UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE TRANSITION PERIOD FROM_____TO_____

Commission File Number 001-40499

Cyteir Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**45-5429901**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
128 Spring St, Building A, Suite 510	
Lexington, MA	**02421**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: 857-285-4140

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	CYT	Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Stock Market on June 30, 2021, was $482,490,328.

The number of shares of Registrant's Common Stock outstanding as of March 10, 2022 was 35,409,028.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A relating to the 2022 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2021. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements. The words “believe,” “may,” “will,” "estimate," “continue,” “anticipate,” “intend,” “expect,” “should,” “could,” “target,” “predict,” “seek” and similar expressions are intended to identify forward-looking statements. We include forward-looking information in our discussion of the following, among other topics, the initiation, timing, progress and results of our current and future preclinical studies and clinical trials, including advancing CYT-0851 into a potentially registrational trial in early 2023, our plan to complete IND-enabling studies with CYT-1853 in the first half of 2022, our plan to file an IND application with the FDA for CYT-1853 by the end of 2022; our plans to develop CYT-0851 in additional tumor settings as both a monotherapy and in combination with other approved cancer therapies; our expectation that our undisclosed target project will reach the drug candidate nomination stage in 2023; our plans to develop patient selection biomarkers; our intention to enter into strategic collaborations; our plans to nominate additional targets from our deoxyribonucleic acid, or DNA, damage repair platform, as well as our research and development programs; our expectations regarding the potential market size and patient populations for any drug candidates that we develop; our plans to develop the manufacturing processes for our drug products; and our estimates regarding expenses, future revenue, capital requirements and needs for additional financing. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy and plans and our objectives for future operations, are forward-looking statements.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those referenced in the section entitled “Item 1A. Risk Factors” in this Annual Report on Form 10-K, which could cause actual results to differ materially. Moreover, we operate in a very competitive and rapidly changing environment and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in or implied by any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report on Form 10-K may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

The forward-looking statements included in this Annual Report on Form 10-K are made only as of the date of this report. You should not rely upon forward-looking statements as predictions of future events. We cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report on Form 10-K to conform these statements to actual results or reflect interim developments, except as required by law.

Summary of Risk Factors

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary and other risks that we face can be found below under the heading "Item 1A. Risk Factors" and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the SEC, before making an investment decision regarding our common stock.

- We have a limited operating history and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and predict our future success and viability.
- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We need substantial additional funding. If we are unable to raise capital when needed, we will be forced to delay, reduce, or eliminate our research and product development programs or future commercialization efforts.
- We have never successfully completed any clinical trials, and we may be unable to do so for any drug candidates we develop.
- Our clinical trials may fail to demonstrate adequately the safety and efficacy of any of our drug candidates, which would delay or prevent further clinical development of those candidates, or prevent marketing approval from FDA or similar regulatory authorities.
- We are developing CYT-0851, and potentially future drug candidates, for use in combination with other therapies, which exposes us to additional risks.
- If we are unable to successfully develop and commercialize companion diagnostic tests for our drug candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our drug candidates.
- Synthetic lethality represents an emerging class of precision medicine targets, and negative perceptions of the efficacy, safety or tolerability of this class of targets, including any that we develop, could adversely affect our ability to conduct our business, advance our drug candidates or obtain regulatory approvals.
- If we are unable to adequately protect and enforce our intellectual property or obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and products may be impaired.
- The continuing outbreak of COVID-19 (including any resurgences, including due to variants, thereof) in the United States and other countries and shortages of qualified healthcare personnel may adversely affect our business and the market price of our common stock.
- Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

PART I

Item 1. Business.

Overview

We are a clinical-stage biotechnology company focused on developing and commercializing the next-generation of precision oncology medicines that inhibit DNA damage repair and cause cancer cell death in specific subsets of cancer patients through a therapeutic strategy known as synthetic lethality.

Our lead program, CYT-0851, was designed to exploit a novel synthetic lethality between overexpression of a family of DNA damaging enzymes called cytidine deaminases, or CD, and functional inhibition of homologous recombination, or HR, a DNA repair pathway critical for the survival of some cancers. We observed preliminary single-agent activity in the dose-escalation phase 1 portion of our phase 1/2 trial, which we completed in November 2021. In January 2022, we initiated patient dosing with CYT-0851 in the phase 2 expansion cohort portion of the phase 1/2 trial in adult patients with hematologic malignancies and solid tumors. If warranted by the phase 1/2 data, and subject to FDA agreement, we could initiate a potentially registrational trial in early 2023 for the treatment of relapsed and/or refractory lymphoma and/or solid tumors. We also plan to develop CYT-0851 in additional tumor settings as both a monotherapy and in combination with approved cancer therapeutics. In January 2022, we initiated patient dosing in the phase 1 portion of the phase 1/2 trial to assess tolerability and preliminary activity of combinations with three standard-of-care therapies.

Cells have complex, coordinated DNA damage repair pathways to ensure genome integrity and cell survival. Several DNA repair pathways have been identified for repairing the myriad forms of DNA damage our cells experience. Double strand DNA, or dsDNA, breaks are particularly toxic, and cells have evolved multiple mechanisms to repair such fatal lesions. The three major dsDNA break repair pathways are non-homologous end joining, or NHEJ, microhomology-mediated end joining, or MMEJ, and HR. NHEJ and MMEJ are considered error-prone repair pathways based on the way they repair dsDNA breaks, while HR is generally thought to be an error-free repair mechanism because the repair is templated by the homologous sister chromosome, thereby restoring the original DNA sequence. Single strand DNA, or ssDNA, damage is also repaired by specific ssDNA repair pathways, including Base Excision Repair, or BER, Nucleotide Excision Repair, or NER, and Mismatch Repair, or MMR, which proofreads and corrects DNA errors introduced during normal DNA replication. Activity of this highly coordinated network of DNA damage sensing and repairing pathways is collectively called the DNA Damage Response, or DDR.

A hallmark feature of cancer cells is the accumulation of DNA damage and genomic instability that leads to DNA mutations that often drive the aggressive characteristics of cancer cells, such as uncontrolled cell proliferation, invasion into surrounding tissues and, importantly, resistance to standard therapies. By their nature, cancer cells suffer excessive DNA damage compared to normal cells, and this increases their dependence on DNA repair processes to prevent the accumulation of genome-wide, catastrophic levels of DNA damage that would otherwise trigger cell death. This dynamic creates the opportunity for selectively targeting these cancers through the therapeutic strategy known as synthetic lethality.

Synthetic lethality is a clinically validated approach to drug development and arises when the occurrence of two cellular conditions is lethal when occurring simultaneously but tolerated when occurring individually. For example, a pre-existing, cancer-specific gene mutation (the first condition) might be synthetically lethal only in the presence of therapeutic inhibition of a specific target protein (the second condition). The existence of the cancer-specific gene mutation makes the therapeutic intervention lethal to the cancer cells, but relatively innocuous to the normal cells that do not express the sensitizing mutation. Leveraging synthetic lethality is a potentially powerful approach in cancer drug discovery because it may lead to better tolerated therapies that preferentially kill cancer cells and it facilitates the identification of patient subpopulations most likely to respond to therapy.

Our approach to drug discovery and development

We are using our expertise in DDR biology and a disciplined approach to select targets for novel, differentiated drug discovery and development programs. Our approach includes:

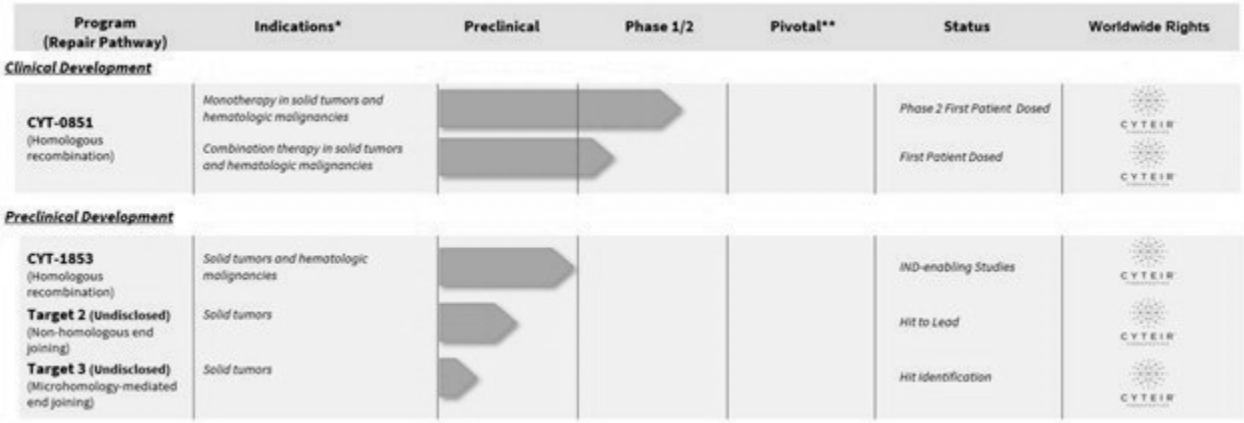
- systematically prioritizing DDR targets based on our deep understanding of DDR biology, coupled with the mining of mutational information collected on diseased tissues and the analysis of results from both internal and external CRISPR-based genetic, chemical and cellular phenotypic synthetic lethality screens;
- elucidating synthetic lethality dependencies of our drug targets and using that information to molecularly define patient populations most likely to benefit from our therapies as a monotherapy, and maximizing tumor selectivity that limits side effects and allows our drugs to be used in combination with other standard anti-cancer therapies;

- developing potent, highly selective, well tolerated, small molecule therapies against these targets and evaluating them in biomarker-selected in vitro and in vivo model systems; and
- expeditiously progressing lead candidates through preclinical studies and into focused clinical trials in defined patient populations using a biomarker-guided approach.

Our core capabilities in discovery biology focusing on DNA damage repair have enabled us to move efficiently from drug discovery to clinical development. We have a management team with successful global registration experience that we believe has the potential to advance our drug candidates to registration. In only three years, we progressed CYT-0851 from discovery to clinical proof of concept. In 2022, we intend to define our registration plan to advance toward the potential approval of CYT-0851, initially as monotherapy in late lines of treatment for certain lymphomas and/or solid tumors. In addition, we may broaden the target patient population in both hematologic malignancies and solid tumors and move to earlier lines of treatment, either alone and/or in combination with standard-of-care anti-cancer therapies.

Our pipeline

The following chart summarizes our clinical and preclinical-drug candidate pipeline. We hold worldwide development and commercialization rights to our drug candidates.



* CYT-0851 monotherapy and combination therapy indications include DLBCL, FL, MM, pancreatic cancer, ovarian cancer, and soft tissue sarcoma; CYT-1853 monotherapy indications to be determined

** Following the phase 1/2 trial, the pivotal trial could be a phase 3 trial, or if the phase 1/2 data warrant and subject to FDA agreement, a phase 2 registrational trial. If the FDA does not agree, or the data do not warrant advancing to a pivotal trial, we may be required to conduct an additional trial before advancing to the pivotal trial.

Our programs

Clinical

Our lead program, CYT-0851, was identified through a phenotypic screening strategy that exploited a novel synthetic lethality between CD overexpression and HR inhibition. The screen was designed to select for compounds that induced synthetic lethality in CD-overexpressing cancer cells while sparing normal cells.

CYT-0851 is a novel, oral, once-daily, small molecule drug candidate that has demonstrated a high therapeutic index. We completed the monotherapy dose-escalation portion of our phase 1/2 trial in November 2021, which included 73 patients enrolled across 12 dose-escalation cohorts. We identified the maximally tolerated dose, or MTD, as 600 mg daily and the recommended phase 2 dose, or RP2D, as 400 mg daily. The dose-escalation portion of the trial was primarily designed to identify the MTD with secondary endpoint measurements that included the formal analysis of anti-tumor activity as assessed by tumor response. As phase 1 trials designed in this way do not compare patients treated with a given investigational drug to those administered standard-of-care or placebo, an analysis of statistical significance cannot be performed and thus phase 1 studies are not powered for statistical significance. Phase 1 response data is not sufficient, nor intended to be used, for drug approval and additional trials will be required to further characterize the safety and efficacy in larger populations. We performed an analysis of all patients in the dose-escalation portion of our phase 1/2 trial as of November 15, 2021. Based on this analysis, 46 patients were considered response-evaluable, and we observed preliminary evidence of clinical benefit with 17 patients achieving stable disease, one patient with follicular lymphoma achieving a complete response, two patients with

diffuse large B-cell lymphoma, or DLBCL, and soft tissue sarcoma achieving partial responses, and the remaining 26 patients having progressive disease. The responses in DLBCL and follicular lymphoma were confirmed by Lugano criteria, and the partial response in soft tissue sarcoma was unconfirmed according to RECIST criteria. Of these 73 patients, 58% reported at least one treatment-related adverse event and only 16% of patients reported at least one Grade 3/4 treatment-related adverse event. The three most common treatment-related adverse events were fatigue (21% of patients), hyperuricemia (11%), and nausea (11%). In January 2022, we initiated patient dosing with CYT-0851 in the phase 2 expansion cohort portion of the phase 1/2 trial, with six tumor-specific cohorts. If warranted by the phase 1/2 data, and subject to FDA agreement, we could initiate a potentially registrational trial in early 2023 for the treatment of relapsed and/or refractory lymphoma and/or solid tumors.

To expand the therapeutic potential of CYT-0851 beyond monotherapy use, we conducted preclinical studies to explore combinations with a variety of standard-of-care anti-cancer drugs. We have observed both additive and synergistic treatment effects in preclinical studies with a variety of agents, including alkylating agents such as bendamustine, and anti-metabolites such as gemcitabine and 5-fluorouracil. We believe the encouraging preclinical results in conjunction with the favorable monotherapy clinical activity and tolerability of CYT-0851 to date provide a strong rationale for the development of a combination therapy in the future. In January 2022, we initiated patient dosing of CYT-0851 in combination with approved standard-of-care anti-cancer therapies in the phase 1 portion of the phase 1/2 trial.

Preclinical

Our next-generation program, CYT-1853, was designed to exploit the same novel synthetic lethality targeted by CYT-0851. Importantly, in preclinical models, CYT-1853 was active across a range of cancer cell lines and exhibited improved potency compared to CYT-0851. We expect to complete IND-enabling studies with CYT-1853 in the first half of 2022 and if the data supports an overall risk-benefit improvement and differentiation from CYT-0851, we plan to file an IND application with the FDA by year-end 2022.

In 2021, we advanced two additional drug discovery projects focused on identifying inhibitors of DNA damage repair targets that exploit specific synthetic lethalities. The first of these undisclosed targets (Target 2) plays a key role in Non-Homologous End Joining, or NHEJ, and the second (Target 3) in Microhomology-Mediated End Joining, or MMEJ, DNA repair pathways. For both targeted drug discovery projects, we have identified subsets of cancers that, we believe, uniquely depend on the target of interest for their survival and we are working to identify patient selection biomarkers to identify sensitive cancer subsets for use in clinical development. Both undisclosed target projects are preclinical stage, and we anticipate reaching the drug candidate nomination stage in 2023.

Additionally, we continually monitor the DDR and synthetic lethality landscape for promising and differentiated new target opportunities to initiate in-house or in-license to enrich our drug candidate pipeline.

Our management team

We have assembled a management team of biopharmaceutical industry veterans with extensive experience in developing novel oncology therapies, including advancing drug candidates from preclinical research through clinical development and ultimately regulatory approval and commercialization. Our executive management team includes veterans from Amgen Inc., ArQule Inc., AstraZeneca, Aton Pharma, Celgene Corporation, Chiron, Genzyme, ImmunoCellular Therapeutics, MedImmune, Merck & Co., Inc., McKinsey & Co., OSI Pharmaceuticals, Pharmacia, Pharmacyclics, Pharmion Corporation, PricewaterhouseCoopers, LLP, Roche Pharmaceuticals, Sanofi, and Searle & Co. Inc.

Strategy

Our goal is to be the leading biopharmaceutical company developing and commercializing next-generation precision oncology medicines that inhibit DDR and cause cancer cell death through synthetic lethality. We employ an integrated drug discovery approach with a streamlined drug development process with the aim to build a patient-centric portfolio of effective cancer therapies.

The key elements of our strategy are to:

- **Build upon the differentiated profile and encouraging preliminary single-agent activity of our lead drug candidate, CYT-0851, to advance it through clinical development and regulatory approval.** We are currently in a phase 1/2 trial for both hematologic malignancies and solid tumors and, depending on the cancer type, we may develop a biomarker for patient enrichment. If warranted by the phase 1/2 data, and subject to FDA agreement, we could initiate a potentially registrational trial in early 2023 for the treatment of relapsed and/or refractory lymphoma and/or solid tumors. In addition, we intend to advance our next-generation program, CYT-1853, through clinical development and regulatory approval to complement CYT-0851. We expect to complete IND-enabling studies with CYT-1853 in the first half of 2022 and if the data supports an overall risk-benefit improvement and differentiation from CYT-0851, we plan to file an IND application with the FDA by year-end 2022.

- **Leverage CYT-0851's favorable monotherapy clinical activity and tolerability to develop it in combination with standard-of-care anti-cancer therapies.** In parallel with monotherapy development, we are evaluating CYT-0851 in combination with standard-of-care anti-cancer drugs. We have selected three regimens for our initial combination evaluation that include: (1) rituximab plus bendamustine, (2) gemcitabine, and (3) capecitabine. We are currently dosing cohorts of patients as part of the ongoing phase 1 portion of the phase 1/2 trial to explore tolerability and preliminary activity of the above combinations.

- **Utilize our deep understanding of DDR and tumor biology to identify novel drug candidates and expand our pipeline.** We have initiated high-throughput screening on two additional drug discovery projects focused on identifying inhibitors of DNA damage repair that exploit specific synthetic lethalities. The first of these undisclosed targets (Target 2) plays a key role in NHEJ and the second (Target 3) in MMEJ DNA repair pathways. For both targeted drug discovery projects, we have identified subsets of cancers that, we believe, uniquely depend on the target of interest for their survival and we are working to identify patient selection biomarkers to identify sensitive cancer subsets for use in clinical development. Both undisclosed target projects are preclinical stage, and we anticipate reaching the drug candidate nomination stage in 2023.

  Additionally, we continually monitor the DDR and synthetic lethality landscape for promising and differentiated new target opportunities to initiate in-house or in-license to enrich our drug candidate pipeline.

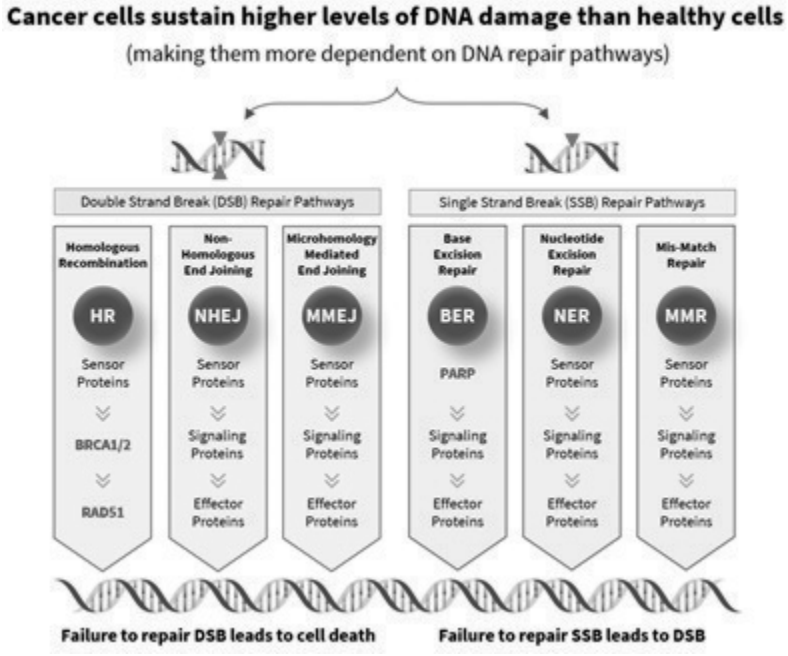
- **Maximize the value of our drug candidates and pipeline while selectively evaluating strategic collaborations.** We own all worldwide rights to our pipeline of precision-oncology programs, and we intend to commercialize our drug candidates, if approved, in key geographies. In the future, we may selectively enter into strategic collaborations around certain targets, drug candidates, disease areas or geographies if we believe these collaborations could maximize the value of our drug candidates. Additionally, we continually monitor the DDR and synthetic lethality landscape for promising and differentiated new target opportunities to initiate in-house or in-license to enrich our drug candidate pipeline.

