and could further severely impact our ability to raise additional capital on a timely basis, or at all, or enter into partnerships with pharmaceutical companies.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the COVID-19 may impact our business, including our clinical trials, manufacturing and supply chains and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the U.S. and other countries, business closures or business disruptions and the effectiveness of actions taken in the U.S. and other countries to contain and treat the disease.

To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this section and in the “Risk Factors” sections of our Annual Report on Form 10-K for the year ended December 31, 2019 and subsequent Quarterly Reports on Form 10-Q.

Cautionary Note Regarding Forward-Looking Statements

This prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements. All statements other than statements of historical fact contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are forward-looking statements, including, without limitation, statements regarding:

- our ability to obtain and maintain regulatory approvals for our product candidates, including cirmtuzumab, TK216 and our ROR1-targeted CAR-T therapy candidate;
- the expected timing for achieving key milestones, including commencing, completing and announcing results of clinical trials of our product candidates;
- the timing or likelihood of regulatory filings and approvals;
- the estimated size of the patient population and anticipated market potential for our product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and our ability to operate our business without infringing upon the intellectual property rights of others;
- the plans and objectives of management for future operations and future results of anticipated products;
- the impact the COVID-19 pandemic has had on our business and the U.S. and global economies;
- our estimates regarding the sufficiency of our cash resources and our expenses, capital requirements and need for additional financing, and our ability to obtain additional financing; and
- our intended use of the net proceeds of the offering.

These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “would,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this this prospectus supplement and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading “Risk Factors.” The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Use of Proceeds

We estimate that we will receive net proceeds of approximately $ million from the sale of the shares of common stock offered by us in this offering, or approximately $ million if the underwriter exercises in full its option to purchase additional shares of common stock, after deducting the underwriting discounts and commissions and estimated offering costs payable by us.

We intend to use the net proceeds from this offering for general corporate purposes, including expenses related to the clinical and preclinical development of cirmtuzumab and TK216, preclinical development of our ROR1 CAR-T program, and for working capital.

The amounts and timing of our actual expenditures will depend on numerous factors, including interactions with and feedback from regulatory authorities, the timing of initiation and progress of our clinical trials and results of such trials, other development efforts for our product candidates, and other factors, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

Dilution

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. As of September 30, 2020, our net tangible book value was $15.7 million, or $0.70 per share, based on 22,346,766 shares of our common stock outstanding as of September 30, 2020. Our net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of our common stock outstanding as of September 30, 2020.

Our pro forma net tangible book value as of September 30, 2020, was approximately $36.1 million, or $1.22 per share, after giving effect to our sale on November 20, 2020, of 7,258,065 shares of common stock at an offering price of $3.10 per share, after deducting underwriting discounts and commissions and offering expenses payable by us.

After giving further effect to our sale in this offering of shares of common stock at an offering price of $ per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of September 30, 2020 would have been $ million, or $ per share. This represents an immediate increase of net tangible book value of $ per share to our existing stockholders and an immediate dilution of $ per share to new investors purchasing our common stock in this offering. The following table illustrates this per share dilution.

Public offering price per share		$
Net tangible book value per share at September 30, 2020	$0.70	
Pro forma increase in net tangible book value per share attributable to pro forma adjustments for the November 2020 offering described above	$0.52	
Pro forma net tangible book value per share at September 30, 2020, before giving effect to this offering	$1.22	
Increase in pro forma net tangible book value per share attributable to investors purchasing shares in this offering		
Pro forma, as adjusted, net tangible book value per share as of September 30, 2020, after giving effect to this offering		
Dilution per share to investors purchasing our common stock in this offering		$

If the underwriter exercises in full its option to purchase up to an additional shares of our common stock, the pro forma, as adjusted net tangible book value after this offering would be $ per share, representing an increase in net tangible book value of $ per share to our existing stockholders and immediate dilution in net tangible book value of $ per share to new investors purchasing shares in this offering.