Cancer treatments moving toward targeted therapeutics but unmet need remains

Advances in the molecular and genetic understanding of cancer have driven a fundamental shift away from cytotoxic chemotherapy treatments toward more targeted therapies that address aberrations in the cellular pathways and proteins necessary for cancer cell growth, proliferation, and survival. These targeted therapies provide a precise method for treating the patients who are most likely to clinically benefit from them. For example, certain patients with lung cancer express mutated forms of epidermal growth factor receptor, or EGFR, which have been validated targets for EGFR-directed therapies. Other targeted therapies address dysregulated pathways that are shared among an entire disease specific population, such as the use of vascular endothelial growth factor inhibitors in renal cell carcinoma. Despite their successes, targeted therapies have had limited utility in cancers that (1) have no identifiable therapeutic targets, (2) have an identifiable target, but it is not "druggable" given the limitations of current technologies, or (3) ultimately develop resistance through mutations, the use of alternative pathways or the loss of the target. Combining therapies and treating cancer through orthogonal pathways with multiple agents can limit the development of resistance to targeted therapies; however, the overlapping toxicity profile of many targeted agents has prevented their use in combination with chemotherapy, immunotherapy and/or radiation. We believe that DNA damage repair, essential for the survival of many cancer cells and for the progression of tumors, provides a unique opportunity to improve patient outcomes by expanding the number of addressable targets and allowing for combination with current standard-of-care therapies.

The importance of DNA damage repair

DNA is constantly under barrage by DNA damaging agents, including ultraviolet radiation in sunlight, carcinogens found in pesticides and tobacco smoke, and even naturally occurring substances produced by our cells during the normal processes of cell growth and division. This damage can occur on one or both strands of DNA, and it has been estimated that every cell in our body endures tens of thousands of DNA damaging events per day.

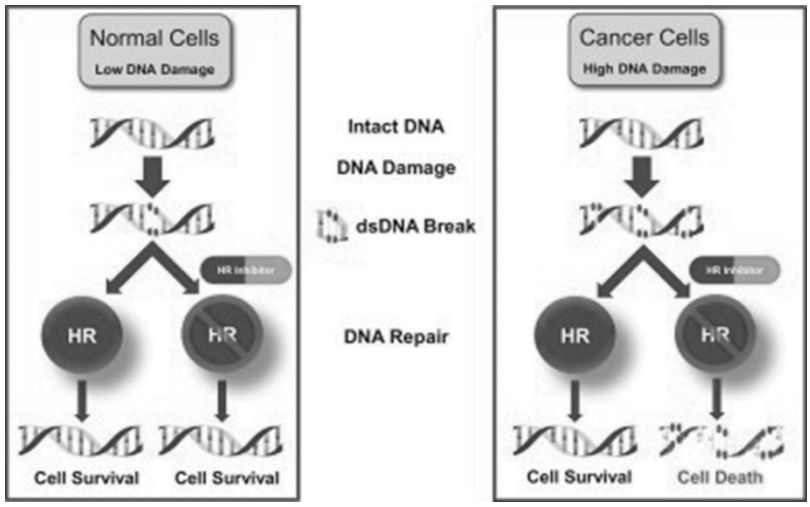


Different DNA repair pathways sense and repair the myriad types of DNA damage that all cells incur daily. Some of the better characterized DNA repair pathways shown above include dsDNA repair pathways such as HR, NHEJ, MMEJ, and ssDNA repair pathways such as BER, NER, and MMR.

Dependence on DNA damage repair creates a therapeutic opportunity in cancer

A hallmark feature of cancer is genomic instability driven by extensive DNA damage that must be repaired for cancer cells to survive. By selectively inhibiting DNA repair, DDR-targeted cancer therapies can cause the massive accumulation of unrepaired DNA damage in cancer cells, ultimately inducing cell death through a process known as mitotic catastrophe. Normal cells are generally not as predisposed to DDR-driven cell death because they express a full complement of overlapping DNA repair pathways as well as fully functional cell cycle checkpoint safeguards—these pathways, sensing DNA damage, direct the cell to stop dividing until its DNA is properly repaired, thereby avoiding mitotic catastrophe. The figure below depicts how cells utilize DDR pathways to repair damaged DNA, and how the increased levels of DNA damage that cancer cells incur can make them more dependent on specific DNA damage repair pathways, such as HR, and more sensitive to DDR-targeted therapies.

Cancer cells become dependent on DNA damage repair pathways



Harnessing the therapeutic potential of synthetic lethality in DDR

Synthetic lethality is a clinically validated approach to drug development and arises when the occurrence of two cellular conditions is lethal when occurring simultaneously but tolerated when occurring individually. For example, a pre-existing, cancer-specific gene mutation (the first condition) might be synthetically lethal only in the presence of therapeutic inhibition of a specific target protein (the second condition). The existence of the cancer-specific gene mutation makes the therapeutic intervention lethal to the cancer cells, but relatively innocuous to the normal cells that do not express the sensitizing mutation. Because DDR defects are common in nearly all cancers, DNA repair pathways are fertile areas to discover novel synthetic lethal targets for the development of effective targeted cancer therapies.

A clinically validated example of synthetic lethality is the use of poly (ADP-ribose) polymerase, or PARP, inhibitors to treat a subset of tumors that harbor certain HR deficiencies. For example, in subsets of ovarian, breast, prostate, and pancreatic cancers, pre-existing mutations in the Breast Cancer Genes, or BRCA, functionally impair HR and render those cancer cells sensitive to treatment with PARP inhibitors. The co-existence of both conditions – the pre-existing loss-of-function BRCA mutation and the therapeutic targeting of PARP – creates synthetic lethality that leads to cancer-specific cell death. The FDA and foreign regulatory authorities have approved four PARP inhibitors for the treatment of patients, including those with BRCA-mutant ovarian cancer, breast cancer, pancreatic cancer and prostate cancer. Global sales of PARP inhibitors in 2021 totaled more than $3.5 billion.

Synthetic lethality opportunities for CYT-0851

Activation-Induced Cytidine Deaminase, or AID, is a member of a larger family of enzymes referred to as CDs. CDs are tightly regulated nucleic acid damaging enzymes that convert cytidine into uridine by removing an amine group, a process known as deamination. The deamination of cytidine to uridine in DNA creates base pair mismatching that fosters DNA mutations and dsDNA breaks. In normal B cells, AID is transiently expressed and tightly regulated to concentrate its mutagenic action on the DNA encoding our antibody genes, a beneficial effect that ultimately improves our immunity. When AID becomes constitutively overexpressed and dysregulated, as it often does in certain forms of cancer, such as B-cell lymphomas, it leads to genome-wide DNA damage and collateral mutations beyond our antibody genes. To avoid mitotic catastrophe, cancer cells frequently rely on DNA damage repair pathways, including HR, to properly repair the harmful damage incurred to genes vital for the cancer's survival. This increased dependency on HR presents a therapeutic opportunity in those cancers overexpressing AID, including B-cell lymphomas.

In addition to subsets of B-cell lymphoma, CDs are also often highly expressed in subsets of solid tumors, such as head and neck, breast, and lung cancers. This observation supports our belief that therapies targeting HR and exploiting the synthetic lethality relationship created by CD overexpression might have broad utility across both hematologic malignancies and solid tumor cancers.

Beyond CD gene overexpression, it is plausible that additional cellular conditions exist in subsets of cancers, such as specific defects in alternative DNA damage repair pathways or cell cycle checkpoint genes that create synthetic lethality with HR inhibition. Such conditions may provide additional therapeutic opportunities for our lead program and are being explored.

Synthetic lethality opportunities for CYT-0851 in combination therapy

Monotherapy treatment relying on the synthetic lethality described above requires pre-existing, intrinsic defects in the cancer cells. Combination therapy, on the other hand, can create the synthetic lethality in cancer cells without any pre-existing defects in DDR pathways. Such combination therapy potentially could be used broadly across cancer types and with multiple classes of chemotherapy drugs and other DDR agents.

We are currently dosing patients in the phase 1 portion of the phase 1/2 trial evaluating CYT-0851 in combination with standard-of-care chemotherapeutic drugs including: (1) rituximab plus bendamustine, (2) gemcitabine and (3) capecitabine for the treatment of either hematologic malignancies or solid tumors.

Initial chemotherapy combinations support potential treatment in a broad range of cancers

Chemotherapy		Potential Addressable Disease Indications
Rituximab + Bendamustine	Lymphoma	DLBCL, FL
Capecitabine	Solid Tumors	Colorectal, Pancreatic, and Breast Cancers
Gemcitabine	Solid Tumors	Pancreatic, Sarcoma, Breast, Ovarian, NSCLC

The clinical utility of such a combination approach in the past has been limited by the overlapping toxicities of DDR inhibitors, such as PARP inhibitors or other experimental agents, and chemotherapy, particularly with respect to myelosuppression. We believe that the observed safety profile of CYT-0851, particularly the lack of clinically significant myelosuppression, nausea and vomiting observed to date in the ongoing phase 1/2 trial, may allow such combinations to be feasible.

CYT-0851

Program overview

CYT-0851 is a novel, oral, once-daily, small molecule drug candidate currently in phase 1/2 clinical trials for the treatment of hematologic malignancies and solid tumors.

In preclinical studies, CYT-0851 has demonstrated potent anti-tumor activity, cancer cell selectivity, and favorable safety and pharmacokinetic profiles that support its potential as a novel therapy that could address the serious unmet need in multiple cancers. We efficiently and expeditiously advanced CYT-0851 into the clinic with a development strategy designed to support the potential regulatory approval for treatment of patients with certain hematologic malignancies or solid tumors.

We are currently conducting a phase 1/2 trial, which we refer to as Study CYT-0851-01, enrolling patients with either hematologic malignancies or solid tumors. The first portion of the trial established 400 mg daily as the RP2D and schedule of CYT-0851 as a monotherapy. The phase 2 expansion cohort portion of the trial, for which we began patient dosing in January 2022, is evaluating the preliminary anti-tumor activity of CYT-0851 monotherapy at this dose and schedule in various hematologic malignancies and solid tumors including diffuse large B-cell lymphoma, or DLBCL, follicular lymphoma, or FL, multiple myeloma, or MM, ovarian cancer, soft tissue sarcoma and pancreatic cancer and confirming the safety of the RP2D. This study is intended to provide these necessary insights to support our broad development program of CYT-0851.

In the dose-escalation portion of our trial to date, CYT-0851 has demonstrated the potential for achieving anti-tumor effects in a variety of advanced solid tumors or hematologic malignancies while maintaining a favorable safety profile. If warranted by the phase 1/2 data, and subject to FDA agreement, we could initiate a potentially registrational trial in early 2023 for the treatment of relapsed and/or refractory lymphoma and/or solid tumors.

We also are enrolling patient cohorts in the phase 1 dose-escalation of CYT-0851 in combination with standard-of-care chemotherapeutic drugs including: 1) rituximab plus bendamustine 2) gemcitabine and 3) capecitabine for the treatment of either hematologic malignancies or solid tumors.

Hematologic malignancies and the current standard of care

Hematologic malignancies are a heterogeneous group of disorders, characterized as cancers arising from cells originating in the bone marrow or lymphoid tissues. Given their cell of origin, these cancers readily spread throughout the body through the cardiovascular and lymphatic systems and typically require a systemic approach for treatment and cannot be

cured by surgery or localized radiation therapy in most cases. Certain diseases such as DLBCL, the most common type of non-Hodgkin lymphoma, or NHL, are potentially curable with aggressive therapies even in the most advanced setting, while other disorders such as FL and MM are treated with the goal of long-term disease and symptom control because cure typically has not been possible. The first line of treatment for the majority of these disorders consists of combination therapy comprised of chemotherapy, targeted agents and/or radiation. When the disease progresses, commonly referred to as relapsed or refractory disease, alternative regimens and combinations are employed, but typically with reduced rates of success and shorter duration of benefit at each progression until the patient exhausts their therapeutic options, is no longer in a physical condition to receive treatment or elects to discontinue active treatment of their disease.

Hematologic malignancies market opportunity

In 2022, according to the American Cancer Society, 184,000 newly diagnosed hematologic malignancy cases and more than 57,000 deaths are expected in the United States. MM is expected to account for more than 34,000 of these new cases. DLBCL and FL are expected to account for about 42,400 new cases. These three indications included in our phase 2 expansion cohort study of CYT-0851 are expected to account for an estimated 20,000 deaths in 2022, indicative of the large ongoing unmet need.

Hematologic Malignancy	2022 estimated incidence	2022 estimated mortality
MM	34,470	12,640
DLBCL	24,600	6,000
FL	17,800	1,330
Totals:	76,870	19,970

Hematologic malignancies: CYT-0851 development plan

We are enrolling patients with DLBCL, FL and MM in the phase 2 expansion cohort study of our phase 1/2 clinical trial for CYT-0851. If warranted by the phase 1/2 data, and subject to FDA agreement, we intend to initiate a potentially registrational trial in early 2023 for the treatment of relapsed and/or refractory lymphoma.

In December 2021, we initiated the phase 1 evaluation of CYT-0851 in combination with rituximab and bendamustine for the treatment of non-Hodgkin lymphoma.

Solid tumors and the current standard of care

Solid tumors are cancers originating from an organ or tissue outside the blood and lymphatic systems. These tumors are further classified, named and ultimately treated based on their tissue of origin, such as breast, ovarian or pancreatic cancer. Solid tumors are responsible for the vast majority of cancers and account for more than 1.7 million new diagnoses in the United States annually. Unlike hematologic malignancies, some solid tumors are identified early through screening procedures or symptomatic presentation prior to spreading throughout the body. In these instances, the cancer can often be removed by surgical excision to ultimately cure the patient's disease. Outcomes for early-stage disease are highly variable across tumor types, with most early-stage colorectal and breast cancers being cured and almost all pancreatic cancers recurring and metastasizing even despite early intervention. Once solid tumors metastasize, or spread to other sites in the body, the goal of therapy often shifts to long-term control and palliation since cures are typically unattainable. In this incurable setting, the most effective therapies are typically used in combination with the first lines of treatment, and subsequent lines of treatment typically become progressively less effective. The number of available lines of therapy is disease type-specific and generally ranges from as low as one to two lines of therapy in pancreatic cancer and soft tissue sarcoma to more than five lines of therapy in hormone-receptor positive breast cancer. Patients remain on treatment until they have exhausted all therapeutic options, develop symptoms that preclude further treatment or elect to stop further treatment of their cancer.

Solid tumor market opportunity

According to the American Cancer Society, the 2022 estimated United States annual incidence and mortality of the three types of malignancies included in our phase 2 expansion cohort study of CYT-0851 are expected to exceed 92,000 and 66,000, respectively, indicative of the large unmet need.

Tumor Type	2022 estimated incidence	2022 estimated mortality
Pancreatic Cancer	62,200	49,800
Ovarian Cancer	19,900	12,800
Soft Tissue Sarcoma	10,500	4,100
Totals:	92,600	66,700

Solid tumors: CYT-0851 development plan

The solid tumor phase 2 monotherapy expansion cohorts of our CYT-0851 phase 1/2 trial include patients with pancreatic and ovarian cancers and soft tissue sarcomas. If warranted by the phase 1/2 data, and subject to FDA agreement, we could initiate one or more potentially registrational trials in 2023 for the treatment of either relapsed or refractory lymphoma or solid tumors.

We are currently dosing patients in the phase 1 portion of the phase 1/2 trial that evaluates two cohorts of combinations of CYT-0851 with gemcitabine or capecitabine for the treatment of solid tumors.

CYT-0851 monotherapy clinical trial design (Study CYT-0851-01)

Study CYT-0851-01 is a phase 1/2 clinical trial of both hematologic malignancies and solid cancers evaluating CYT-0851 in advanced cancer patients who have exhausted standard therapies. In November 2021 we completed enrollment in the phase 1 dose-escalation portion of the study, utilizing a standard 3+3 design to establish a single monotherapy dose for all malignancies. Seventy-three patients have been treated in 12 dose levels and 600 mg daily was established as the MTD and 400 mg daily was selected as the monotherapy RP2D. Upon identification of the monotherapy RP2D, we initiated phase 1 dose-escalation cohorts of CYT-0851 in combination with standard dosing of three standard-of-care chemotherapies: (1) rituximab plus bendamustine, (2) gemcitabine and (3) capecitabine. The starting dose of CYT-0851 with each combination is 100 mg daily, which will be escalated in each cohort independently according to a standard 3+3 design to a maximum of 400 mg daily. The primary endpoint for phase 1 is dose-limiting toxicities, or DLTs, to identify the MTD. Secondary endpoints are pharmacokinetics, safety, and preliminary anti-tumor activity. Our design also includes pharmacodynamic backfill cohorts that allow us to enroll up to 12 patients in total at any dose level to further characterize the safety, pharmacokinetic, and pharmacodynamic profiles for dose selection, as well as collect additional tumor biopsies for biomarker development.

Trial design for the phase 1 portion of the trial

Endpoints	
Primary	• Incidence of Dose-Limiting Toxicities
Secondary	• Objective Response and duration of response • Safety (AEs and changes in lab values and ECGs) • Pharmacokinetics
Exploratory	• Pharmacodynamics • Correlation between biomarker status and response • Evaluation of biomarkers

Tumors	Dose Escalation	Pharmacodynamic Backfill*
Hematologic	B-Cell NHL	DLBCL
	CLL	B-Cell Malignancies
	Multiple Myeloma	
Solid	Breast	Pancreatic Cancer
	Head and Neck	Small-cell Lung Cancer
	Soft tissue sarcoma	HPV+ HNSCC
	Ovarian	

3+3 Escalation Design

Dose Level	Total Daily Dose
1	30 mg**
2	40 mg**
3	60 mg**
4	90 mg**
5	90 mg
6	130 mg
7	200 mg
8	300 mg
9	400 mg
10	600 mg
11	800 mg**
12	1200 mg**

*Dose Levels 5+ may be expanded with up to 12 total patients to further evaluate safety, PK and PD

** Dose Levels split into BID dosing. At levels 11 and 12 due to number of capsules required.

Upon selection of a RP2D we initiated the phase 2 expansion phase of the study in January 2022 and are currently dosing patients. The primary endpoint for this phase is the objective response rate to characterize the anti-tumor activity of CYT-0851 in six disease-specific expansion cohorts: DLBCL, MM, FL, soft-tissue sarcoma, ovarian and pancreatic cancers. We made a strategic decision to delay opening the mantle cell lymphoma and triple negative breast cancer, or TNBC, cohorts based on the evolving treatment and regulatory landscapes. The secondary endpoints for this portion of the study include further assessment

of the clinical activity in terms of duration of response, progression-free survival, and overall survival, as well as safety and pharmacokinetics.

To assess the primary endpoint, each phase 2 cohort will proceed with a Simon two-stage design. This approach minimizes the number of patients to be enrolled. This design enrolls and evaluates the response in a set number of patients in the first stage. The proportion of responding patients is assessed and, if sufficient, enrollment into the second stage proceeds to further evaluate the response rate. Our target response rates for each indication are based on historical benchmarks for standard of care. Each cohort will independently guide future development for each disease indication and may include further expansion of the cohort in the current trial, commencement of randomized trials, pursuit of an accelerated approval registration pathway, therapeutic combination strategies or some permutation thereof.