The above discussion and table are based on 22,346,766 shares outstanding as of September 30, 2020, and excludes as of that date:

- 3,521,438 shares of common stock issuable upon the exercise of outstanding warrants with a weighted average exercise price of $10.96 per share;
- 2,340,939 shares of common stock issuable upon the exercise of outstanding stock options with a weighted average exercise price of $7.73 per share;
- 842,837 shares of common stock reserved for future issuance under our 2019 Incentive Award Plan.

In addition, the above discussion excludes the 435,484 shares of our common stock issuable upon exercise of warrants issued on November 20, 2020.

In addition, the number of shares of our common stock to be outstanding after this offering excludes shares (or if the underwriter exercises its option to purchase additional shares in full) of common stock issuable upon exercise of warrants to be issued to the underwriter with an exercise price of $ per share, as described in "Underwriting."

To the extent that outstanding options or warrants are exercised, you 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 we raise additional capital by issuing equity or convertible debt securities, your ownership will be further diluted.

Underwriting

Pursuant to the underwriting agreement with H.C. Wainwright & Co., LLC, as the underwriter, we have agreed to issue and sell, and the underwriter has agreed to purchase, shares of common stock, less the underwriting discounts and commissions, on the closing date, subject to the terms and conditions contained in the underwriting agreement,. The underwriting agreement provides that the obligations of the underwriter is subject to certain customary conditions precedent, representations and warranties contained therein.

Pursuant to the underwriting agreement, the underwriter has agreed 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 underwriter's option to purchase additional shares of common stock described below. The underwriter has advised us that it does not intend to confirm sales to any account over which it exercises discretionary authority.

Discounts, Commissions and Expenses

The underwriter may offer the shares of common stock from time to time to purchasers directly or through agents, or through brokers in brokerage transactions on The Nasdaq Capital Market, or to dealers in negotiated transactions or in a combination of such methods of sale, or otherwise, at a fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices, subject to receipt and acceptance by it and subject to its right to reject any order in whole or in part. The difference between the price at which the underwriter purchases shares from us and the price at which the underwriter resells such shares may be deemed underwriting compensation. If the underwriter effects such transactions by selling shares of common stock to or through dealers, such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriter and/or purchasers of shares of common stock for whom they may act as agents or to whom they may sell as principal.

The underwriter is offering the shares, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters and other conditions specified in the underwriting agreement. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

We have granted to the underwriter an option to purchase up to an additional shares of common stock (up to 15% of the shares of common stock in this offering) at the public offering price, less the underwriting discounts and commissions. The option is exercisable for 30 days.

Any shares sold by the underwriter to securities dealers will be sold at the public offering price less a selling concession not in excess of per share.

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 underwriter's option to purchase additional shares.

		Total	
	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discounts and commissions payable by us	$	$	$
Proceeds, before expenses, to us	$	$	$

We have also agreed to pay the underwriter a management fee equal to 1% of the aggregate gross proceeds in this offering. We have agreed to reimburse the expenses of the underwriter in the non-accountable sum of $40,000 in connection with this offering, reimburse the expenses of the underwriter, including its legal fees, up to $100,000 in connection with this offering, and $12,900 for the clearing expenses of the underwriter in connection with this offering.

Underwriter Warrants

In addition, we have agreed to issue to the underwriter warrants to purchase up to shares of common stock, or shares of common stock if the underwriter exercises its option to purchase additional securities in full, which represents 6% of the aggregate number of shares of common stock sold in this offering, at an exercise price of $ per share (representing 125% of the public offering price per share of common stock to be sold in this offering). The underwriter warrants will be exercisable immediately and for five years from the date of commencement of sales in this offering.

Tail Financing Payments

In the event that any investors that participate in this offering or were introduced to this offering by the underwriter provides any capital to us in a public or private offering or capital-raising transaction within 12 months following the closing of this offering, we shall pay the underwriter the cash compensation provided above on the gross proceeds from such investors.

Indemnification

We have agreed to indemnify the underwriter against certain liabilities, including civil liabilities under the Securities Act of 1933, as amended, or the Securities Act, or to contribute to payments that the underwriter may be required to make in respect of those liabilities.