Trial design for the phase 2 expansion cohorts

Endpoints	
Primary	• Objective response
Secondary	• Duration of response, PFS, and OS • Safety (AEs and changes in lab values and ECGs) • Pharmacokinetics
Exploratory	• Pharmacodynamics • Correlation between biomarker status and response • Evaluation of biomarkers

Cohort	Stage 1 (N)	Stage 2 (N)	Total (N)
DLBCL	12	13	25
Follicular Lymphoma	15	17	32
Multiple Myeloma	12	13	25
Ovarian Cancer	7	11	18
Pancreatic Cancer	13	21	34
Soft Tissue Sarcoma	13	21	34
Total	72	96	168

Current phase 1/2 trial (Study CYT-0851-01) interim results

As of November 15, 2021, we had treated 73 patients across 12 dose-escalation cohorts. We identified 600 mg daily as the MTD and selected 400 mg daily as the monotherapy RP2D. We performed an aggregated analysis for the safety and clinical activity.

Safety assessment

CYT-0851 has a favorable safety profile characterized by infrequent, primarily low-grade (Grade 1 or 2) and reversible adverse events, or AEs. Only 58% of patients have reported any treatment-related adverse events, or TRAEs, the majority of which were low-grade (Grade 1-2) and manageable. The most common CYT-0851-related AEs were primarily low grade and included fatigue (21% of patients), hyperuricemia (11%), and nausea (11%). We believe that these results support development of CYT-0851 not only as a monotherapy but also in combination with other anti-cancer agents given the lack of overlapping toxicities such as clinically significant myelosuppression, neuropathy, vomiting and diarrhea that typically preclude combination strategies.

Treatment related adverse events experienced by more 5% of patients on trial

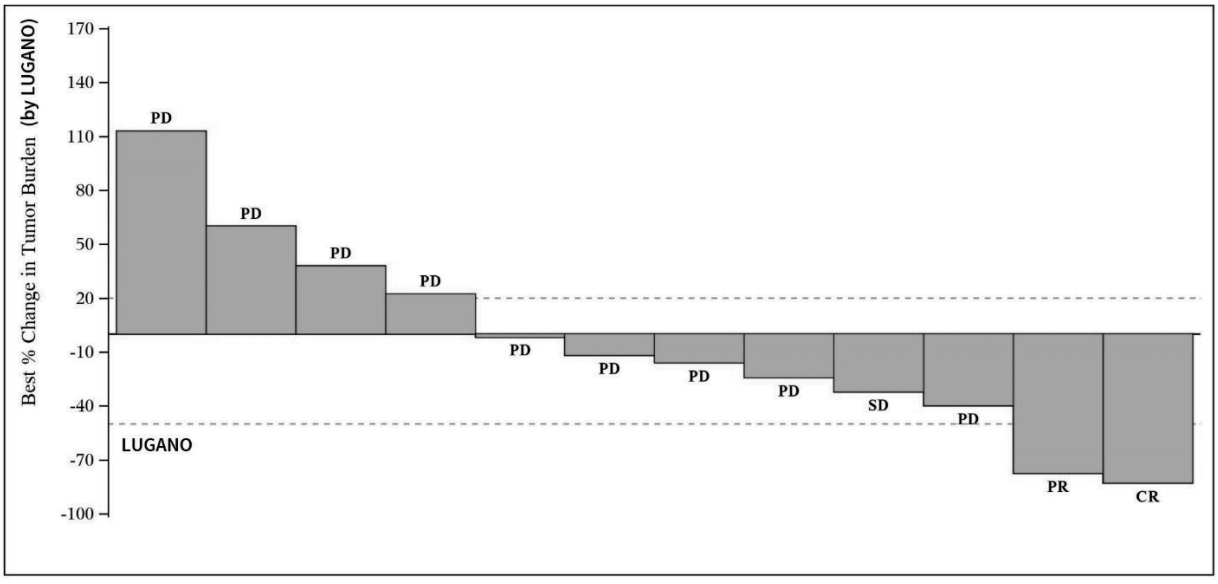
Adverse Event (Occurring in > 5% of pts)	Total Grade N (%)	Grade 3/4 N (%)
Fatigue	15 (20.5%)	3 (4.1%)
Hyperuricaemia	8 (11.0%)	0
Nausea	8 (11.0%)	0
Alopecia	7 (9.6%)	0
Constipation	6 (8.2%)	0
Headache	6 (8.2%)	0
Anaemia	5 (6.8%)	1 (1.4%)
Blood alkaline phosphatase increased	5 (6.8%)	0
Blood creatinine increased	5 (6.8%)	0
Lymphocyte count decreased	5 (6.8%)	0
Aspartate aminotransferase increased	4 (5.5%)	0
Blood bilirubin increased	4 (5.5%)	0

Efficacy assessment

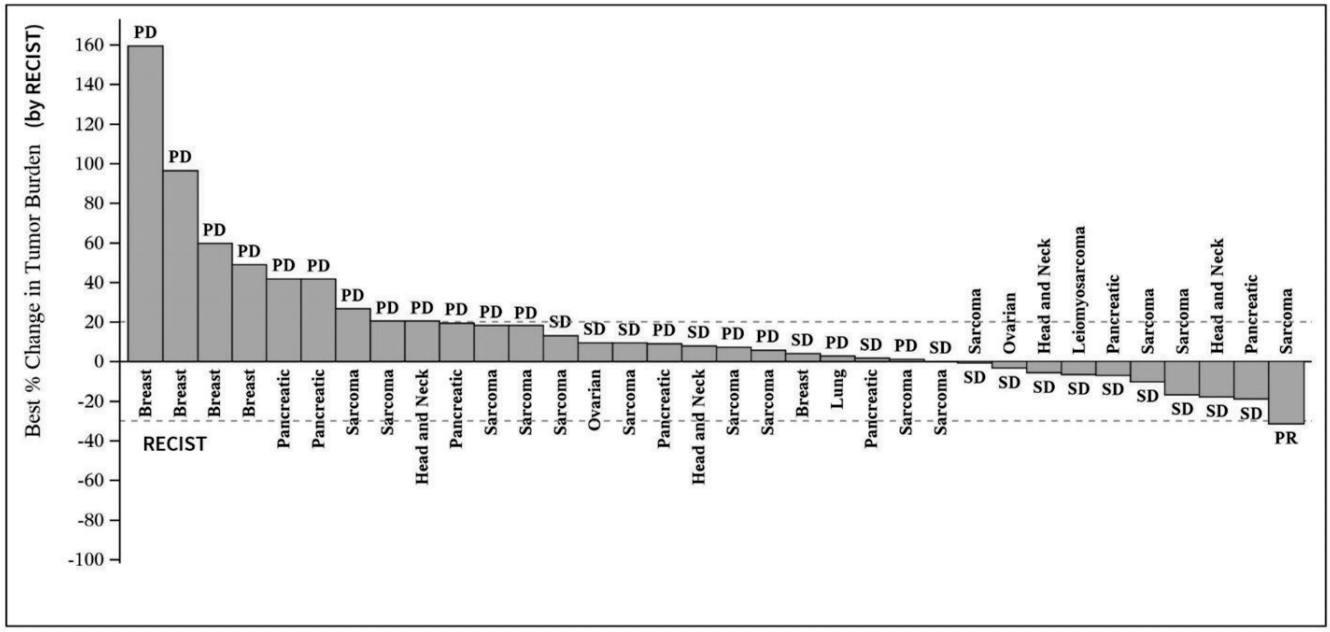
As of November 15, 2021, 46 patients were considered response-evaluable per protocol (treated with CYT-0851 and had at least one post-baseline disease assessment). One patient experienced a complete response, or CR, and two patients experienced partial responses, or PR. Seventeen of these patients had stable disease, or SD, and twenty-six of these patients experienced progressive disease, or PD, as their best overall response according to disease specific criteria (RECIST v1.1 or modified Lugano response criteria). The CR in FL and PR in DLBCL were confirmed by Lugano criteria, and the PR in soft tissue sarcoma was unconfirmed according to RECIST criteria.

Response evaluable Non Hodgkin Lymphoma patients and their best overall change in tumor size by Lugano criteria

PD: progressive disease; SD: stable disease; PR: partial response; CR: confirmed response



Response evaluable solid tumor patients and their best overall change in tumor size by RECIST criteria



Pharmacokinetic assessment

Preliminary pharmacokinetic analyses of CYT-0851 demonstrated approximately dose-proportional systemic exposure. A mean plasma effective half-life of approximately three days supported transition from twice daily to once daily administration. Furthermore, the minimum exposure projected to be clinically active, based on preclinical studies, was reached at 90 mg total daily dose.

Mechanism of action

CYT-0851 was identified through a phenotypic screening strategy that exploited a novel synthetic lethality between CD overexpression and HR inhibition. The screen was designed to select for compounds that induced synthetic lethality in CD-overexpressing cancer cells while sparing normal cells. By its nature, this type of screening strategy does not depend on, nor directly lead to, a precise understanding of where active drug candidates bind, nor their precise mechanism of action. While CYT-0851 advances in clinical testing, we continue to make progress on elucidating its molecular target and mechanism of action.

CYT-0851 initial patient targeting

Hematologic malignancies

We are initially targeting patients with DLBCL, FL and MM. CYT-0851 has several features that may differentiate it from other drugs on the market and in development for these indications. CYT-0851 is orally delivered and, if approved, would be dosed as an outpatient treatment. Many of the currently approved therapies are intravenous, require hospitalization or specialized centers for administration, have limited durations of treatment due to cumulative treatment side effects, or may not be feasibly administered in the community setting. The lack of clinically significant myelosuppression and the overall safety observed to date for CYT-0851 may allow prolonged dosing strategies and treatment of patients who are elderly or frail or have limited bone marrow and end organ reserve from prior therapies. We have not identified cumulative toxicities in humans treated up to 17 months at our RP2D or below. CYT-0851 can also be potentially combined with other therapies to both delay the onset of resistance and improve efficacy.

Our estimates described below for potentially addressable patient populations, where included, are based on a combination of third-party estimates, our internal estimates and management's experience. Starting with the annual incidence for our target indications, we estimated the number of patients that receive each line of treatment based on statistics reported in journal articles or specialized disease reports and then matched our proposed CYT-0851 treatment profile to each addressable patient line to estimate a total addressable population for CYT-0851. If we ultimately use one or more

biomarkers to select patients for future trials, we will adjust these addressable market estimates for the expected frequency of the biomarkers.

If approved, CYT-0851 may initially be available as a third or later line of treatment in DLBCL patients whose disease has progressed after two lines of standard therapy, or in patients who cannot tolerate standard first- or second-line therapies due to age, frailty or other factors. We estimate that there may be up to approximately 9,500 patients meeting these treatment criteria annually in the U.S.

In FL, CYT-0851 may initially be available for refractory patients as a third or later line of treatment. If CYT-0851 proves tolerable in FL patients, enabling a long duration of treatment, we believe the addressable FL market could be substantial. We estimate that there may be up to approximately 8,500 patients meeting these treatment criteria annually in the U.S.

We are including MM patients in our phase 2 expansion cohort study of CYT-0851. If results are positive, we anticipate targeting MM patients previously treated with three prior therapies, including a proteasome inhibitor, an immunomodulatory agent, or IMiD, and an anti-CD38 antibody.

Malignancy	Initial treatment opportunity
DLBCL	• 3rd Line+ • 1st/2nd Line+ for elderly/frail patients
FL	• 3rd Line+ • 1st/2nd Line+ for elderly/frail patients
MM	• Treated with three prior therapies including a proteosome inhibitor, IMiD and anti-CD38 antibody

Solid tumors

To date in our phase 1/2 clinical trial of CYT-0851, we have observed decreases in tumor burden in 10 patients with solid tumors including a partial response in a patient with soft tissue sarcoma (30% reduction). These observations are consistent with our preclinical data indicating that a subset of solid tumor cancer models, including pancreatic and breast cancer PDX models, is sensitive to CYT-0851. We are further evaluating the activity of CYT-0851 in patients with pancreatic and ovarian cancers, as well as soft tissue sarcomas, in our phase 2 expansion cohort study.

We currently define the initial target patient population in pancreatic cancer to be second and later line treatments. We estimate that there may be up to approximately 32,500 patients meeting these treatment criteria annually in the U.S.

In ovarian cancer, we could initially target patients who are progressing after platinum-based chemotherapy and PARP inhibitors for patients who are HR deficient. As the majority of patients are receiving both of these agents as part of a first-line regimen, we believe we could target second and later lines as an initial target population. We estimate that there may be up to approximately 13,000 patients meeting these treatment criteria annually in the U.S.

Soft tissue sarcomas are a heterogeneous collection of tumors from both a cell-of-origin and genetic standpoint. In the phase 1 dose-escalation portion of Study CYT-0851-01, in 15 response evaluable patients, we have observed seven sarcoma patients with SD, seven with PD and one with a partial response by RECIST criteria. Based on these observations, and the unmet need, we believe a path toward accelerated approval of CYT-0851 may be possible. Based on these initial clinical results, we anticipate the initial target population in soft tissue sarcomas will be second or later line treatment.

Tumor type	Initial treatment opportunity
Metastatic or recurrent pancreatic cancer	• 2nd Line+
Advanced ovarian cancer	• 2nd Line+
Soft tissue sarcoma	• 2nd Line+

Preclinical Programs

CYT-1853

Program overview

Our next-generation compound, CYT-1853, was designed to exploit the same novel synthetic lethality targeted by CYT-0851. The primary goal of the program was to discover and develop a more potent compound. Our rationale was that a more potent compound might not only demonstrate improved anti-cancer activity in sensitive tumor types but may also be effective in cancers relatively insensitive to the first-generation compound. After extensive screening efforts, CYT-1853 was selected as our more potent next-generation drug candidate. We expect to complete IND-enabling studies with CYT-1853 in the first half of 2022 and, if the data supports an overall risk-benefit improvement and differentiation from CYT-0851, we plan to file an IND application with the FDA by year-end 2022. Evaluation of the potential differentiation of CYT-1853 from CYT-0851 will include consideration of results of ongoing pre-clinical evaluation of CYT-1853 as well as ongoing clinical evaluation of CYT-0851. For example, if the potential clinical benefits of CYT-0851 are observed to be greater than originally hypothesized the comparative benefits of CYT-1853 could be reduced which could lead to a decision to not move CYT-1853 into the clinic.

Preclinical data

To identify compounds more potent than our first generation drug candidate, we used a cell-based screening assay to measure and compare the potency of novel compounds to that of CYT-0851. In the original phenotypic screening assay, CYT-1853 was 34-fold more potent than CYT-0851 at inhibiting in vitro cell proliferation of the AID-overexpressing Daudi Burkitt's lymphoma cell line.

Beyond Burkitt's lymphoma, CYT-1853 has demonstrated broad-spectrum anti-cancer activity across a panel of over 400 diverse human cancer cell lines, generally displaying about 10-fold improved potency over CYT-0851 across the cell line panel. The observation that most of the cell lines were more sensitive to CYT-1853 than CYT-0851 supports the possibility that CYT-1853 may be able to treat tumor types where CYT-0851 lacks sufficient efficacy. Importantly, CYT-1853 has also demonstrated dose-dependent in vivo anti-cancer activity in multiple mouse models of human cancer at tolerated doses. Additional in vitro and in vivo preclinical studies are underway to further characterize and evaluate the overall risk-benefit profile of CYT-1853 and potential differentiation from CYT-0851.

Undisclosed Targets 2 & 3

Program overview

In 2021, we advanced two additional drug discovery projects focused on identifying inhibitors of DNA damage repair. Rather than using a phenotypic screening paradigm as we did for CYT-0851 and CYT-1853, in both of these projects we are using a more traditional drug discovery approach by first identifying the molecular target of interest. The first of these undisclosed targets (Target 2) plays a key role in NHEJ and the second (Target 3) in MMEJ DNA repair pathways. For both targeted drug discovery projects, we have identified subsets of cancers that, we believe, uniquely depend on the target of interest for their survival and we are working to confirm patient selection biomarkers to identify these cancer subsets for use in drug candidate development. Both undisclosed target projects are preclinical stage, and we anticipate reaching the drug candidate nomination stage in 2023.

Additionally, we continually monitor the DDR and synthetic lethality landscape for promising and differentiated new target opportunities to initiate in-house or in-license to enrich our drug candidate pipeline.

Competition

While we believe that our technology, drug development expertise and deep understanding of DDR biology provide us with certain competitive advantages, we face competition from many pharmaceutical and biotechnology companies, as well as academic institutions that are involved in the discovery, development, and commercialization of oncology therapeutics.

Many other companies are advancing oncology therapeutics that target DNA repair, including AbbVie, Artios Pharma, AstraZeneca, BeiGene, Breakpoint Therapeutics, Bristol Myers Squibb, Clovis Oncology, EMD Serono, Foghorn Therapeutics, Genentech, GlaxoSmithKline, IDEAYA Biosciences, Merck & Co, Pfizer, Rain Therapeutics, Repare Therapeutics, Ryvu Therapeutics, and Tango Therapeutics. In addition, academic and other non-profit organizations have early-stage ongoing drug discovery efforts that target DNA repair, such as Cancer Research UK, University of Chicago, and Dana Farber Cancer Institute. In addition, to gain market acceptance for our drug candidates, if they are approved for

commercial sale, we will face competition from numerous companies that are developing novel cancer therapeutics using a variety of modalities other than targeting DNA repair.

Our success will be based upon our ability to advance CYT-0851 and our portfolio of DDR drug candidates through clinical development to regulatory approval and successful commercialization. We believe our therapeutics have the potential to be more tolerable and more effective than competing products in our target indications both as a monotherapy and in combination with standard-of-care chemotherapy. Our competitive position will also depend on our ability to attract and retain qualified personnel relative to peer companies in light of the highly competitive market for talent in the biopharmaceutical industry, to obtain and maintain patent protection or otherwise to develop proprietary products and protect and enforce our intellectual property, and to secure sufficient capital to support our research and development efforts in a way that allows us achieve our preclinical and clinical development goals relative to our competitors.

We could see a reduction or elimination in our commercial opportunity if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, or are less expensive than our drug candidates. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Intellectual property

We strive to obtain, maintain, protect, enforce and enhance the proprietary technology, inventions and improvements that we believe are commercially important to the development of our business, including by seeking, maintaining, enforcing and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how, and continuing technological innovation to develop, strengthen and maintain our proprietary position in our field.

Our future commercial success depends, in part, on our ability to: obtain and maintain patent and other intellectual property and proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our intellectual property and proprietary rights, in particular our patents rights; preserve the confidentiality of our trade secrets; operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and other intellectual property and proprietary rights of third parties; and prevent others from infringing, misappropriating or otherwise violating our intellectual property and proprietary rights. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents, trade secrets or other intellectual property or proprietary rights that cover these activities.

As of February 3, 2022 we owned four issued U.S. patents, one allowed U.S. non-provisional patent application, five pending U.S. non-provisional patent applications, two pending U.S. provisional patent application, two issued foreign patents, one allowed foreign patent application, 69 pending foreign patent applications, and one pending Patent Cooperation Treaty, or PCT, applications, as detailed in the table below.