Lock-Up Agreements

We have agreed to not sell any shares of our common stock or any securities convertible into or exercisable or exchangeable into share of common stock, subject to certain exceptions, for a period of 90 days after the date of this prospectus supplement, and to not effect or enter into an agreement to effect any variable rate transaction for a period of one year after the closing of this offering, without the prior written consent of the underwriter. This consent may be given at any time without public notice.

Price Stabilization, Short Positions and Penalty Bids

In connection with this offering, the underwriter may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions and penalty bids in connection with our common stock.

Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum.

Overallotment transactions involve sales by the underwriter of shares of common stock in excess of the number of shares the underwriter is 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 underwriter is not greater than the number of shares that it may purchase in the overallotment option. In a naked short position, the number of shares involved is greater than the number of shares in the overallotment option. The underwriter may close out any short position by exercising its overallotment option 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. Such a naked short position would be closed out by buying securities in the open market. A naked short position is more likely to be created if the underwriter is concerned that there could be downward pressure on the price of the securities in the open market after pricing that could adversely affect investors who purchase in the offering.

Penalty bids permit the underwriter to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a stabilizing or syndicate covering transaction 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 underwriter make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on The Nasdaq Capital Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

In connection with this offering, the underwriter also may engage in passive market making transactions in our common stock in accordance with Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of the distribution. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for that security. However, if all independent bids are lowered below the passive market maker's bid that bid must then be lowered when specific purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Electronic Distribution

A prospectus in electronic format may be made available on the websites maintained by the underwriter, if any, participating in this offering and the underwriter may distribute prospectuses electronically. 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 form a part, has not been approved or endorsed by us or the underwriter, and should not be relied upon by investors.

Other Relationships

From time to time, certain of the underwriter and its affiliates have provided, and may provide in the future, various advisory, investment and commercial banking and other services to us in the ordinary course of business, for which they have received and may continue to receive customary fees and commissions. The underwriter served as our exclusive placement agent in connection with our registered direct offerings we consummated in May 2020, July 2020, September 2020 and November 2020 for which it received compensation. However, except as disclosed in this prospectus supplement, we have no present arrangements with the underwriter for any further services.

Transfer Agent

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Nasdaq Capital Market Listing

Our shares of common stock are listed on The Nasdaq Capital Market under the symbol "ONCT."

Legal Matters

The validity of the issuance of the securities offered hereby will be passed upon by our counsel, Latham & Watkins LLP, San Diego, California. Haynes and Boone LLP, New York, New York is acting as counsel to the underwriter in connection with this offering.

Experts

The consolidated financial statements of Oncternal Therapeutics, Inc. as of December 31, 2019 and 2018 and for the years then ended and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2019, incorporated by reference in this prospectus supplement have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm (the report on the consolidated financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

Where You Can Find More Information; Information Incorporated By Reference

Available Information

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus supplement forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement and the accompanying prospectus certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus supplement and the accompanying prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is http://www.sec.gov.

Our website address is www.oncternal.com. The information on, or accessible through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement and the accompanying prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement and accompanying prospectus to the extent that a statement contained in this prospectus supplement or the accompanying prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the

"Exchange Act" in this prospectus supplement, between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus supplement and the accompanying prospectus incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on March 16, 2020;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2020, June 30, 2020 and September 30, 2020, filed with the SEC on May 7, 2020, August 6, 2020 and November 4, 2020, respectively;
- the information specifically incorporated by reference into our Annual Report on Form 10-K from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 29, 2020;
- our Current Reports on Form 8-K filed with the SEC on March 18, 2020, April 2, 2020, May 19, 2020, May 21, 2020, June 15, 2020, June 30, 2020, July 21, 2020, July 31, 2020, August 27, 2020, August 31, 2020, November 19, 2020 and December 7, 2020; and
- the description of our Common Stock contained in our registration statement on Form 8-A, filed with the SEC on January 13, 2004 and any amendment or report filed with the SEC for the purpose of updating the description, including Exhibit 4.5 to our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on March 16, 2020.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement and the accompanying prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address

Oncternal Therapeutics, Inc.
Attn: Corporate Secretary
12230 El Camino Real, Suite 300
San Diego, California 92130
(858) 434-1113

Table of Contents

PROSPECTUS

$150,000,000
Common Stock
Warrants

From time to time, we may offer up to $150,000,000 of shares of our common stock and warrants to purchase our common stock, either individually or in combination. We may also offer common stock upon the exercise of warrants.

We will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you buy any of the securities being offered.

Our common stock is listed on The Nasdaq Capital Market under the symbol "GTXI." On December 21, 2017, the last reported sale price of our common stock was $12.72 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on The Nasdaq Capital Market or other securities exchange of the securities covered by the prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

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

The securities may be sold directly by us to investors, through agents designated from time to time or to or through agents, underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any agents, underwriters or dealers are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents, underwriters or dealers and any applicable fees, commissions, 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 we expect to receive from such sale will also be set forth in 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 January 5, 2018.

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration process. Under this shelf registration statement, we may, from time to time, offer and sell, in one or more offerings, any combination of the securities described in this prospectus for total gross proceeds of up to $150,000,000. This prospectus provides you with a general description of the securities we may offer.

Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to read carefully this prospectus, any applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the section entitled "Incorporation by Reference," before buying any of the securities being offered.

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

You should rely only on the information contained in, or incorporated by reference into, this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different or additional information. 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.

The information appearing in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus incorporates by reference market data, industry statistics and other data that have been obtained from, or compiled from, information made available by third parties. We have not independently verified their data. This prospectus and the information incorporated herein by reference includes trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section entitled “Where You Can Find More Information.”

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus (as supplemented and amended), including the financial data and related notes, risk factors and other information incorporated by reference in this prospectus, before making an investment decision. Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus to "GTx," "the company," "we," "us," "our" or similar references mean GTx, Inc.

GTx, Inc.

We are a biopharmaceutical company dedicated to the discovery, development and commercialization of small molecules for the treatment of muscle-related diseases and other serious medical conditions. Our current strategy is focused on the further development of selective androgen receptor modulators, or SARMs. Our lead product candidate is enobosarm (GTx-024). Enobosarm is the generic name given to the compound by the USAN Council and the World Health Organization and is the first compound to receive the SARM stem in its name, recognizing enobosarm as the first in this new class of compounds.

Additionally, in 2015, we entered into an exclusive worldwide license agreement with the University of Tennessee Research Foundation to develop its proprietary selective androgen receptor degrader, or SARD, technology which we believe has the potential to provide compounds that can degrade multiple forms of androgen receptor by inhibiting tumor growth in patients with progressive castration-resistant prostate cancer, including those patients who do not respond to or are resistant to current therapies.

We were originally incorporated under the name Genotherapeutics, Inc. in Tennessee in September 1997. We changed our name to GTx, Inc. in 2001, and we reincorporated in Delaware in 2003. Our principal executive office is located at 175 Toyota Plaza, 7th Floor, Memphis, TN 38103, and our telephone number is (901) 523-9700. Our website address is www.gtxinc.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus.

The Securities We May Offer

We may offer shares of our common stock and warrants to purchase our common stock, either individually or in combination, with a total value of up to $150,000,000 from time to time under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. We may also offer common stock upon the exercise of warrants. This prospectus provides you with a general description of the securities we may offer. Each time we offer 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 the aggregate offering price.

A prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference into this prospectus. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

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

- the names of those underwriters, dealers or agents;
- 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 ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

Common Stock. We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock.

Warrants. We may issue warrants for the purchase of common stock in one or more series. We may issue warrants independently or together with common stock. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the warrants. A form of warrant agreement and warrant certificate containing the terms of the warrants that may be offered has been filed as an exhibit to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that describe the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Warrants may be issued under a warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if any, in the applicable prospectus supplement relating to a particular series of warrants.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and discussed under the section entitled "Risk Factors" contained in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with a specific offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition or results of operations could be seriously harmed. This could cause the trading price of our securities to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled "Special Note Regarding Forward-Looking Statements."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain 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 Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements are based on our management's beliefs and assumptions and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. All statements, other than statements of historical facts, are forward-looking statements for purposes of these provisions, including, without limitation, any statements relating to:

- the implementation of our business strategies, including our ability to preserve or realize any significant value from our SARM and SARD programs;
- the therapeutic and commercial potential of, and our ability to advance the development of, SARMs and our SARD program;
- the timing, scope and anticipated initiation, enrollment and completion of our ongoing clinical trials, and any other future clinical trials that we may conduct;
- our ability to establish and maintain potential new collaborative, partnering or other strategic arrangements for the development and commercialization of our product candidates;
- the anticipated progress of our preclinical and clinical programs, including whether our ongoing clinical trials will achieve clinically relevant results;
- the timing of regulatory discussions and submissions, and the anticipated timing, scope and outcome of related regulatory actions or guidance;
- our ability to obtain and maintain regulatory approvals of our product candidates and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to market, commercialize and achieve market acceptance for our product candidates;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- our estimates regarding the sufficiency of our cash resources and our expenses, capital requirements and need for additional financing, and our ability to obtain additional financing;
- our projected operating and financial performance; and

- our intended use of the net proceeds from offerings of our securities under this prospectus.

In some cases, you can identify forward-looking statements by terms such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance, time frames or achievements to be materially different from the information expressed or implied by these forward-looking statements. While we believe that we have a reasonable basis for each forward-looking statement, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. We discuss many of these risks, uncertainties and other factors in greater detail under the heading “Risk Factors” contained in any applicable prospectus supplement, in any free writing prospectuses we authorize for use in connection with a specific offering, and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus, any applicable prospectus supplement and any free writing prospectuses we authorize for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading “Incorporation by Reference,” completely and with the understanding that our actual future results may be materially different from what we expect. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our business, results of operations and financial condition. We hereby qualify all of our forward-looking statements by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently anticipate using the net proceeds from the sale of securities under this prospectus, if any, for clinical development and other research and development activities and for working capital and general corporate purposes. As of the date of this prospectus, we cannot specify with certainty all of the particular uses of the proceeds from the sale of the securities under this prospectus. Accordingly, we will retain broad discretion over the use of such proceeds. Pending these uses, we intend to invest the net proceeds in investment-grade, interest-bearing instruments.

DESCRIPTION OF CAPITAL STOCK

General

As of the date of this prospectus, our authorized capital stock consists of 60,000,000 shares of common stock, $0.001 par value per share, and 5,000,000 shares of preferred stock, $0.001 par value per share. As of December 15, 2017, there were 21,541,909 shares of our common stock outstanding and no shares of preferred stock outstanding.

On December 5, 2016, we effected a one-for-ten reverse stock split of our outstanding common stock. At the effective time of the reverse stock split, every ten shares of our issued and outstanding common stock was automatically combined and reclassified into one issued and outstanding share of common stock. No fractional shares of our common stock were issued and each holder of our common stock who would otherwise have been entitled to a fraction of a share of our common stock received a cash payment. In addition, as a result of the reverse stock split, proportionate adjustments were made to the per share exercise price and/or the number of shares issuable upon the exercise or vesting of all stock options, restricted stock units and warrants issued by us and outstanding immediately prior to the effective time of the reverse stock split, which resulted in a proportionate decrease in the number of shares of our common stock reserved for issuance upon exercise or vesting of such stock options, restricted stock units and

warrants, and, in the case of stock options and warrants, a proportionate increase in the exercise price of all such stock options and warrants. The number of shares reserved for issuance under our equity compensation plans immediately prior to the effective time of the reverse stock split was reduced proportionately. All share and per share information included in this prospectus has been retroactively adjusted to give effect to the reverse stock split.

The following summary description of our capital stock is based on the provisions of our certificate of incorporation and bylaws, the applicable provisions of the General Corporation Law of the State of Delaware, or DGCL, and the agreements described below. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our certificate of incorporation and bylaws, the DGCL and such agreements. For information on how to obtain copies of our certificate of incorporation, bylaws and such agreements, which are exhibits to the registration statement of which this prospectus is a part, see the section entitled “Where You Can Find More Information.”

Common Stock

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. The holders of our common stock do not have cumulative voting rights in the election of directors. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock.

The rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of holders of shares of any preferred stock that we may designate and issue in the future.