Related To	Type of IP protection	Application / Patent No.	Jurisdiction	Status	Expiration Date
Early analogs of CYT-0851	Composition of matter	2018301381	Australia	Pending	7/11/2038 (expected)
Early analogs of CYT-0851	Composition of matter	3069003	Canada	Pending	7/11/2038 (expected)
Early analogs of CYT-0851	Composition of matter	201880058652.7	China	Pending	7/11/2038 (expected)
Early analogs of CYT-0851	Composition of matter	18746518.2	EPO	Pending	7/11/2038 (expected)
Early analogs of CYT-0851	Composition of matter	2020-523682	Japan	Pending	7/11/2038 (expected)
Early analogs of CYT-0851	Composition of matter	MX/A/2020/000367	Mexico	Pending	7/11/2038 (expected)
Early analogs of CYT-0851	Composition of matter	16/623,850	United States	Allowed	7/11/2038 (expected)
CYT-0851	Composition of matter	20180102580	Argentina	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	107131953	Taiwan	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	10,590,122	United States	Issued	9/11/2038
CYT-0851	Composition of matter	10,336,746	United States	Issued	9/11/2038
CYT-0851	Use	11,084,812	United States	Issued	9/11/2038
CYT-0851	Composition of matter and use	17/363,099	United States	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	2018328818	Australia	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	BR112020004828-3	Brazil	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	3075062	Canada	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	201880072664.5	China	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	18782257.2	EPO	Allowed	9/11/2038 (expected)
CYT-0851	Composition of matter	62020015272	Hong Kong	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	273156	Israel	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	202027013549	India	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	2020-514206	Japan	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	10-2020-7010585	South Korea	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	MX/a/2020/002745	Mexico	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	762501	New Zealand	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	1-2020-550079	Philippines	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	2020113064	Russia	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	11202002069W	Singapore	Issued	9/11/2038
CYT-0851	Composition of matter	10202107087Y	Singapore	Issued	9/11/2038
CYT-0851	Composition of matter	2020/01436	South Africa	Pending	9/11/2038 (expected)
CYT-0851	Composition of matter	2021/04029	South Africa	Pending	9/11/2038 (expected)
CYT-1853	Composition of matter	109108203	Taiwan	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	11247988	United States	Issued	3/12/2040
CYT-1853	Composition of matter	17/552,577	United States	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	2020235089	Australia	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	BR112021017336-6	Brazil	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	202080035279.0	China	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	20768883.9	EPO	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	285889	Israel	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	202127038778	India	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	2021-553834	Japan	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	10-2021-7032591	South Korea	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	MX/a/2021/010916	Mexico	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	779502	New Zealand	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	1-2021-552147	Philippines	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	2021129476	Russia	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	11202109399S	Singapore	Pending	3/12/2040 (expected)
CYT-1853	Composition of matter	2021/06284	South Africa	Pending	3/12/2040 (expected)

Related To	Type of IP protection	Application / Patent No.	Jurisdiction	Status	Expiration Date
CYT-0851	Use	109110065	Taiwan	Pending	3/25/2040 (expected)
CYT-0851	Use	16/829,099	United States	Pending	3/25/2040 (expected)
CYT-0851	Use	2020244809	Australia	Pending	3/25/2040 (expected)
CYT-0851	Use	BR112021017325-0	Brazil	Pending	3/25/2040 (expected)
CYT-0851	Use	3133005	Canada	Pending	3/25/2040 (expected)
CYT-0851	Use	202080038048.5	China	Pending	3/25/2040 (expected)
CYT-0851	Use	20718118.1	EPO	Pending	3/25/2040 (expected)
CYT-0851	Use	285927	Israel	Pending	3/25/2040 (expected)
CYT-0851	Use	202127043210	India	Pending	3/25/2040 (expected)
CYT-0851	Use	2021-557340	Japan	Pending	3/25/2040 (expected)
CYT-0851	Use	10-2021-7034165	South Korea	Pending	3/25/2040 (expected)
CYT-0851	Use	MX/a/2021/011689	Mexico	Pending	3/25/2040 (expected)
CYT-0851	Use	779894	New Zealand	Pending	3/25/2040 (expected)
CYT-0851	Use	1-2021-552205	Philippines	Pending	3/25/2040 (expected)
CYT-0851	Use	2021130781	Russia	Pending	3/25/2040 (expected)
CYT-0851	Use	11202109844Q	Singapore	Pending	3/25/2040 (expected)
CYT-0851	Use	2021/06741	South Africa	Pending	3/25/2040 (expected)
CYT-0851	Use	109121113	Taiwan	Pending	6/22/2040 (expected)
CYT-0851	Use	16/907,430	United States	Pending	6/22/2040 (expected)
CYT-0851	Use	2020296195	Australia	Pending	6/22/2040 (expected)
CYT-0851	Use	BR112021025491-9	Brazil	Pending	6/22/2040 (expected)
CYT-0851	Use	3143716	Canada	Pending	6/22/2040 (expected)
CYT-0851	Use	20737805	EPO	Pending	6/22/2040 (expected)
CYT-0851	Use	288707	Israel	Pending	6/22/2040 (expected)
CYT-0851	Use	TBD	Japan	Pending	6/22/2040 (expected)
CYT-0851	Use	10-2022-7002235	South Korea	Pending	6/22/2040 (expected)
CYT-0851	Use	MX/a/2021/016049	Mexico	Pending	6/22/2040 (expected)
CYT-0851	Use	783444	New Zealand	Pending	6/22/2040 (expected)
CYT-0851	Use	1-2021-553132	Philippines	Pending	6/22/2040 (expected)
CYT-0851	Use	11202113720W	Singapore	Pending	6/22/2040 (expected)
CYT-0851	Use	2021/10265	South Africa	Pending	6/22/2040 (expected)
CYT-0851	Use	110107561	Taiwan	Pending	3/3/2041 (expected)
CYT-0851	Use	17/191,220	United States	Pending	3/3/2041 (expected)
CYT-0851	Use	63/148,683	United States	Pending	3/3/2041 (expected)
CYT-0851	Use	PCT/US2021/020661	PCT	Pending	3/3/2041 (expected)
CYT-0851	Use	63/234,293	United States	Pending	8/18/2042 (expected)

A subset of our patent portfolio relates to CYT-0851 and includes patents and patent applications directed to CYT-0851 and certain methods of use. As of February 3, 2022, we owned three issued U.S. patents, four pending U.S. non-provisional patent applications, two pending U.S. provisional patent applications, two issued foreign patents, one allowed foreign patent application, 47 pending foreign patent applications, and one pending PCT application related to CYT-0851. As of February 3, 2022, we owned one issued U.S. patent, one pending U.S. non-provisional patent application, and 16 pending foreign patent applications related to CYT-1853. The foregoing patents and patent applications will, if issued, have statutory expiration dates between 2038 and 2042, excluding any patent term adjustments or patent term extensions that may be available.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file patent applications, including the U.S., the patent term is 20 years from the earliest date of filing a non-provisional patent application. In addition, in the U.S., in certain instances, a patent term can be extended by a patent term adjustment to recapture a portion of the U.S. Patent and Trademark Office, or the USPTO, review period in issuing the patent and/or by patent term extension to account for a portion of the term effectively lost as a result of the FDA regulatory review period, and a patent term may be shortened if a patent is terminally disclaimed over an earlier filed patent. As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our drug candidates will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our owned and licensed pending patent applications, and any patent applications that we may in the future file or license from third parties, may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our owned or licensed patents or whether such claims, if issued, will cover our drug candidates, provide sufficient protection from competitors or otherwise provide any competitive advantage. Any issued patents that we may receive or in-license in the future may be challenged, invalidated, narrowed, held unenforceable, infringed or circumvented. In addition, because of the extensive time required for clinical development and regulatory review of a drug candidate we may develop, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide.

We cannot be certain of the priority of inventions covered by our owned or licensed patents and pending patent applications, in part because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and because publication of discoveries in the scientific or patent literature often lags behind actual discoveries and patent application filings. Accordingly, we may not have been the first to invent the subject matter disclosed in some of our patents and patent applications or the first to file patent applications covering such subject matter.

In addition to patent protection, we rely upon unpatented trade secrets and confidential know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and confidential know-how are difficult to protect. We seek to protect our proprietary information, in part, using confidentiality agreements with any collaborators, scientific advisors, employees and consultants and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with consultants, scientific advisors and collaborators who are involved in the creation of our technology. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, grant us ownership of technologies that are developed through our relationship with the counterparty. However, these agreements may not provide meaningful protection, and we cannot guarantee that we have executed such agreements with all applicable counterparties. These agreements may also be breached, and we may not have an adequate remedy for any such breach. In addition, our trade secrets and/or confidential know-how may become known or be independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or to obtain or use information that we regard as proprietary. Although we take steps to protect our proprietary information, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information.

See “Risk Factors – Risks Related to our Intellectual Property” for a more comprehensive description of risks related to our intellectual property.

Manufacturing

We currently rely and expect to continue relying on contract development and manufacturing organizations, or CDMOs, to manufacture our drug substances and drug products for preclinical and clinical testing and for future commercial manufacturing of our products. We require the CDMOs manufacturing our drug substances and drug products for clinical testing to comply with current good manufacturing practices, or cGMP, requirements. We have assembled a team of experienced employees and consultants to provide the required technical, quality, and regulatory oversight over our CDMOs. The development of our analytical methods to control and analyze our products is maintain at a phase appropriate level corresponding to the clinical development.

Our drug substances are small molecules and our CDMOs manufacture them by synthetic processes from available starting materials. We expect to continue the development of the manufacturing processes of our drug substances at CDMOs and to produce them in a cost-effective manner and meeting all regulatory requirements.

Government regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, recordkeeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs. We, along with our vendors, contract research organizations and contract manufacturers, will be required to navigate the various preclinical, clinical, manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our drug candidates. The process of obtaining regulatory approvals of drugs and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

In the United States, where we are initially focusing our drug development, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, as amended, its implementing regulations and other laws. If we fail to comply with applicable FDA or other requirements at any time with respect to product development, clinical testing, approval or any other legal requirements relating to product manufacture, processing, handling, storage, quality control, safety, marketing, advertising, promotion, packaging, labeling, export, import, distribution, or sale, we may become subject

to administrative or judicial sanctions or other legal consequences. These sanctions or consequences could include, among other things, the FDA's refusal to approve pending applications, issuance of clinical holds for ongoing studies, suspension or revocation of approved applications, warning or untitled letters, product withdrawals or recalls, product seizures, relabeling or repackaging, total or partial suspensions of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution.

The process required by the FDA before our drug candidates are approved as drugs for therapeutic indications and may be marketed in the United States generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies
- conducted in accordance with good laboratory practice, or GLP, requirements;
- completion of the manufacture, under current good manufacturing practices, or cGMP, conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical trials may begin;
- approval by an institutional review board, or IRB, or independent ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with applicable IND regulations, good clinical practice, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of a new drug application, or NDA;
- a determination by the FDA within 60 days of its receipt of an NDA, to accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the sponsor and the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potentially, satisfactory completion of FDA audit of the clinical trial sites that generated the data in support of the NDA;
- payment of user fees for FDA review of the NDA; and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States.

Preclinical studies and clinical trials for drugs

Before testing any drug in humans, the drug candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as in vitro and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulation, including GLP requirements for safety/toxicology studies. The results of the preclinical studies, together with manufacturing information and analytical data, must be submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before clinical trials may begin. Some long-term preclinical testing may continue after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a full or partial clinical hold. FDA must notify the sponsor of the grounds for the hold and any identified deficiencies must be resolved before the clinical trial can begin. Submission of an IND may result in the FDA not allowing clinical trials to commence or not allowing clinical trials to commence on the terms originally specified in the IND. A clinical hold can also be imposed once a trial has already begun, thereby halting the trial until the deficiencies articulated by FDA are corrected.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, who generally are physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among

other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable compared to the anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may recommend to the sponsor to halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as a lack of observed efficacy. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trials to public registries. For example, information about clinical trials, including results for clinical trials other than phase 1 investigations, must be submitted within specific timeframes for publication on www.ClinicalTrials.gov, a clinical trials database maintained by the National Institutes of Health.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, FDA will nevertheless accept the results of the study in support of an NDA if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials to evaluate therapeutic indications to support NDAs for marketing approval are typically conducted in three sequential phases, which may overlap.

- *Phase 1*—Phase 1 clinical trials involve initial introduction of the investigational product into healthy human volunteers or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism, distribution, and excretion of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- *Phase 2*—Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the drug's potential efficacy, to determine the optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. It is common to combine phase 1 and phase 2 studies in oncology drug development.
- *Phase 3*—Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labeling.

Post-approval trials, sometimes referred to as phase 4 clinical trials or post-marketing studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of phase 4 clinical trials as a condition of NDA approval.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators fifteen days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human volunteers and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug candidate and finalize a process for manufacturing

the drug product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

U.S. marketing approval for drugs

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA package requesting approval to market the product for one or more indications. An NDA is a request for approval to market a new drug for one or more specified indications and must contain proof of the drug's safety and efficacy for the requested indications. The marketing application is required to include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA must approve an NDA before a drug may be marketed in the United States.

The FDA reviews all submitted NDAs before it accepts them for filing and may request additional information rather than accepting the NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt, and such decision could include a refusal to file by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective for the indications sought and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. Under the goals and polices agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of a new molecular entity NDA and respond to the applicant, and six months from the filing date of a new molecular entity NDA for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Further, under PDUFA, as amended, each NDA must be accompanied by a substantial user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy, or REMS, if it believes that a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug outweigh its risks. A REMS can include use of risk evaluation and mitigation strategies like medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk-minimization tools.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling,

require that post-approval studies, including phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the product available in the United States for the disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan products are eligible for certain incentives, including tax credits for qualified clinical testing and waiver of application fees.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to a seven-year period of marketing exclusivity during which the FDA may not approve any other applications to market the same therapeutic agent for the same indication, except in limited circumstances, such as a subsequent product's showing of clinical superiority over the product with orphan exclusivity or where the original applicant cannot produce sufficient quantities of product. Competitors, however, may receive approval of different therapeutic agents for the indication for which the orphan product has exclusivity or obtain approval for the same therapeutic agent for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for the same therapeutic agent for the same indication before we do, unless we are able to demonstrate that our product is clinically superior. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Further, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited development and review programs for drugs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients more quickly than standard FDA review timelines typically permit.

A new drug is eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed. Rolling review means that the agency may review portions of the marketing application before the sponsor submits the complete application. In addition, a new drug may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient drug development program beginning as early as phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including Priority Review designation and Accelerated Approval. A product is eligible for Priority Review, once an NDA is submitted, if the drug that is the subject of the marketing application has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under priority review, the FDA's goal date to take action on the marketing application is six months compared to ten months for a standard review. Products are eligible for Accelerated Approval if they can be shown to have an effect on a surrogate endpoint that is

reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

Accelerated Approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit. The FDA may withdraw approval of a drug or an indication approved under Accelerated Approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, the FDA generally requires, as a condition for Accelerated Approval, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period. After the 120-day period has passed, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval, though they may expedite the development or review process.

Pediatric information and pediatric exclusivity

The Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, as amended, certain NDAs and NDA supplements must contain data that can be used to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The FD&C Act requires that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the phase 3 or phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

A drug can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing marketing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

U.S. post-approval requirements for drugs

Drugs manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, reporting of adverse experiences with the product, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the generation of additional data or the conduct of additional preclinical studies and clinical trials.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-market testing, including phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. In addition, drug manufacturers and their subcontractors involved

in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements. Failure to comply with statutory and regulatory requirements may subject a manufacturer to legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution. There is also a continuing, annual prescription drug product program user fee.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs; or mandated modification of promotional materials and labeling and issuance of corrective information.

Patent term restoration and extension

Depending upon the timing, duration and specifics of FDA approval of our drug candidates, some of a sponsor's U.S. patents may be eligible for limited patent term extension, or PTE, under the Hatch-Waxman Amendments. As compensation for patent term lost during product development and the FDA regulatory review process, the Hatch-Waxman Amendments permit a patent restoration term, which is limited to a maximum of five years, or less if the extended patent term would exceed 14 years after the date of the regulatory approval of the product. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA, less any time the sponsor did not act with due diligence during the period and the approval of that application less any time the sponsor did not act with due diligence during the period. Only one patent applicable to an approved drug or drug product is eligible for the extension, only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended, and the application for the extension must be submitted prior to the expiration of the patent. Moreover, a given patent may only extended once based on a single product. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, we may intend to apply for restoration of a patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA. However, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. There can be no assurance that we will benefit from any PTE or favorable adjustment to the term of any of our patents. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

Marketing exclusivity

Market exclusivity provisions authorized under the FD&C Act can delay the submission or the approval of certain marketing applications. The FD&C Act provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for

review an abbreviated new drug application, or ANDA, or an NDA submitted under Section 505(b)(2), or 505(b)(2) NDA, submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FD&C Act alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

In addition, pediatric exclusivity and orphan drug exclusivity, as described above, may offer a six-month or seven-year period of exclusivity, respectively, except in certain circumstances.

Regulation of companion diagnostics

Companion diagnostics are diagnostic tests designed to identify patients who may be most likely to benefit from a particular therapeutic product, identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product, or monitor response to treatment with a particular therapeutic product. On August 6, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance document, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although the FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, the FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. The FDA also issued a draft guidance in July 2016 setting forth the principles for co-development of an in vitro companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding in vitro companion diagnostic.

Companion diagnostics are regulated as medical devices by the FDA. In the United States, the FD&C Act, and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification, or 510(k), and approval of a premarket approval application, or PMA.

To obtain 510(k) clearance for a medical device, or for certain modifications to devices that have received 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or to a pre-amendment device that was in commercial distribution before May 28, 1976, or a predicate device, for which the FDA has not yet called for the submission of a PMA. In making a determination that the device is substantially equivalent to a predicate device, the FDA compares the proposed device to the predicate device and assesses whether the subject device is comparable to the predicate device with respect to intended use, technology, design and other features which could affect safety and effectiveness. If the FDA determines that the subject device is substantially equivalent to the predicate device, the subject device may be cleared for marketing. The 510(k) premarket notification pathway generally takes from three to twelve months from the date the application is completed, but can take significantly longer.

A PMA must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the quality system regulation, or QSR, which requires manufacturers to follow design, testing, control,

documentation and other quality assurance procedures. The FDA's review of an initial PMA is required by statute to take between six to ten months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny the approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

Once cleared or approved, the companion diagnostic device must adhere to post-marketing requirements including the requirements of the FDA's QSR, adverse event reporting, recalls and corrections along with product marketing requirements and limitations. Like drug makers, companion diagnostic makers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and the company's facilities for compliance with its authorities.

Other regulatory matters

Manufacturing, sales, promotion and other activities of drug candidates following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, which may include the Centers for Medicare & Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

Other healthcare laws

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below.

- The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid; a person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

- The federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using, or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs.

- The federal civil monetary penalties laws impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary, if the person knows or should know it is

likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies.