Preferred Stock

Our certificate of incorporation provides that our board of directors has the authority, without further action by the stockholders, to designate and issue up to 5,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, and to determine or alter for each such series, such voting powers, full or limited, or no voting powers, and such designation, preferences, and relative, participating, optional, or other rights and such qualifications, limitations, or restrictions thereof, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deterring or preventing a change in control of GTx or making removal of management more difficult, and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock.

Registration Rights

In September 2017, we completed a private placement of immediately separable units comprised of an aggregate of 5,483,320 shares of our common stock and warrants to purchase an aggregate of 3,289,988 shares of our common stock. Pursuant to the terms of the securities purchase agreement we entered into in connection with this private placement, we agreed to file as many registration statements with the SEC as may be necessary to cover the resale of all of the shares of common stock that we issued to, or are issuable upon the exercise of warrants that we issued to, the investors in the private placement, to use our reasonable best efforts to have all such registration statements declared effective as required by and within the timeframes set forth in the securities purchase agreement, and to keep such registration statements effective for up to two years following the closing date of the private placement. In October 2017, we filed a registration statement under the Securities Act registering the resale of all 8,773,308 shares of common stock that we issued to, or are issuable upon the exercise of warrants that we issued to, the investors in the private placement. In the event that any required registration statements are not filed or declared effective within the

timeframes set forth in the securities purchase agreement, or any such effective registration statements subsequently become unavailable, we would, subject to certain limited exceptions, be required to pay liquidated damages equal to 1.0% of the aggregate unit purchase price under the securities purchase agreement per month for each default (up to a maximum of 10% of such aggregate unit purchase price). In addition, J.R. Hyde, III, a member of our board of directors, and an affiliate of Mr. Hyde's, have rights under a separate registration rights agreement with us to require us to file resale registration statements covering an additional 785,297 shares of our common stock held in the aggregate or to include these shares in registration statements that we may file for ourselves or other stockholders. The foregoing registration rights do not apply or have been waived with respect to the registration statement of which this prospectus is a part, and no shares held by or issuable to the foregoing investors are registered for resale hereunder.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents

Delaware Takeover Statute. We are subject to Section 203 of the DGCL. Section 203 generally prohibits a public Delaware corporation such as us from engaging in a "business combination" with an "interested stockholder" for a period of three years following the time that the stockholder became an interested stockholder, unless:

- prior to the time the stockholder became an interested stockholder, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which 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 number of shares outstanding (a) shares owned by persons who are directors and also officers and (b) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to the time the stockholder became an interested stockholder, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66-2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, lease, exchange, mortgage, pledge, transfer or other disposition (in one transaction or a series of transactions) involving the interested stockholder of 10% or more of the assets of the corporation (or its majority-owned subsidiary);
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect, directly or indirectly, of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit, directly or indirectly (except proportionately as a stockholder of such corporation), of any loans, advances, guarantees, pledges or other financial benefits, other than certain benefits set forth in Section 203, provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person that is an affiliate or associate of such entity or person.

Charter Documents. Our certificate of incorporation and bylaws provide that our board of directors be divided into three classes of directors, as nearly equal in number as possible, with each class serving a staggered three-year

term. The classification system of electing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us since the classification of the board of directors generally increases the difficulty of replacing a majority of directors. In addition, our certificate of incorporation and bylaws:

- provide that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by any consent in writing;
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon at a stockholder meeting;
- provide that the authorized number of directors may be changed only by resolution of the board of directors; and
- provide that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer or our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors.

The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote is required to amend a corporation's bylaws, unless a corporation's certificate of incorporation requires a greater percentage or also confers the power upon the corporation's directors. Our bylaws may be amended or repealed by:

- the affirmative vote of a majority of our directors then in office; or
- the affirmative vote of the holders of at least 66-2/3% of the voting power of all then-outstanding shares of our capital stock entitled to vote generally in the election of directors.

The foregoing provisions of our certificate of incorporation may only be amended or repealed by the affirmative vote of a majority of our directors and the affirmative vote of the holders of at least 66-2/3% of the voting power of all then-outstanding shares of our capital stock entitled to vote generally in the election of directors.