- The Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for knowingly and willfully executing a scheme, or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, or falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, impose, among other things, specified requirements on covered entities and their business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.
- The Physician Payments Sunshine Act, which imposes annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, for certain payments and "transfers of value" provided to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Since January 1, 2022, these reporting obligations extend to include transfers of value made in the previous year to certain non-physician providers such as physician assistants and nurse practitioners.
- Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers.
- Analogous state and foreign laws and regulations may be broader in scope than the provisions described above and may apply regardless of payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and relevant federal government compliance guidance; require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers; restrict marketing practices or require disclosure of marketing expenditures and pricing information. State and foreign laws may govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

Coverage and reimbursement by third-party payors

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a drug candidate is approved, sales of the product will depend, in part, on the extent to which

third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. In the United States, the Medicare and Medicaid programs are increasingly used as models for how private and other governmental payors develop their coverage and reimbursement policies for drugs. No uniform policy of coverage and reimbursement for drug products exists, however, among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, which will require additional expenditure above and beyond the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, drug candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Current and future healthcare reform legislation

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments to the Affordable Care Act in the future. For example, tax reform legislation was enacted at the end of 2017 that eliminated the tax penalty established under the Affordable Care for individuals who do not maintain mandated health insurance coverage beginning in 2019. The Affordable care Act has also been subject to judicial challenge. In On June 17, 2021, the U.S. Supreme Court dismissed the latest judicial challenge to the Affordable Care Act brought by several states without specifically ruling on the constitutionality of the Affordable Care Act.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. In addition, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, including bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal legislation

designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Although a number of these measures may require additional authorization to become effective, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

On July 24, 2020, President Trump announced a number of executive orders related to prescription drug pricing that attempt to implement several of the Administration's proposals, including a policy that would tie Medicare Part B drug prices to international drug prices; one that directs HHS to finalize the Canadian drug importation proposed rule previously issued by HHS and makes other changes allowing for personal importation of drugs from Canada; and one that directs HHS to finalize the rulemaking process on modifying the anti-kickback law safe harbors for plans, pharmacies, and pharmaceutical benefit managers after HHS confirms that the action is not projected to increase federal spending, Medicare beneficiary premiums, or patients' total out-of-pocket costs. The Biden administration has focused on reforms that would address the high cost of drugs. In response to an Executive Order from President Biden, the Secretary of HHS issued a comprehensive plan for addressing high drug prices that describes a number of legislative approaches and identifies administrative tools to address the high cost of drugs. And Democrats included drug pricing reform provisions reflecting elements of the plan in a broader proposed spending package in late 2021 - such as capping Medicare Part D patients out-of-pocket costs; establishing penalties for drug prices that increase faster than inflation in Medicare; and authorizing the federal government to negotiate prices on certain, select high cost drugs under Medicare Parts B and D.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Healthcare reform efforts have been and may continue to be subject to scrutiny and legal challenge. For example, revisions to regulations under the federal anti-kickback statute would remove protection for traditional Medicare Part D discounts offered by pharmaceutical manufacturers to pharmacy benefit managers and health plans. Pursuant to court order, the removal was delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Other U.S. environmental, health and safety laws and regulations

We may be subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Government regulation of drugs outside of the United States

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things,

clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution would apply to any product that is approved outside the United States.

Facilities

Our corporate headquarters is located at 128 Spring St, Building A, Suite 510, Lexington, MA 02421, where we lease and occupy approximately 20,167 square feet of office and laboratory space. The current term of our 128 Spring St. lease expires in 2025.

To meet the future needs of our business, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

Human Capital

As of December 31, 2021, we had 40 full-time employees. Twenty-one of our employees have M.D. or Ph.D. degrees. Within our workforce, 30 employees are engaged in research and development and 10 are engaged in business development, finance, legal, human resources, and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital priorities and objectives include, as applicable, attracting, recruiting, retaining, and developing our staff. We seek to create and maintain a workplace with an inclusive culture that provides challenging and rewarding work, and creates the opportunity for everyone to contribute their best on behalf of patients and all stakeholders we serve. The principal purposes of our equity incentive plans are to support these objectives, and to recognize staff member performance and align it to the growth and success of the company. Share-based compensation awards and cash-based performance bonus awards are extended to selected employees, consultants and directors.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and related notes appearing at the end of this Annual Report on Form 10-K, before deciding to invest in our common stock. Some of the following risks and uncertainties are, and will be, exacerbated by the COVID-19 pandemic (including any resurgences, including due to variants, thereof) and any worsening of the global business and economic environment as a result. If any of the events or developments described below were to occur, our business, prospects, operating results and financial condition could suffer materially, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks related to our financial position and need for additional capital

We have a limited operating history and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and predict our future success and viability.

We are a clinical-stage biopharmaceutical company with a limited operating history. We were incorporated in 2012, and our operations to date have been focused on developing our initial drug candidates, organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, obtaining, maintaining, protecting and enforcing our intellectual property, identifying potential drug candidates, undertaking preclinical and clinical studies and establishing arrangements with third parties for the manufacture of initial quantities of our drug candidates and component materials. We have not yet demonstrated an ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization.

In addition, as a research and development stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. If our drug candidates have successful clinical trial results and are able to obtain marketing approvals, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and results of operations to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since our inception, we have devoted all of our efforts to research and development and we have incurred significant operating losses. As of December 31, 2021, we had an accumulated deficit of $92.1 million. To date we have financed our operations primarily through private placements of our preferred stock and proceeds from our initial public offering. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- advance ongoing and planned development of our lead drug candidate, CYT-0851, including the enrollment of phase 2 monotherapy expansion cohorts and enrollment of patient cohorts to assess tolerability and preliminary activity of CYT-0851 combinations with three standard-of-care cancer therapies;
- advance our preclinical drug candidate CYT-1853 toward an investigational new drug, or IND, application, submission and into clinical trials;
- continue the preclinical development of additional drug candidates from our current research programs;
- initiate preclinical testing for any new drug candidates we identify and develop;
- pursue potential in-licensing opportunities for preclinical assets;
- obtain, maintain, expand, enforce, defend and protect our trade secrets and intellectual property portfolio;
- hire additional research and development personnel;

- add operational, legal, compliance, financial and management information systems and personnel to support our research, product development and operations as a public company;
- increase our laboratory facilities and office space to support the above;
- operate as a public company;
- expand our research capabilities and operations internationally;
- seek marketing approvals for any of our drug candidates that successfully complete clinical trials; and
- ultimately, establish a sales, marketing, pharmacovigilance, medical affairs, regulatory and distribution infrastructure to commercialize any products for which we may obtain marketing approval.

We expect that it will be many years, if ever, before we have a drug candidate ready for commercialization. To become and remain profitable, we must develop and, either directly or through collaborators, eventually commercialize a medicine or medicines with significant market potential. This will require us to be successful in a range of challenging activities, including identifying drug candidates, completing preclinical testing and clinical trials of drug candidates, obtaining marketing approval for these drug candidates, manufacturing, marketing, and selling those medicines for which we may obtain marketing approval, and satisfying any post-marketing regulatory requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. We are unable to predict the extent of any future losses or when we will become profitable, if at all. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We will need substantial additional funding. If we are unable to raise capital when needed, we will be forced to delay, reduce, or eliminate our research and drug development programs or future commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate clinical trials of, and seek marketing approval for, our drug candidates. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we will be forced to delay, reduce, or eliminate our research and product development programs or future commercialization efforts.

Additional fundraising efforts, when needed, may divert our management's attention from their day-to-day activities, which may adversely affect our ability to advance our drug candidates or develop new drug candidates. If we raise additional capital through future collaborations, strategic alliances or third-party licensing arrangements, we may have to relinquish certain valuable rights to our intellectual property, future revenue streams, research programs or drug candidates, or grant licenses on terms that may not be favorable to us.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to obtain funding on a reasonable and timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs, clinical research, or the commercialization of any drug candidate, or grant rights to develop and market drug candidates that we would otherwise develop and market ourselves. We may be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

We have never generated revenue from product sales and may never be profitable.

We are currently only in the phase 2 expansion portion of the phase 1/2 clinical trial for our most advanced drug candidate, CYT-0851. We expect that it will be many years, if ever, before CYT-0851 or any other drug candidate is ready for commercialization. To become and remain profitable, we must succeed in developing, obtaining marketing approval for and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including advancing CTY-0851 through clinical development as a monotherapy or in combination with other drugs, completing preclinical testing and clinical trials of our current or future drug candidates, establishing and maintaining arrangements with third parties for the manufacture of clinical supplies of our drug candidates, obtaining marketing approval for our drug candidates and manufacturing, marketing, selling and obtaining reimbursement for any products for which we may obtain marketing approval, and maintaining regulatory requirements while a product is on the market. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Our future ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial net operating losses, or NOLs, during our history and we may not achieve profitability prior to the time that certain of our NOLs expire. U.S. federal and certain state NOLs generated in years beginning after December 31, 2017 are not subject to expiration. Federal NOLs generally may not be carried back to prior taxable years except that, under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, federal NOLs generated in 2018, 2019, and 2020 may be carried back to each of the five taxable years preceding the taxable year in which the loss arises. Additionally, for taxable years beginning after December 31, 2020, the deductibility of federal NOLs generated in taxable years beginning after December 31, 2017 is limited to 80% of our taxable income in such taxable year. NOLs generated in taxable years beginning before January 1, 2018 may still be used to offset future taxable income without regard to the 80% limitation, although they have the potential to expire without being utilized if we do not achieve profitability in the future. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset a portion of future taxable income, if any, subject to expiration in the case of carryforwards generated prior to January 1, 2018. Additionally, we continue to generate business tax credits, including research and development tax credits, which generally may be carried forward to offset a portion of future taxable income, if any, subject to expiration of such credit carryforwards. Furthermore, under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. Our equity offerings and other changes in our stock ownership may have resulted in such ownership changes. We may also experience ownership changes in the future as a result of future shifts in our stock ownership, some of which may be outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOLs or other pre-change tax attributes to offset U.S. federal taxable income may be subject to limitations described above, which could potentially result in increased future tax liability to us. There is a risk that under existing tax laws, changes thereto, regulatory changes, or other unforeseen reasons, our existing NOLs or business tax credits could expire or otherwise be unavailable to offset future income tax liabilities. At the state level, there may also be periods during which the use of NOLs or business tax credits is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For these reasons, we may not be able to realize a tax benefit from the use of our NOLs or tax credits, even if we attain profitability.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets, including inflation. A severe or prolonged economic downturn, or additional global financial crises, could result in a variety of risks to our business, including weakened demand for our drug candidates, if approved, or our ability to raise additional capital when needed on acceptable terms, if at all. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets. Similarly, the recent significant volatility associated with the ongoing COVID-19 pandemic has caused significant instability and disruptions in the capital and credit markets. Furthermore, the February 2022 armed conflict between Russia and Ukraine and potential consequences such as sanctions, embargoes, regional instability, geopolitical shifts and adverse effects on macroeconomic conditions, currency exchange rates and financial markets could also substantially disrupt the capital and credit markets. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Risks related to discovery and development

We have limited experience as a company in conducting clinical trials, and we may be unable to do so for any additional drug candidates we develop.

We have limited experience as a company in conducting clinical trials. In part because of this lack of experience, we cannot be certain that our clinical trials will begin or be completed on time, if at all. Large-scale clinical trials require significant additional financial and management resources and reliance on third-party clinical investigators, contract research organizations, or CROs, and consultants. Relying on third-party clinical investigators, CROs and consultants may force us to encounter delays that are outside of our control. We may be unable to identify and contract with sufficient investigators, CROs and consultants on a timely basis or at all. We may be unable to negotiate and enter into any master services agreement with CROs, as necessary, on terms that are acceptable to us on a timely basis or at all.

We have not yet demonstrated an ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing, pharmacovigilance and distribution activities necessary for successful product commercialization. To date, we only have one drug candidate in clinical development, CYT-0851. We observed preliminary single-agent activity in the dose-escalation phase 1 portion of our phase 1/2 trial, which we completed in November 2021. In January 2022, we initiated patient dosing with CYT-0851 in the phase 2 expansion cohort portion of the phase 1/2 trial in adult patients with hematologic malignancies and solid tumors. If warranted by the phase 1/2 data, and subject to FDA agreement, we could initiate a potentially registrational trial in early 2023 for the treatment of relapsed and/or refractory lymphoma and/or solid tumors. We also plan to develop CYT-0851 in additional tumor settings as both a monotherapy and in combination with approved cancer therapeutics. In January 2022, we initiated patient dosing in the phase 1 portion of the phase 1/2 trial to assess tolerability and preliminary activity of combinations with three standard-of-care therapies.

If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our drug candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Clinical product development is a lengthy and expensive process with an uncertain outcome.

It is impossible to predict when or if any of our drug candidates will prove effective and safe in humans or will receive regulatory approval. The majority of drug candidates in phase 1/2 clinical trials in oncology do not reach regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design, implement, and execute, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing.

Our data or the data quality may not meet the standards for regulatory approval. The outcome of preclinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drug candidates. Our preclinical studies and future clinical trials may not be successful.

In addition, we may experience regulatory delays or rejections due to changes in regulatory policy during the period of our drug candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

We may not be able to file INDs or IND amendments to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or a comparable foreign regulatory may not permit us to proceed.

We may not be able to file INDs for any of our drug candidates on the timelines we expect, if at all. Moreover, we cannot be sure that submission of an IND will result in the U.S. Food and Drug Administration, or FDA, allowing further clinical trials to begin, or that, once begun, issues will not arise that require us to suspend or terminate clinical trials. Commencing each of these clinical trials will be subject to finalizing the trial design and selection of relevant endpoints based on discussions with the FDA and other regulatory authorities. Any guidance we receive from the FDA or other regulatory authorities is subject to change. These regulatory authorities could change their position, including, on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional clinical trials or impose stricter approval conditions than we currently expect. Successful completion of our clinical trials is a prerequisite to submitting a new drug application, or NDA, to the FDA for each drug candidate and, consequently, the ultimate approval and commercial marketing of each drug candidate. Even if completed, our ongoing or any future clinical trials of drug candidates may not be successful or may not generate positive clinical data.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

We may experience delays in completing our preclinical studies and initiating or completing clinical trials, and we may experience numerous unforeseen events during, or as a result of, any future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

- FDA or other regulatory authorities may disagree with the design, protocol or conduct of our clinical trials;
- regulators, institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- data from one trial may not be reproduced in another study. Contradictory results in clinical trials may result in the requirement for additional trials or the failure to obtain regulatory approval of the drug;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators or IRBs or ethics committees may require us or our investigators to, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements, a finding that our drug candidates may have undesirable side effects or other unexpected characteristics that expose the participants to unacceptable health risks, or reports may arise from preclinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our drug candidates;
- the cost of clinical trials of our drug candidates may be greater than we anticipate;
- inflationary pressures could increase costs for our clinical trials; and
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate.

We could encounter delays if a clinical trial is suspended or terminated by us, including based on a recommendation by the Data Safety Monitoring Board, or DSMB, for such trial, by the IRBs of the institutions at which such trials are being conducted or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination or clinical hold due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial, superior efficacy of a competing product in development for the same indication, or marketing approval of a superior product that reduces the pool of patients with an unmet need that seek out clinical trials. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates. Further, the FDA may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

Our product development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our future clinical trials will begin as planned, or whether any of our current or future clinical trials will need to be restructured or will be completed on schedule, if at all. Significant preclinical study or clinical trial delays, including those caused by the COVID-19 pandemic, also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and results of operations. Any delays in

our preclinical or future clinical development programs may harm our business, financial condition and prospects significantly.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In particular, our ability to enroll patients has been, and may continue to be significantly delayed by global events such as the COVID-19 pandemic, and we cannot know or predict the extent and scope of such delays at this point. In January 2022, we experienced delays in our clinical trial enrollment as a result of the impact of the omicron variant of COVID.

We have and may continue to experience difficulties in identifying and enrolling patients as a result of competition for patients with other ongoing clinical trials, particularly with respect to enrollment of patients for treatment of lymphoma. In addition to the competitive trial environment, the eligibility criteria of our planned clinical trials may further limit the pool of available trial participants. Additionally, the process of finding patients may prove costly. We also may not be able to identify, recruit and enroll a sufficient number of patients to complete our clinical trials because of the perceived risks and benefits of the drug candidates under study, the availability and efficacy of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective patients, and the patient referral practices of physicians. If patients are unwilling to participate in our studies for any reason or if we are not able to enroll a sufficient number of patients who remain in the study until its conclusion, the timeline for recruiting patients, conducting studies and obtaining regulatory approval for our drug candidates may be delayed.

Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the clinical trial in question;
- the intensity of study procedures a patient has to go through during study participation;
- the frequency and number of visits required for study participants;
- the number of patients with the disease or condition being studied;
- the approval of new alternative treatments that reduce the number of available study patients;
- the identification and availability of an appropriate patient selection test;
- the other clinical trials competing for the same patients;
- the perceived risks and benefits of the drug candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- our ability to obtain and maintain patient consents;
- the ability to monitor patients adequately during and after treatment, which may be worsened by pandemics such as COVID-19;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before completion of their treatment or study follow-up visits, especially during a pandemic such as COVID-19;
- the proximity and availability of clinical trial sites for prospective patients; and
- factors we may not be able to control, such as current or potential future global health crises that may limit patients, principal investigators or staff or clinical site availability (for example, the ongoing COVID-19 pandemic).

Interim, "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, top-line or preliminary data from our clinical trials. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim, top-line and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Positive results from the clinical trials and preclinical studies of our drug candidates are not necessarily predictive of the results of later clinical trials or preclinical studies. If we cannot replicate the positive results from our clinical trials and preclinical studies of our drug candidates in our later clinical trials preclinical studies, we may be unable to successfully develop, obtain regulatory approval for and commercialize our drug candidates.

Any positive results from clinical trials and preclinical studies of our drug candidates may not necessarily be predictive of the results from later clinical trials and preclinical studies. Similarly, even if we are able to complete the planned clinical trials and preclinical studies of our drug candidates according to our current development timeline, the positive results from such trials and studies may not be replicated in subsequent trials and studies.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we may not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their drug candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain approval from the FDA or other regulatory authorities.

Our clinical trials may reveal significant adverse events not seen in our preclinical or nonclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of our drug candidates.

Before obtaining regulatory approvals for the commercial sale of any products, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our drug candidates are both safe and effective for use in each target indication. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of drug candidates proceeding through clinical trials. Drug candidates in later stages of clinical trials also may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial early-stage clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most drug candidates that commence clinical trials are never approved as products and there can be no assurance that any of our current or future clinical trials will ultimately be successful or support further clinical development of any of our drug candidates.

As is the case with many treatments for cancer, it is possible that there may be side effects associated with the use of our drug candidates. Our phase 1/2 clinical trial for CYT-0851 includes cancer patients who are very sick and whose health is deteriorating, and we expect that additional clinical trials of our other drug candidates will include similar patients with deteriorating health. Some of these patients may experience adverse side effects, and some patients may die during our clinical trials for various reasons, including as a result of receiving our drug candidates, because the patient's disease is too advanced, or because the patient experiences medical problems that may not be related to our drug candidate. Even if the deaths are not related to our drug candidates, the deaths could affect perceptions regarding the safety of our drug candidate. In addition, due to the lack of a clear mechanism of action with respect to our drug candidates, we may find it difficult or impossible to mitigate against any adverse side effects resulting from toxicity, which could lead to developmental delays, added costs from increased safety monitoring and decreased study enrollment and difficulties in the identification of patient populations likely to benefit from our drug candidates, which could in turn lead to reduced efficacy and ultimately impact our ability to receive regulatory approval.

If significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients into our clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of one or more drug candidates altogether. We, the FDA or other applicable regulatory authorities, or an IRB may suspend or terminate clinical trials of a drug candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its unfavorable tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects.

We are developing CYT-0851, and potentially future drug candidates, for use in combination with other therapies, which exposes us to additional risks.

We are developing CYT-0851, and potentially future drug candidates, for use in combination with one or more chemotherapies or other oncology treatments. Combination therapies are commonly used for the treatment of cancer, and we are subject to additional risks as we develop any of our drug candidates for use in combination with other drugs or for indications other than cancer. The use of CYT-0851 in combination with other cancer therapies may unmask unforeseen adverse side effects that could make further development difficult or impossible. CYT-0851 may also reduce the metabolism of other drugs by inhibiting the activity of a human liver enzyme required to metabolize other drugs, including some anti-cancer drugs, which may result in higher exposure to those drugs and potential adverse side effects. Even if any drug candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to bear the risks that the FDA or similar foreign regulatory authorities could revoke approval of the therapy used in combination with our drug candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially.

We may also evaluate future drug candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA or similar foreign regulatory authorities. We will not be able to market and sell any drug candidate we develop in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval. If the FDA or similar foreign regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, manufacturing, or supply issues arise with, the drugs we choose to evaluate in combination with our drug candidates, we may be unable to obtain approval of or market our drug candidates.

If the FDA or comparable foreign regulatory authorities do not approve or revoke their approval of, or if safety, efficacy, manufacturing, or supply issues arise with, therapies we choose to evaluate in combination with any of our drug candidates, we may be unable to obtain regulatory approval of or to commercialize such drug candidates in combination with these therapies.

If we are unable to successfully develop and commercialize companion diagnostic tests for our drug candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our drug candidates.

Because predictive biomarkers may be used to select patients for our drug candidates, we believe that our success may depend, in part, on the development and commercialization of companion diagnostic tests. While we were granted an Investigational Device Exemption for use of an investigational companion diagnostic in our phase 1/2 clinical trial of CYT-0851, we have no experience in the development and commercialization of companion diagnostic tests and may not be successful in developing and commercializing appropriate companion diagnostic tests to pair with CYT-0851 or any of our drug candidates that receive marketing approval. Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval prior to commercialization. We may encounter difficulties in identifying biomarkers that are predictive of response to our therapies or may never identify a biomarker at all. We may not be able to develop assays that consistently measure our biomarkers in clinical trials and some biomarkers may not be able to be measured in certain tumor types precluding development in those indications. Even if our biomarkers prove effective for patient selection we may still encounter difficulties developing and obtaining regulatory approval for the companion diagnostic tests, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. While our drug candidates will have their marketing applications reviewed by FDA's Center for Drug Evaluation and Research, or CDER, companion diagnostics require separate marketing applications under the primary jurisdiction of FDA's Center for Devices and Radiological Health, or CDRH. This parallel

jurisdiction and separate marketing applications could result in coordination issues, require additional time and effort, or result in delays or failure to obtain marketing approval for either the companion diagnostic or related drug indications.

Any failure to develop or obtain regulatory approval of the companion diagnostic tests could delay or prevent approval of our drug candidates. If we, or any third parties that we may in the future engage to assist us, are unable to successfully develop and commercialize companion diagnostic tests for our drug candidates, or experience delays in doing so:

- the development of our drug candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our drug candidates may not receive marketing approval if safe and effective use of a therapeutic drug candidate depends on an *in vitro* diagnostic; or
- we may not realize the full commercial potential of any drug candidates that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from treatment with our drugs.

If any of these events were to occur, our business would be materially harmed.

Synthetic lethality represents an emerging class of precision medicine targets, and negative perceptions of the efficacy, safety or tolerability of this class of targets, including any that we develop, could adversely affect our ability to conduct our business, advance our drug candidates or obtain regulatory approvals.

Aside from PARP inhibitors, such as Lynparza, Rubraca, Zejula and Talzenna, no synthetically lethal small molecule inhibitor therapeutics have been approved to date by the FDA or other comparable regulators. Adverse events in future clinical trials of our drug candidates or in clinical trials of others developing similar products and the resulting publicity, as well as any other adverse events in the field of synthetic lethality, or other products that are perceived to be similar to synthetic lethality, such as those related to gene therapy or gene editing, could result in a decrease in the perceived benefit of one or more of our programs, increased regulatory scrutiny, decreased confidence by patients and CROs in our drug candidates, and less demand for any product that we may develop. Our synthetic lethality drug candidates could result in a greater quantity of reportable adverse events or other reportable negative clinical outcomes, manufacturing reportable events or material clinical events that could lead to clinical delays or holds by the FDA or applicable regulatory authority or other clinical delays, any of which could negatively impact the perception of one or more of our synthetic lethality programs, as well as our business as a whole. In addition, responses by U.S. federal or foreign governments to negative public perception may result in new legislation or regulations that could limit our ability to develop any drug candidates or commercialize any approved products, obtain or maintain regulatory approval, or otherwise achieve profitability. More restrictive statutory regimes, government regulations, or negative public opinion would have an adverse effect on our business, financial condition, results of operations, and prospects, and may delay or impair the development of our drug candidates and commercialization of any approved products or demand for any products we may develop.

We may in the future conduct clinical trials for our drug candidates outside the United States, and the FDA and similar foreign regulatory authorities may not accept data from such trials.

We may in the future choose to conduct additional clinical trials outside the United States. The acceptance of trial data from clinical trials conducted outside the United States by the FDA may be subject to certain conditions. In cases where data from clinical trials conducted outside the United States are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the trials were performed in accordance with Good Clinical Practices, or GCPs, and by clinical investigators of recognized competence and (iii) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any similar foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any similar foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our drug candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

The market opportunities for certain of our drug candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small, and the incidence and prevalence for target patient populations of our drug candidates have not been established with precision. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be materially and adversely affected.

Cancer therapies are sometimes characterized as first line, second line or third line, and the FDA often approves new therapies initially only for later line use where there are not good therapeutic alternatives. When cancers are detected and require systemic treatment, these are treated with the first line therapy. This generally consists of chemotherapy, radiation, antibody drugs, tumor targeted small molecules, or a combination of these. In addition, sometimes a bone marrow transplant may also be used. If the patient's cancer progresses or relapses, then they are given a second line or third line therapy, which can consist of more chemotherapy, radiation, antibody drugs, tumor targeted small molecules, or a combination of these, or bone marrow transplant. Generally, as patients progress through lines of therapy, the number of patients deriving benefit decreases, as does the time that the treatment controls their cancer. We are targeting a wide range of cancer populations in our clinical trials of CYT-0851, including patients with hematologic malignancies or solid tumors; the line of therapy we will pursue for potential registration for CYT-0851 will depend on the target disease indication and the size of benefit observed for patients receiving CYT-0851, but in most cases is likely to be positioned initially as a second or later line therapy.

We are currently evaluating the safety and tolerability of CYT-0851 as a monotherapy and in combination with standard-of-care chemotherapies in a phase 1/2 dose escalation study in patients with relapsed and/or refractory B-cell malignancies and advanced solid tumors. We believe that CYT-0851 has the potential to be approved in multiple monotherapy and combination therapy settings for both hematologic malignancies and solid tumors.

In the future, if CYT-0851 advances to earlier lines of treatment as either a monotherapy or as a combination therapy, it could potentially address additional patients annually in the U.S. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with CYT-0851, or any of our drug candidates, are based on estimates.

The total addressable market opportunity will ultimately depend upon, among other things, the treatment criteria included in the final label. Even if our drug candidates are approved for sale for these indications, acceptance by the medical community may be lower than estimated and patient access, product pricing and reimbursement may hinder sales and lead to lower sales. The number of patients with cancers and solid tumors may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. We may not be successful in our efforts to identify additional drug candidates. Due to our limited resources and access to capital, we must prioritize development of certain drug candidates, which may prove to be the wrong choice and may adversely affect our business.

Although we intend to explore other therapeutic opportunities in addition to the drug candidates that we are currently developing, we may fail to identify viable new drug candidates for clinical development for a number of reasons. Failure to identify additional potential drug candidates could materially harm our business.

In addition to our drug candidates that are currently under development, we continue to build and direct our DDR biology expertise and discovery and translational research capabilities and capacity to generate additional discovery programs. We currently have two undisclosed target discovery projects undergoing chemical series testing and medicinal chemistry and continue to evaluate external preclinical-stage programs for in-licensing. Research programs to identify new disease targets and drug candidates require substantial technical, financial and human resources whether or not they are ultimately successful. We may not find potential additional drug candidates using this approach or such potential drug candidates may not be clinically validated. Our research programs may initially show promise in identifying potential indications and/or drug candidates, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or drug candidates;
- potential drug candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective products; or
- it may take greater human and financial resources than we possess to identify additional therapeutic opportunities for our drug candidates or to develop suitable potential drug candidates through internal research programs, thereby limiting our ability to develop, diversify and expand our product portfolio.

Because we have limited financial and human resources, we have initially focused on research programs and drug candidates for a limited set of indications. As a result, we may forgo or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater likelihood of clinical success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our drug candidates or to develop suitable potential drug candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential drug candidates or other potential programs that ultimately prove to be unsuccessful.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our drug candidates, we will not be able to commercialize, or will be delayed in commercializing, our drug candidates, and our ability to generate revenue will be materially impaired.

Our drug candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Before we can commercialize any of our drug candidates, we must obtain marketing approval. Currently, all of our drug candidates are in development, and we have not received approval to market any of our drug candidates from regulatory authorities in any jurisdiction. It is possible that our drug candidates, including any drug candidates we may seek to develop in the future, will never obtain regulatory approval. We have only limited experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third-party CROs and/or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. It requires quality assurance and control systems that meet regulatory standards, and publishing know-how to submit the regulatory applications and gain approval. We have limited experience building quality systems and publishing new drug applications and will rely on third-party CROs and vendors to establish these controls and systems. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our drug candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. In addition, regulatory authorities may find fault with our manufacturing processes or facilities or that of third-party contract manufacturers. We may also face greater than expected difficulty in manufacturing our drug candidates.

The process of obtaining regulatory approvals, both in the United States and abroad, is expensive and often takes many years. If the FDA or a comparable foreign regulatory authority requires that we perform additional preclinical or clinical trials, or manufacturing changes, approval, if obtained at all, may be delayed. The length of such a delay varies substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted application may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies or make manufacturing changes. Our drug candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may not be able to enroll a sufficient number of patients in our clinical studies;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication or a related companion diagnostic is suitable to identify appropriate patient populations;
- the results of clinical trials may not meet the level of statistical significance or the degree of benefit required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the purity of our product;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may fail to accept the preclinical pharmacology, safety and toxicology evaluation as adequate to support approval of the drugs; and
- the approval policies, the interpretation of the regulatory approval guidelines by the reviewers, or regulations of the FDA or comparable foreign regulatory authorities may significantly change such that our clinical and non-clinical data are insufficient for approval.

Even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, or may not allow us to present all safety and efficacy data in the drug label, thereby narrowing the commercial potential of the drug candidate. In addition, regulatory authorities may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our drug candidates, the commercial prospects for our drug candidates may be harmed and our ability to generate revenues will be materially impaired.

While we continue to pursue a further understanding of the molecular binding mechanism of our drug candidates, we do not currently, and may never, fully understand, the precise mechanism of action of our inhibitors.

Our lead candidates, CYT-0851 and CYT-1853, were discovered from a phenotypic screen and the exact mechanism of action by which they function is not currently known and may never be known. While this knowledge is not required for regulatory approval, the lack thereof could still pose significant development challenges that result in delays in our development or our ability to commercialize our products, including difficulties managing any unexpected toxicities should they arise. The effects on RAD51 and DNA repair may be secondary to other direct action of our lead drug candidates. Without a clear understanding of the mechanism of action of these candidates, and given that there may be a direct mechanistic action of these candidates on targets that we do not understand, we may find it difficult or impossible to mitigate against any adverse side effects resulting from toxicity, which could lead to developmental delays, added costs from increased safety monitoring and decreased study enrollment.

Our business substantially depends upon the successful development of drug candidates generated through the application of our platform, and in particular, our lead drug candidate, CYT-0851. If we are unable to obtain regulatory approval for, and successfully commercialize, products developed through the application of our platform, our business may be materially harmed.

Our lead drug candidate, CYT-0851, was developed through the application of our platform. All of our drug candidates to date were derived based on the same principle of synthetic lethality. As such, negative results in the development of CYT-0851 may also impact our ability to obtain regulatory approval for our other drug candidates, either at all or within anticipated timeframes because, although other drug candidates may target different indications, the underlying technology platform, manufacturing process and development process is the same for all of our drug candidates. Accordingly, a failure in any one program may decrease trust in our technology and affect the ability to obtain regulatory approval to continue or conduct clinical programs for other drug candidates. If CYT-0851 shows unexpected adverse events or a lack of efficacy in the indications we intend to treat, or if we experience other regulatory or developmental issues, our development plans and business could be significantly harmed.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs or modifications to approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most foreign inspections of manufacturing facilities and products, and subsequently, on March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials, which has since been further updated and is being refreshed on a periodic basis. As of June 23, 2020, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals and conducting "mission–critical" domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards.

Most recently, as of July 2020, utilizing a rating system to assist in determining when and where it is safest to conduct such inspections based on data about the virus's trajectory in a given state and locality and the rules and guidelines that are put in place by state and local governments, the FDA is either continuing to, on a case-by-case basis, conduct only "mission-critical" inspections, or, where possible to do so safely, resuming prioritized domestic inspections, which generally include pre-approval inspections. Foreign pre-approval inspections that are not deemed mission-critical remain postponed, while those deemed mission-critical will be considered for inspection on a case-by-case basis. The FDA will use similar data to inform resumption of prioritized operations abroad as it becomes feasible and advisable to do so. The FDA's assessment of whether an inspection is mission-critical considers many factors related to the public health benefit of U.S. patients having access to the product subject to inspection, including whether the products are used to diagnose, treat, or prevent a serious disease or medical condition for which there is no other appropriate substitute. Both for-cause and pre-approval inspections can be deemed mission-critical. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks related to the commercialization of our drug candidates

We face substantial competition, which may result in others developing or commercializing drugs before or more successfully than us.

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly as they develop novel approaches to treating disease indications that our drug candidates are also focused on treating. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel therapeutics or to in-license novel therapeutics that could make the drug candidates that we develop obsolete. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our drug candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our drug candidates are efficacy, safety, tolerability, reliability, convenience of use, price and reimbursement.

We face competition from companies in segments of the pharmaceutical, biotechnology and other related markets that are advancing oncology therapeutics that target DNA repair, including AbbVie, Artios Pharma, AstraZeneca, BeiGene, Breakpoint Therapeutics, Bristol Myers Squibb, Clovis Oncology, EMD Serono, Foghorn Therapeutics, Genentech, GlaxoSmithKline, IDEAYA Biosciences, Merck & Co, Pfizer, Rain Therapeutics, Repare Therapeutics, Ryvu Therapeutics, and Tango Therapeutics. In addition, academic and other non-profit organizations have early-stage ongoing drug discovery efforts that target DNA repair, such as Cancer Research UK, University of Chicago, and Dana Farber Cancer Institute. In addition, to gain market acceptance for our drug candidates, if they are approved for commercial sale, we will face competition from numerous companies that are developing novel cancer therapeutics using a variety of modalities other than targeting DNA repair.

We anticipate that we will continue to face intense and increasing competition as new treatments enter the market and advanced technologies become available. Our competitors may be currently developing, or may in the future develop, products that are equally or more effective or are more economically attractive than any of our current or future drug candidates. Competing products may gain faster or greater market acceptance than our products, if any, and medical advances or rapid technological development by competitors may result in our drug candidates becoming non-competitive or obsolete before we are able to recover our research and development and commercialization expenses. If we or our drug candidates do not compete effectively, it may have a material adverse effect on our business, financial condition and results of operations.

Our estimates for potentially addressable patient populations presented in this Annual Report on Form 10-K are subject to inherent challenges and uncertainties. If we have overestimated the sizes of the potentially addressable patient populations or the various markets in which we operate or plan to operate, our future growth opportunities may be limited.

Our estimates for potentially addressable patient populations presented in this Annual Report on Form 10-K are calculated based on a combination of third-party estimates, our internal estimates and management's experience. Accordingly, they are subject to uncertainty and are based on assumptions that may not prove to be accurate. In particular, we calculated our estimates for potentially addressable patient populations based on, among other parameters, the annual incidence of our target indications. The information for these parameters is derived from a combination of third-party reports and management assessment, and is subject to significant assumptions and estimates, which may change or prove to be inaccurate. While we believe the information and assumptions on which we base our estimates for potentially addressable patient populations are reasonable, such information is inherently imprecise. In addition, our expectations, assumptions and estimates of future opportunities are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in this Annual Report on Form 10-K. If third-party or internally generated data prove to be inaccurate, or if we make errors in our assumptions based on that data, our future growth opportunities may be different from our expectations. Moreover, if our estimates for potentially addressable patient populations, or the size of any of the various markets in which we operate or plan to operate, proves to be inaccurate, there could be a material adverse effect on our prospects. Additionally, we are working to identify patient selection biomarkers to identify defined patient populations for potential use in our clinical trials and drug candidate development. If we ultimately use one or more biomarkers to select patients for future trials, our addressable market estimates may change and may be smaller than our current estimates.

We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we identify for specific indications among many potential options. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate. Any such event could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We currently have no marketing and sales organization and have no experience as a company in marketing products. Failure to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our drug candidates, if approved, would impair our ability to generate product revenue.

We currently have no sales, marketing or distribution capabilities and have no experience in marketing products. We intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue arrangements with third-party sales, marketing, and distribution collaborators regarding the sales and marketing of our products, if approved. However, we may not be able to establish or maintain such arrangements on favorable terms or if at all, or if we are able to do so, these third-party arrangements may not provide effective sales forces or marketing and distribution capabilities. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our drug candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our drug candidates.

We may not be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

Risks related to employee matters, managing growth and information technology

We are highly dependent on our key personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

We are highly dependent on Markus Renschler, M.D., our President and Chief Executive Officer. In addition, the loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business.

Despite our efforts to retain Dr. Renschler and other valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice.

Because of the specialized scientific nature of our business, our ability to develop our drug candidates largely depends upon our ability to attract, retain and motivate highly qualified managerial and key scientific personnel. If we are unable to retain the services of one or more of the principal members of senior management or other key employees, our ability to implement our business strategy could be materially harmed. We face intense competition for qualified employees from biopharmaceutical companies, research organizations and academic institutions. Attracting, retaining or replacing these personnel on acceptable terms may be difficult and time-consuming given the high demand in our industry for similar personnel. We believe part of being able to attract, motivate and retain personnel is our ability to offer a competitive compensation package, including equity incentive awards. If we cannot offer a competitive compensation package to attract and retain the qualified personnel necessary for the continued development of our business, we may not be able to maintain our operations or grow our business.

We will need to grow the size of our organization, and we may experience difficulties in achieving or managing this growth.

As of December 31, 2021, we had 40 full-time employees. We intend to hire new employees to assume activities and responsibilities within the company, including conducting our research and performing development activities in the future.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We conduct our operations at our facilities in Lexington, Massachusetts. The Massachusetts region is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market is intense and limits our ability to hire and retain highly qualified personnel on acceptable terms or at all. Changes to U.S. immigration and work authorization laws and regulations, including those that restrain the flow of scientific and professional talent, can be significantly affected by political forces and levels of economic activity. Our business may be materially adversely affected if legislative or

administrative changes to immigration or visa laws and regulations impair our hiring processes and goals or projects involving personnel who are not U.S. citizens.

Any delay or disruption in hiring such new employees could result in delays in our research and development activities and would harm our business. We rely on third-party recruiters to help us fill the positions. The recruiters may not perform which may delay hiring. As our development and commercialization plans and strategies develop, and as we continue to operate as a public company, we expect to need additional managerial, operational, sales, marketing, quality, regulatory affairs, financial and other personnel, as well as additional facilities to expand our operations.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, or if we are not able to effectively build out new facilities to accommodate this expansion, we may not be able to successfully execute the tasks necessary to further develop and commercialize our drug candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our internal computer systems, or those used by our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of the development programs of our drug candidates.

Our internal computer systems and those of our current and future CROs and other vendors, contractors and consultants are vulnerable to damage from data breaches, computer viruses, cybersecurity threats (such as denial-of-service attacks, cyber-attacks, cyber-intrusions, hacking, phishing and other social engineering attacks), unauthorized access or use, natural disasters, terrorism, war and telecommunication and electrical failures. Because the techniques used to obtain unauthorized access, disable or degrade service or sabotage systems change frequently and often are not recognized until launched against a target, we and our vendors may be unable to anticipate these techniques or to implement adequate preventative measures. As we become more dependent on information technologies to conduct our operations, such incidents, including deliberate attacks and attempts to gain unauthorized access to such computer systems and networks, may increase in frequency and sophistication. Further, we do not have any control over the operations of the facilities or technology of our vendors, including any vendors that collect, transmit, store and otherwise process personal information on our behalf. Our and our vendors' systems, servers and platforms are vulnerable to computer viruses or physical or electronic break-ins that our or their security measures may not detect. For example, while we have not experienced any such material system failure or security breach at our company to date, one of our clinical trial CROs had an incident but had adequate mechanisms to recover all of our data. Such a security breach and related interruptions in our operations or the operations of one of our CROs or vendors, could result in the unauthorized disclosure of or access to personally identifiable information or individually protected health information, which could result in a material disruption of our development programs and our business operations. For example, the loss of data from completed or future preclinical studies and clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our drug candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our vendors' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our drug candidates could be delayed. We may also need to expend significant resources to protect against security breaches or to mitigate the impact of any such breaches. We or our third-party providers may not be successful in preventing security breaches or successfully mitigating their effects.