These and other provisions contained in our certificate of incorporation and bylaws could delay or discourage some types of transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares over then current prices, and may limit the ability of stockholders to remove current management or approve transactions that stockholders may deem to be in their best interests and, therefore, could adversely affect the price of our common stock.

Transfer Agent and Registrar

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

DESCRIPTION OF WARRANTS

The following description, together with the additional information that we include in any applicable prospectus supplement and in any related free writing prospectus that we may authorize to be distributed to you, summarizes the material terms and provisions of the warrants that we may offer under this prospectus. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered under this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed a form of warrant agreement and warrant certificate containing the terms of the warrants that may be offered as an exhibit to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that describe the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance

of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectus, and the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

The warrants may be issued independently or together with any common stock. The warrants may be issued under a warrant agreement that we enter into with a warrant agent, all as shall be set forth in a prospectus supplement relating to the particular series of warrants being offered pursuant to this prospectus and such prospectus supplement.

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

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the number of warrants issued with each share of common stock;
- the number of shares of common stock purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of shares of common stock issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrants may be modified;
- a discussion of any material or special United States federal income tax consequences of holding or exercising the warrants; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of our common stock, including the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any. Accordingly, holders of warrants will not be entitled, by virtue of being such holders, to vote, consent, receive dividends, receive notices as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter, or to exercise any rights whatsoever as our stockholders.

Exercise of Warrants

Each warrant will entitle the holder to purchase shares of our common stock at such exercise price as will in each case be set forth in, or be determinable as set forth in, the applicable prospectus supplement relating to the warrants offered thereby. The warrants may be exercised as set forth in the applicable prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the common stock purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

Governing Law

Unless we otherwise specify in the applicable prospectus supplement, the warrants will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the common stock purchasable upon exercise of, its warrants.

Outstanding Warrants

As of December 15, 2017, we had outstanding warrants to purchase an aggregate of 3,289,988 shares of our common stock having a per share exercise price of $9.02. These warrants have a five year term expiring on September 29, 2022. As of December 15, 2017, we also had outstanding warrants to purchase an aggregate of 6,430,948 shares of our common stock having a per share exercise price of $8.50. These warrants have a four year term expiring on May 6, 2019.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, “at-the-market” offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers. A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any over-allotment or other options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement. Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. If a dealer is used in the sale of securities, we or an underwriter 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. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time, including in “at-the-market” offerings or otherwise. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide underwriters, dealers and agents with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the underwriters, dealers or agents may make with respect to these liabilities. Underwriters, dealers and agents, or their affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on The Nasdaq Capital Market may engage in passive market making transactions in the securities on The Nasdaq Capital Market in accordance with Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker’s bid, however, the passive market maker’s bid must then be lowered when certain purchase limits are exceeded.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Cooley LLP, San Francisco, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, and the effectiveness of our internal control over financial reporting as of December 31, 2016, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities we are offering under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits filed as a part of the registration statement. You may read and copy the registration statement, as well as our reports, proxy statements and other information, at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, including GTx. The SEC's website can be found at www.sec.gov. We maintain a website at www.gtxinc.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 000-50549):

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, filed with the SEC on March 24, 2017;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 from our definitive proxy statement on Schedule 14A for our 2017 Annual Meeting of Stockholders, filed with the SEC on March 31, 2017;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017, June 30, 2017 and September 30, 2017 filed with the SEC on May 15, 2017, August 14, 2017 and November 14, 2017, respectively;
- our Current Reports on Form 8-K, filed with the SEC on January 9, 2017, May 3, 2017, May 11, 2017, June 12, 2017, September 13, 2017 and September 29, 2017; and
- the description of our common stock set forth in our registration statement on Form 8-A, filed with the SEC on January 13, 2004, including any further amendments thereto or reports filed for the purposes of updating this description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part

and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to GTx, Inc., Attention: Corporate Secretary, 175 Toyota Plaza, 7th Floor, Memphis, TN 38103. Our phone number is (901) 523-9700.

Shares

Common Stock

PROSPECTUS SUPPLEMENT

, 2020

H.C. Wainwright & Co.