Any security breach or other incident, whether real or perceived, that results in a loss of or accidental, unlawful or unauthorized access to, use of, release of or other processing of personal, proprietary or other sensitive information could impact our reputation, cause us to incur significant liability and costs, including legal expenses, fines and penalties for any noncompliance with any privacy and security laws, harm patient and other stakeholder confidence, hurt our expansion into potential markets, or cause us to incur remediation costs. We do not currently maintain cybersecurity insurance, and any insurance we may maintain against the risk of this type of loss in the future may not be sufficient to cover actual losses, or may not apply to the circumstances relating to any particular loss. Further, increasing use of social media could give rise to liability, breaches of data security or reputational damage.

Risks related to our intellectual property

If we are unable to adequately protect and enforce our intellectual property or obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and products may be impaired.

Our commercial success will depend in part on our ability and the ability of our licensors and collaborators to obtain, maintain, enforce and protect proprietary or intellectual property protection in the United States and other countries for our drug candidates and our core technologies. We rely on patent protection, trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We seek to protect our proprietary drug candidates by filing patent applications in the United States and abroad related to our drug candidates and other proprietary technologies that are important to our business. If we or our licensors are unable to obtain, maintain, protect or enforce patent protection with respect to our current and future drug candidates, competitors and other third parties could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our current drug candidates and other drug candidates that we may pursue may be impaired. As a result, our business, financial condition, results of operations and prospects could be materially harmed.

The degree of patent protection we require to successfully commercialize our drug candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. Our pending patent applications may not issue, and any of our patent applications that have matured or may mature into issued patents may not include claims with a scope sufficient to protect CYT-0851, CYT-1853 or our other current or future drug candidates. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional or international patent application filing date. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such drug candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar or identical to our drug candidates, including generic versions of such drugs.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our owned or in-licensed patent applications, in either case that they may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or until issuance or, in some cases, not published at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty.

In addition, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Further, with respect to many of the pending patent applications covering our drug candidates, prosecution has yet to commence. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office, or USPTO, have often been significantly narrowed by the time they issue, if at all. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

Even if we acquire patent protection that we expect should enable us to maintain a competitive advantage, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third-party submission of prior art to the USPTO challenging the priority of an invention claimed within one of our patents, which submissions may also be made prior to a patent's issuance, precluding the granting of any of our pending patent applications. We may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others from whom we have obtained licenses to such rights. Competitors or other third parties may claim that they invented the inventions claimed in our

issued patents or patent applications prior to us, or may file patent applications before we do. Competitors or other third parties may also claim that we are infringing, misappropriating or otherwise violating their patents or other intellectual property and proprietary rights and that we therefore cannot practice our technology as claimed under our patents, if issued. Competitors or other third parties may also contest our patents, if issued, by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor or other third party could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents.

In addition, we may in the future be subject to claims by our former employees, consultants, advisors or independent contractors asserting an ownership right in our patents, patent applications or technologies, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to our proprietary know-how, information or technology to assign or grant similar rights to their inventions to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy.

An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, without payment to us, or could limit the duration of the patent protection covering our technology and drug candidates. Such challenges may also result in our inability to manufacture or commercialize our drug candidates without infringing, misappropriating or otherwise violating third party patent or other intellectual property rights or require us to license the relevant intellectual property from third parties, which licenses may not be available on commercially reasonable terms, if at all. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates.

Even if our patent portfolio is unchallenged, it may not provide us with any meaningful protection or prevent competitors or other third parties from designing around our patent claims to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. For example, a third party may develop a competitive product that provides benefits similar to one or more of our drug candidates but that has a different composition that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our drug candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our drug candidates could be negatively affected, which would harm our business.

If we are unable to protect the confidentiality of our trade secrets our business and competitive position may be harmed.

In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security on our premises, and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

Our trade secrets could otherwise become known or be independently discovered by our competitors or other third parties. Competitors or other third parties could purchase our drug candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe, misappropriate or otherwise violate our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from

using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' products, our competitive position could be adversely affected, as could our business.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on issued patents and patent applications often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our products or procedures, we may not be able to stop a competitor from marketing products that are the same as or similar to our drug candidates, which would have a material adverse effect on our business.

The intellectual property landscape around our technology is highly dynamic, and third parties may obtain intellectual property rights that could affect our ability to use our technology or otherwise develop and commercialize drug candidates.

Synthetic lethality and the use of inhibitors of specific DNA damage repair pathways in the context of cancer drug development remains a novel approach. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is evolving and in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends upon our ability to develop, manufacture, market, and sell any drug candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of therapies, products or their methods of use or manufacture. There may be third-party patents of which we are currently unaware with claims to technologies, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our drug candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. We may be unable to obtain a license to such patents held by third-parties on commercially reasonable terms or at all. In the event that we are unable to obtain licenses to such patents, our ability to develop and commercialize one or more drug candidates may become severely limited. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us.

We may initiate or become involved in legal proceedings involving allegations that we are infringing, misappropriating or otherwise violating a third party's intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends in part upon our ability and the ability of our collaborators, to develop, manufacture and sell our drug candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and other propriety rights of third parties.

The biotechnology and pharmaceutical industries are characterized by extensive and frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates and technology. Our competitors or other third parties may assert infringement, misappropriation or other claims against us, alleging that our products or technologies are covered by their patents or other intellectual property. Given the vast number of patents in our field of technology, we cannot be certain that we do not infringe, misappropriate or otherwise violate existing patents or that

we will not infringe, misappropriate or otherwise violate patents that may be granted in the future. If a patent holder believes our product or drug candidate infringes, misappropriates or otherwise violates its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect.

If we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we may be enjoined from further developing or commercializing the infringing, misappropriating or otherwise violating products or technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties to continue developing and marketing our drug candidates and technology, pay royalties and/or redesign our infringing products or technologies, which may be impossible or require substantial time and monetary expenditure. In addition, we may choose to obtain one or more licenses from third parties, even in the absence of an action or finding of infringement, misappropriation or other violation. In either case, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease developing and commercializing the infringing, misappropriating or otherwise violating technology or drug candidates. A finding of infringement could prevent us from commercializing our drug candidates or force us to cease some of our business operations, which could materially harm our business. If we lose a foreign patent or other intellectual property lawsuit, alleging our infringement, misappropriation or other violation of a competitor's patents or other intellectual property, we could be prevented from marketing our products in one or more foreign countries, which would have a materially adverse effect on our business. In addition, we may in the future pursue patent challenges with respect to third-party patents, including as a defense against the foregoing infringement, misappropriation or other claims. The outcome of such challenges is unpredictable. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

We may be subject to damages resulting from claims that we or our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers, including our competitors or are in breach of non-competition or non-solicitation agreements with their current or former employers, including our competitors, or claims asserting ownership of what we regard as our own intellectual property.

We could in the future also be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may in the future be subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer, competitor or other third party. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to our management and employees. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drug candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. An inability to incorporate such technologies or features would have a material adverse effect on our business, and may prevent us from successfully commercializing our drug candidates. In addition, we may lose valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our drug candidates, which would have an adverse effect on our business, results of operations and financial condition. Any of the foregoing could harm our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our patent rights and other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our patents, if obtained, and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement, misappropriation or other claims. A court may disagree with our allegations or may refuse to stop the other party from using the technology at issue on the grounds that our or our licensors' patents do not cover the third-party technology in question. Further, such third parties could counterclaim that we or our licensors' infringe, misappropriate or otherwise violate their

intellectual property or that a patent we have asserted against them is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us or our licensors to assert such challenges to our or our licensors' intellectual property rights. The outcome of any such proceeding is generally unpredictable. To counter or defend against such claims can be expensive and time consuming. An adverse result in any litigation proceeding could put one or more of our or our licensors' patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our drug candidates, we would lose at least part, and perhaps all, of the patent protection covering such drug candidate. Competing products may also be sold in other countries in which our patent coverage might neither exist nor be as strong.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or otherwise violating, or from successfully challenging, our intellectual property rights, or we may be unable to successfully defend ourselves from allegations of infringement, misappropriation or other violation. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property proceedings could have a material adverse effect on our ability to compete in the marketplace.

We may not be able to effectively obtain, maintain, protect and enforce our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, maintaining, defending and enforcing patent rights on our drug candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in obtaining, maintaining, protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property rights, particularly those relating to biotechnology products. This could make it difficult for us to stop the infringement, misappropriation or other violation of our patent rights or our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors or other third parties may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patent rights to stop infringing, misappropriating or other violating activities is inadequate. These products may compete with our drug candidates, and our patent rights or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our intellectual property and proprietary rights, including our patent rights, in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business, put our patent rights at risk of being invalidated or interpreted narrowly, put our owned or in-licensed patents and patent applications at risk of not issuing. Furthermore, while we intend to protect our intellectual property rights in the major markets for our drug candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our drug candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate to obtain significant commercial advantage from the intellectual property that we develop or license.

We may be subject to claims challenging the inventorship or ownership of any intellectual property, including any patents we may own or in-license in the future.

We may be subject to claims that former employees, collaborators or other third parties have an interest in any patents we may own or in-license in the future, trade secrets, or other intellectual property as an inventor or co-inventor. We may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our drug candidates or other technologies. We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to an inventorship, such dispute may lead to litigation which could be expensive and time consuming. If we are unsuccessful, in addition to paying monetary damages, we could lose valuable rights in intellectual property that we regard as our own, such as exclusive ownership of, or right to use, intellectual property that is important to our drug candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we do not obtain patent term extension and data exclusivity for any drug candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any of our drug candidates, one or more of our U.S. patents, if obtained, may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our business, financial condition, results of operations and prospects could be materially harmed.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our drug candidates or utilize similar technology but that are not covered by the claims of any patents that may issue to us, our licensors or our collaborators;
- we or our licensors or collaborators, might not have been the first to make the inventions covered by our owned or licensed pending patent applications, or any patents that may issue in the future;
- we or our licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;

- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating or otherwise violating our intellectual property rights;
- it is possible that our owned or licensed present or future pending patent applications will not lead to issued patents;
- issued patents that we hold or license rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties, or may not provide us with any competitive advantages;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent or other intellectual property rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- changes to the patent law and its interpretation in the United States and other jurisdictions could diminish the value of patents in general and may impact the validity, scope or enforceability of our patent rights, thereby impairing our ability to protect our drug candidates;
- we may not develop additional proprietary technologies that are patentable;
- the patents or pending or future patent applications of others, if issued, may harm our business; and
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes to the patent law and its interpretation in the United States and in other jurisdictions could diminish the value of patents in general and impact the validity, scope or enforceability of our patent rights, thereby impairing our ability to protect our drug candidates and technologies.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining, maintaining, protecting and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or in their interpretation in any jurisdiction that we seek patent protection diminish our ability to protect our inventions, obtain, maintain and enforce our intellectual property and proprietary rights and, more generally, may affect the value of our intellectual property and proprietary rights. Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system from a "first to invent" system into a "first to file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier.

Moreover, various courts, including the U.S. Supreme Court, has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce rights in our proprietary technology. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that we may obtain in the future which could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. During trademark registration proceedings, we may receive rejections

of our applications by the USPTO or in other foreign jurisdictions. Although we are given an opportunity to respond to such rejections, we may be unable to overcome them. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, which may not survive such proceedings. Moreover, any name we have proposed to use with our drug candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA or an equivalent administrative body in a foreign jurisdiction objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark.

We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement, misappropriation or other claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, domain name or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

Risks related to our reliance on third parties

We rely, and expect to continue to rely, on third parties, including independent clinical investigators, CROs, and CDMOs to conduct certain aspects of our clinical trials, preclinical studies, development and regulatory filings. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators and third-party CROs and CDMOs, as well as potential collaboration partners to conduct certain aspects of our clinical trials, preclinical studies and discovery programs and to monitor and manage data and conduct randomizations and statistical analyses for our ongoing clinical and preclinical programs. We rely on these parties for execution of our clinical trials and preclinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials and studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors, CROs and CDMOs are required to comply with GCP and GMP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our drug candidates in clinical development. Regulatory authorities enforce these GCPs and GMPs through periodic inspections of trial sponsors, principal investigators, trial sites and manufacturing facilities. If we or any of these third parties, our CROs or our CDMOs fail to comply with applicable GCPs and GMPs, fail to conduct valid randomizations and statistical analyses, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Moreover, our business may be adversely affected if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Further, these investigators, CROs and CDMOs are not our employees and we are not able to control, other than by contract, the amount of resources, including time, which they devote to our drug candidates and clinical trials. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If independent investigators, CROs and CDMOs fail to devote sufficient resources to the development of our drug candidates, if consolidation in the drug manufacturing market results in fewer manufacturers available to us to manufacture the compounds necessary for the development of our drug candidates, or if CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be put on hold by regulatory authorities, extended, delayed or terminated and we may not be able to obtain

regulatory approval for or successfully commercialize our drug candidates. As a result, our operations and the commercial prospects for our drug candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed or precluded entirely.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, we may encounter similar challenges or delays in the future or that these delays or challenges may have a material adverse impact on our business, financial condition and prospects.

We currently rely and expect to rely in the future on the use of manufacturing suites in third-party facilities or third parties to manufacture our drug candidates. Our business could be harmed if we are unable to use third-party manufacturing suites or if the third-party manufacturers fail to provide us with sufficient quantities of our drug candidates or fail to do so at acceptable quality levels or prices.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and we rely on outside vendors to manufacture our drug candidates in clinical quantities. We expect to rely in the future on these third parties to manufacture our products in sufficient commercial quantities if and when the products are ultimately approved by FDA or other regulatory authorities.

Our reliance on third parties for clinical quantities exposes us to a number of risks, including:

- our third-party manufacturers might be unable to timely manufacture our drug candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any;
- contract manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately and incompliance with cGMP; and
- our third-party manufacturers could breach or terminate their agreements with us.

Each of these risks could delay or prevent the completion of our clinical trials or the approval of any of our drug candidates by the FDA or result in higher costs. In addition, we will rely on third parties to perform certain specification tests on our drug candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm and the FDA could place significant restrictions on our company until deficiencies are remedied.

Our third-party manufacturers may also encounter difficulties in production, particularly in scaling up or out to meet commercial demand if and when the products are approved by FDA or other regulatory authorities, validating the production process, and assuring high reliability of the manufacturing process. These problems could include delays or break-downs in logistics and shipping, difficulties with production costs and yields, quality control, product testing, operator error, lack of availability of qualified personnel, or failure to comply with strictly enforced federal, state and foreign regulations.

Our third-party manufacturers are also subject to government inspections and shutdowns by the FDA and other comparable regulatory authorities. If they are unable to reliably produce products to specifications acceptable to the regulatory authorities, we may not obtain or maintain the approvals we need to manufacture our products. Further, our third-party manufacturing facilities may fail to pass government inspections prior to or after the commercial launch of our drug candidates, which would cause significant delays and additional costs required to remediate any deficiencies identified by the regulatory authorities. Any of these challenges could delay approval of our products, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects.

We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;

- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, and safety and pharmacovigilance reporting.

Any medicines that we may develop may compete with other drug candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We have arrangements in place for our supply of active pharmaceutical ingredient from two suppliers. However, we rely on single source suppliers for raw materials needed for our manufacturing process. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our drug candidates or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We anticipate that a portion of the manufacturing of our drug candidates will take place outside the United States through third-party manufacturers. A significant disruption in the operation of those manufacturers, a trade war or political unrest in such countries could materially adversely affect our business, financial condition and results of operations.

We currently contract manufacturing operations to third parties, and it is possible that clinical quantities of our drug candidates will be manufactured by third parties outside the United States, including in China. Any disruption in production or inability of such manufacturers outside the United States to produce adequate quantities to meet our needs, whether as a result of a natural disaster or other causes, could impair our ability to operate our business on a day-to-day basis and to continue our development of our drug candidates. Furthermore, since certain of these manufacturers could be located in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the United States or Chinese governments, political unrest or unstable economic conditions in China. For example, a trade war could lead to tariffs on the chemical intermediates we use that are manufactured in China. Any of these matters could materially and adversely affect our business and results of operations. Any recall of the manufacturing lots or similar action regarding our drug candidates used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third-party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our drug candidates and impair our competitive position. Further, we may be exposed to foreign exchange fluctuations. Future appreciation of such local currencies could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in countries outside the United States.

If our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers. Our manufacturers are subject to numerous environmental, health and safety laws and regulations, including those governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

Our principal investigators, CROs, consultants and employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

Our principal investigators, CROs, consultants and employees may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Business disruptions that affect our third-party CROs and manufacturers could seriously harm our future revenue and financial condition and increase our costs and expenses.

While we rely on multiple CROs for preclinical research and development to mitigate potential impacts that may affect any one of our CROs, we have a single CRO for each clinical trial and single contract manufacturers for multiple steps in the manufacturing or our drugs. CROs and other contractors and consultants could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, pandemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our drug candidates. Our ability to obtain clinical supplies of our drug candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Risks related to regulatory and other legal compliance matters

Our clinical trials may fail to demonstrate adequately the safety and efficacy of any of our drug candidates, which would delay or prevent further clinical development of those candidates, or prevent marketing approval from FDA or similar regulatory authorities.

We have not received approval to market any of our drug candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals. To obtain the requisite regulatory approvals to market and sell any of our drug candidates, including CYT-0851, and any other future drug candidates, we must demonstrate through extensive preclinical studies and clinical trials that our products are both safe and effective in humans. To date, we have only a limited amount of safety and tumor response data in our ongoing phase 1/2 clinical trial of CYT-0851.

Clinical trials that we conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our drug candidates. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same drug candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. The current safety experience of CYT-0851 may not be reflective of the ultimate safety profile of the drug, and rare and sometimes fatal side effects may not be seen until much larger numbers of patients have been treated. If the results of our ongoing or future clinical trials are inconclusive with respect to the efficacy of our drug candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our drug candidates, we may be delayed in obtaining marketing approval, if at all.

Even if the trials are successfully completed, clinical data are often susceptible to varying interpretations and analyses, and we cannot guarantee that the FDA or other comparable foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our drug candidates for approval. We cannot guarantee that the FDA or other comparable foreign regulatory authorities will view our drug candidates as having sufficient efficacy to support the indication studied in the clinical trial even if positive results are observed in early clinical trials. To the extent that the results of the trials are not satisfactory to the FDA or other comparable foreign regulatory authorities for support of a marketing application, approval of our drug candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of our drug candidates. Additionally, any safety or efficacy concerns observed in any of our clinical trials could limit the prospects for regulatory approval of our drug candidates in any disease indication or result in future limitations after approval, which could have a material adverse effect on our business, financial condition and results of operations.

Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our drug candidates, the commercial prospects for our drug candidates may be harmed and our ability to generate revenues will be impaired.

Our relationships with healthcare providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, anti-bribery, physician payment transparency and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.

Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell, and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- federal Anti-Kickback Statute, which prohibits, among other things, persons from offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- federal false claims, false statements and civil monetary penalties laws prohibiting, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment of government funds or knowingly making, or causing to be made, a false statement material to a false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the Physician Payments Sunshine Act, which requires pharmaceutical and medical device companies to report information related to certain payments and transfers of value to certain healthcare providers to the Center for Medicare & Medicaid Services, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback, anti-bribery and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers, as well as other state laws that require companies to comply with specific compliance standards, restrict financial interactions between companies and healthcare providers and require companies to report information related to payments to health care providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices may not comply with healthcare laws and regulations, including, without limitation, certain of our advisory board agreements with physicians who receive stock or stock options as compensation for services provided to us. If our operations are found to be in violation of any of the laws described above or any other government

regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

The U.S. and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval or reimbursement of our current or future drug candidates or any future drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. In particular, in the U.S., there have been and continue to be a number of legislative initiatives at the federal and state level to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, of collectively, the ACA, was enacted, which substantially changed the way healthcare is financed by both government and private payors. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. It is unclear how any efforts to challenge, repeal, or replace the ACA will impact the ACA or our business.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products or (iv) additional record-keeping requirements. Further, healthcare reform may result in changes to payment methodologies, the implementation of pharmaceutical and biological product price controls, and reductions in Medicare and other healthcare funding. If any such changes were to be imposed, they could adversely affect the operation of our business.

The successful commercialization of our drug candidates will depend in part on the extent to which third-party payors establish coverage, adequate reimbursement levels and pricing policies.

Our ability to obtain coverage and adequate reimbursement for our drug candidates by governmental healthcare programs, private health insurers, and other third-party payors will have an effect on our ability to successfully commercialize our drug candidates. We cannot be sure that coverage and reimbursement will be available for our drug candidates or any product that we may develop, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future. No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our drug candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. If reimbursement is not available, is delayed, or is available only at limited levels, we may not be able to successfully commercialize our drug candidates, and may not be able to obtain a satisfactory financial return on our drug candidates.

We, our collaborators and our service providers are subject to a variety of U.S. and international restrictive data privacy and security laws, regulations, contractual obligations and industry standards governing the use, processing and cross-border transfer of data and personal information, which could increase compliance costs and our failure to comply with them could subject us to potentially significant liability, fines or penalties and otherwise harm our business.

We maintain a large quantity of sensitive information, including confidential business information, protected health information and other personal information, and are subject to laws and regulations governing the privacy and security of such information. The global data protection landscape is rapidly evolving, and we and our collaborators and service providers may be affected by or subject to new, amended or existing laws and regulations in the future, including as our operations continue to expand or if we operate in foreign jurisdictions. These laws and regulations may be subject to differing interpretations, which adds to the complexity of processing personal data. Guidance on implementation and compliance practices are often updated or otherwise revised.

In particular, the conduct of our clinical trials may be subject to privacy restrictions based on U.S. and non-U.S. regulations. In many jurisdictions, enforcement actions and consequences for noncompliance are rising. In the United States, these include enforcement actions in response to rules and regulations promulgated under the authority of federal agencies and state attorneys general and legislatures and consumer protection agencies. Laws in all 50 states require businesses to provide notice to customers whose personally identifiable information has been disclosed as a result of a data breach. The

laws are not consistent, and compliance in the event of a widespread data breach is costly. States are also constantly amending existing laws, requiring attention to frequently changing regulatory requirements. For example, we may be subject to the California Consumer Privacy Act, or the CCPA, which became effective on January 1, 2020, and was further amended by the California Privacy Rights Act, or the CPRA, on November 3, 2020. As currently written, the CCPA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. Among other things, the CCPA requires covered companies to provide new disclosures to California residents and provide such residents new data protection and privacy rights, including the ability to opt-out of certain sales of personal information. The CPRA significantly modifies the CCPA by expanding residents' rights with respect to certain personal information and creates a new state agency to oversee implementation and enforcement efforts. Many of the CPRA's provisions will become effective on January 1, 2023. The CCPA provides for civil penalties for violations, as well as a private right of action for certain data breaches. This private right of action may increase the likelihood of, and risks associated with, data breach litigation, including class action litigation.

Additionally, the collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR. The GDPR, which came into effect on May 25, 2018, introduced new data protection requirements in the European Union, as well as potential fines for noncompliant companies of up to the greater of €20 million or 4% of annual global revenue. The regulation imposes numerous new requirements for the collection, use and disclosure of personal information, including more stringent requirements relating to consent and the information that must be shared with data subjects about how their personal information is used, the obligation to notify regulators and affected individuals of personal data breaches, extensive new internal privacy governance obligations and obligations to honor expanded rights of individuals in relation to their personal information (e.g., the right to access, correct and delete their data). Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, and the efficacy and longevity of current transfer mechanisms between the EU and the United States remains uncertain. For example, in 2016, the EU and United States agreed to a transfer framework for data transferred from the EU to the United States, called the Privacy Shield, but the Privacy Shield was invalidated in July 2020 by the Court of Justice of the European Union. At this time, we do not believe we are subject to the GDPR, but should this change, the GDPR will increase our responsibility and potential liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, in June 2016, the UK held a referendum and voted in favor of leaving the EU and, on January 31, 2020, the UK exited the EU and the implementation period or transition period ended on December 31, 2020. This referendum and exit has created political and economic uncertainty, particularly in the UK and the EU, and this uncertainty may last for years. Further, following the withdrawal of the United Kingdom from the EU and the European Economic Area, or the EEA, on January 31, 2020 and the end of the transition period, we will have to comply with the GDPR and separately the GDPR as implemented in the United Kingdom, each regime having the ability to fine up to the greater of €20 million/£17 million or 4% of global turnover. The relationship between the United Kingdom and the EU and the EEA in relation to certain aspects of data protection law remains unclear, including how data transfers between EU and EEA member states and the United Kingdom will be treated. Our business could be affected during this period of uncertainty, and perhaps longer, by the impact of the UK's referendum and exit.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with U.S. and international data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

We may face potential liability if we obtain identifiable patient health information from clinical trials sponsored by us.

Most healthcare providers, including certain research institutions from which we may obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the HITECH. We are not currently classified as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-

abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. In addition, in the future, we may maintain sensitive personally identifiable information, including health information, that we receive throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who may enroll in patient assistance programs if we choose to implement such programs. As such, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA.

The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, the United Kingdom's decision to leave the European Union, referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated now that the United Kingdom has left the European Union.

Furthermore, certain health privacy laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Patients about whom we or our collaborators may obtain health information, as well as the providers who may share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

If we or third-party CMOs, CROs or other contractors or consultants fail to comply with applicable federal, state/provincial or local regulatory requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our therapeutic candidates and could harm or prevent sales of any affected therapeutics that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing and marketing our therapeutics. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business.

Even if we receive regulatory approval of any drug candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drug candidates.

If any of our drug candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, other marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our drug candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including phase 4 clinical trials and surveillance to monitor the safety and efficacy

of the drug candidate. The FDA may also require a REMS program as a condition of approval of our drug candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Comparable foreign regulatory authorities may also have programs similar to REMS. In addition, if the FDA or a comparable foreign regulatory authority approves our drug candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our drug candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our drug candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA does restrict manufacturer's communications on the subject of off-label use of their products. The policies of the FDA and of comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

A variety of risks associated with operating internationally could materially adversely affect our business or that of our collaborators.

Our business strategy includes potentially expanding internationally if any of our drug candidates receives regulatory approval. Doing business internationally involves several risks, including, but not limited to:

- multiple, conflicting, and changing laws and regulations, such as privacy regulations, tax laws, export and import restrictions, economic sanctions laws and regulations, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;

- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses, including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, its books and records provisions, or its anti-bribery provisions, as well as other applicable laws and regulations prohibiting bribery and corruption.

Any of these factors could significantly harm any future international expansion and operations and, consequently, our results of operations.

Risks related to our common stock

An active trading market may not be sustained.

If a market for our common stock is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall. An inactive market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock or fails to publish reports on us regularly, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Insiders have substantial influence over us, which could limit your ability to affect the outcome of key transactions, including a change of control.

As of December 31, 2021, our directors and executive officers and their affiliates beneficially owned shares representing approximately 31% of our outstanding common stock. As a result, these stockholders, if they act together, are able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

We do not expect to pay any dividends for the foreseeable future.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years following our IPO. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are

applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders is different than the information that is available with respect to other public companies. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies.

Further, even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. In addition, if we are a smaller reporting company at the time we no longer qualify as an emerging growth company, we would continue to not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act. These exemptions and reduced disclosures in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock prices may be more volatile.

Provisions in our amended and restated certificate of incorporation, our amended and restated by-laws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation, amended and restated by-laws and Delaware law contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. Our amended and restated certificate of incorporation and by-laws, include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may be removed for cause only;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorized our board of directors to modify, alter or repeal our amended and restated by-laws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock.

In addition, because we are incorporated in the State of Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation designates the state or federal courts within the State of Delaware as the exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state or federal courts within the State of Delaware will be exclusive forums for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated by-laws, (4) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws or (5) any other action asserting a claim against us that is governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or to any claim for which the federal courts have exclusive jurisdiction. Our amended and restated certificate of incorporation also provides that, unless we consent in writing to the selection of an alternative forum, the U.S. federal district courts shall be the exclusive forum for the resolution of any claims arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees.

Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

The market price of our common stock has been volatile and could subject us to securities class actions litigation.

Since shares of our common stock were sold in our IPO in June 2021, the price per share of our common stock has ranged from as low as $3.25 to as high as $23.10. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive drug candidates or technologies;
- the timing and results of clinical trials and preclinical studies for any drug candidates that we may develop;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of drug candidates of our competitors, or announcements about new research programs or drug candidates of our competitors;
- developments or changing views regarding synthetic lethality or the use of PARP inhibition in the context of cancer drug development;
- commencement or termination of collaborations for our product development and research programs;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;

- the level of expenses related to any of our research programs, clinical development programs, or drug candidates that we may develop;
- the results of our efforts to develop additional drug candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and global market conditions; and
- the other factors described in this "Risk Factors" section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future.

We will continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We are continuing to hire additional accounting, finance, and other personnel in connection with our efforts to comply with the requirements of being a public company, and our management and other personnel devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and make some activities more time-consuming and costly. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes Oxley Act, we will be required to furnish a report by our management on our internal control over financial reporting with the SEC. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

The continuing outbreak of COVID-19 (including any resurgences, including due to variants, thereof) in the United States and other countries and shortages of qualified healthcare personnel may adversely affect our business and the market price of our common stock.

The recent COVID-19 pandemic is impacting worldwide economic activity, particularly economic activity in the United States, and poses the risk that we or our employees, contractors, suppliers, or other partners may be prevented or delayed from conducting business activities for an indefinite period of time, including due to shutdowns that may be requested or mandated by governmental authorities. The ongoing COVID-19 pandemic and the measures taken by the governments of countries affected by it could disrupt the supply chain and the manufacture or shipment of both drug substance and finished drug product for our drug candidates for preclinical testing or clinical trials, cause diversion of healthcare resources away from the conduct of preclinical and clinical trial matters to focus on pandemic concerns, limit travel in a manner that interrupts key trial activities, such as trial site initiations and monitoring, delay regulatory filings with regulatory agencies in affected areas or adversely affect our ability to obtain regulatory approvals. These disruptions could also affect other facets of our business, including but not limited to:

- our ability to recruit employees from outside of the United States;
- the ability of our CROs to conduct clinical trials and preclinical studies in countries outside of the United States;
- our ability to important materials from outside of the United States, including raw materials required to manufacture our drug;
- our ability to export materials to our CROs and other third-parties located outside of the United States;
- our ability to identify suitable clinical sites or open those sites for enrollment due to competing business needs;
- our ability to enroll patients due to their fear of coming into medical facilities and their perceived risk of becoming infected at such facilities;
- our ability to initiate clinical trial sites and actively enroll patients due to shortages of healthcare personnel as a result of competition we may face for qualified personnel, labor shortages and reallocation of resources by hospitals from clinical trials to COVID-19 care; and
- our ability to monitor the clinical data generated at clinical sites, required for completion of clinical trials.

The COVID-19 outbreak and mitigation measures also may have an adverse impact on global economic conditions, which could adversely impact our business, financial condition or results of operations. Additionally, the COVID-19 outbreak has resulted in significant financial market volatility and uncertainty. A continuation or worsening of the levels of market disruption and volatility seen in the recent past as a result of the COVID-19 outbreak could have an adverse effect on our ability to access capital and on the market price of our common stock.

Risks related to general legal matters

Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

The use of any medicine drug candidates we may develop in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- significant costs to defend the litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize a drug candidate;

- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- decreased market demand for any product; and
- loss of revenue.

The product liability insurance we currently carry, and any additional product liability insurance coverage we acquire in the future, may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any drug candidate, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim, or series of claims, brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operation and business, including preventing or limiting the commercialization of any precision medicine drug candidates we develop.

U.S. federal income tax reform could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, on March 27, 2020, the United States enacted the CARES Act, which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 coronavirus outbreak, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. Additionally, on December 22, 2017, the United States enacted the Tax Cuts and Jobs Act, or the TCJA, which significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. The TCJA included significant changes to corporate and individual taxation, some of which could adversely impact an investment in our common stock. Many of the provisions of the TCJA and CARES Act still require guidance through the issuance or finalization of regulations by the U.S. Treasury Department in order to fully assess their effects, and there may be substantial delays before such regulations are promulgated or finalized, increasing the uncertainty as to the ultimate effects of the TCJA and CARES Act on us and our stockholders. There also may be technical corrections legislation or other legislative changes proposed with respect to the TCJA and CARES Act, the effects of which cannot be predicted and may be adverse to us or our stockholders. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We may also have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant share price volatility in recent years. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters is located at 128 Spring St, Building A, Suite 510, Lexington, MA 02421, where we lease and occupy approximately 20,167 square feet of office and laboratory space. The current term of our 128 Spring St. lease expires in 2025.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock trades under the symbol "CYT" on the Nasdaq Global Select Market and has been publicly traded since June 18, 2021. Prior to this time, there was no public market for our common stock.

Holders of Record

As of March 1, 2022, there were approximately 48 holders of record of our common shares. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include shareholders whose shares may be held in trust by other entities.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans will be included in our definitive proxy statement for our 2022 annual meeting of shareholders to be filed with the SEC and is incorporated into this Annual Report on Form 10-K by reference.

Dividend Policy

We have never declared or paid any cash dividends on our common shares. We currently intend to retain future earnings to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial conditions, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Recent Sales of Unregistered Equity Securities

None.

Use of Proceeds from our Public Offering of Common Shares

On June 22, 2021, we completed our initial public offering ("IPO") pursuant to which we issued and sold 7,400,000 of our common shares, at a public offering price of $18.00 per share. On July 1, 2021, we sold an additional 885,644 shares of our common stock at a public offering price of $18.00 per share.

The offer and sale of all of our common shares were registered under the Securities Act pursuant to a registration statement on Form S-1, as amended (File No. 333-256601), which was declared effective by the SEC on June 17, 2021. J.P. Morgan Securities LLC, Morgan Stanley & Co. LLC and BofA Securities, Inc. acted as joint book-running managers of the offering and as representatives of the underwriters.

We received aggregate gross proceeds from our IPO of $149.1 million, or aggregate net proceeds of $136.1 million after deducting underwriting fees and offering costs. None of the offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates.

There has been no material change in our planned use of the net proceeds from the IPO as described in our final prospectus dated June 17, 2021 (the "Final Prospectus").

Issuer Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Reserved.

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the related notes to those statements included elsewhere in this Annual Report on Form 10-K. The following discussion and analysis and other parts of this Annual Report on Form 10-K contains forward-looking statements that involve risks, uncertainties and assumptions. Some of the numbers included herein have been rounded for the convenience of presentation. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including those discussed under "Risk Factors" and elsewhere in this Annual Report on Form 10-K.

Overview

We are a clinical-stage biotechnology company focused on developing and commercializing the next-generation of precision oncology medicines that inhibit DNA damage repair and cause cancer cell death in specific subsets of cancer patients through a therapeutic strategy known as synthetic lethality. Synthetic lethality is a clinically validated approach to drug development and arises when the occurrence of two cellular conditions is lethal when occurring simultaneously but tolerated when occurring individually.

Our lead program, CYT-0851 was designed to exploit a novel synthetic lethality between overexpression of a family of DNA damaging enzymes called cytidine deaminases, or CD, and functional inhibition of homologous recombination, or HR, a DNA repair pathway critical for the survival of some cancers. We observed preliminary single-agent activity in the dose-escalation phase 1 portion of our phase 1/2 trial, which we completed in November 2021. In January 2022, we initiated patient dosing with CYT-0851 in the phase 2 expansion cohort portion of the phase 1/2 trial in adult patients with hematologic malignancies and solid tumors. If warranted by the phase 1/2 data, and subject to FDA agreement, we could initiate a potentially registrational trial in early 2023 for the treatment of relapsed and/or refractory lymphoma and/or solid tumors. We also plan to develop CYT-0851 in additional tumor settings as both a monotherapy and in combination with approved cancer therapeutics. In January 2022, we initiated patient dosing in the phase 1 portion of the phase 1/2 trial to assess tolerability and preliminary activity of combinations with three standard-of-care therapies.

Since our inception in 2012, we have focused primarily on organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of novel therapeutics. We do not have any drug candidates approved for sale and have not generated any revenue from product sales. Since our inception, we have funded our operations primarily with proceeds from the sale of redeemable convertible preferred stock and have raised an aggregate of approximately $141.0 million of gross proceeds from the sale of redeemable convertible preferred stock and approximately $149.1 million of gross proceeds from the sale of common stock in our initial public offering, as of December 31, 2021.

We have incurred significant operating losses since inception, including net losses of $42.1 million and $20.8 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021 and 2020, we had an accumulated deficit of $92.1 million and $49.9 million, respectively. These losses have resulted primarily from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. We expect to continue to generate operating losses and negative operating cash flows for the foreseeable future as we:

- continue the research and development of our drug candidates;
- initiate and conduct additional preclinical studies and clinical trials for our drug candidates;
- further develop and refine the manufacturing processes for our drug candidates;
- seek regulatory approvals and pursue commercialization for any of our drug candidates that successfully complete clinical trials;
- seek to identify and validate additional drug candidates and their associated biomarkers;
- obtain, maintain, protect and enforce our intellectual property portfolio;
- seek to attract and retain new and existing skilled personnel;
- acquire or in-license other drug candidates and technologies;

- create additional infrastructure to support our operations as a public company and incur increased legal, accounting, investor relations and other expenses; and
- experience delays or encounter issues with any of the above.

We will not generate any revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for one or more of our drug candidates, if ever. If we obtain regulatory approval for any of our drug candidates, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing and distribution.

As of December 31, 2021, we had cash and cash equivalents of $189.7 million. We believe that our existing cash and cash equivalents as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "Liquidity and Capital Resources."

COVID-19 business update

In response to the ongoing COVID-19 pandemic, we established a cross-functional task force and have implemented business continuity plans designed to address and mitigate the impact of the COVID-19 pandemic on our employees and our business, including our clinical trials. Our operations are considered an essential business and we have been allowed to continue operating under current governmental restrictions during this period. We have taken measures to secure our research and development activities, while our work in laboratories and facilities has been organized to reduce risk of COVID-19 transmission. The extent of the impact of the COVID-19 pandemic on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, trial sites, contract research organizations, or CROs, contract manufacturing organizations, or CMOs, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. While we are experiencing limited financial impacts at this time, given the global economic slowdown, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic, our business, financial condition and results of operations ultimately could be materially adversely affected. We continue to closely monitor the COVID-19 pandemic as we evolve our business continuity plans, clinical development plans and response strategy.

Components of results of operations

Revenue

To date, we have not generated any revenue from product sales. If our development efforts for our drug candidates and preclinical programs are successful and result in regulatory approval, we may generate revenue in the future from product sales.

Operating expenses

Research and development expenses

Research and development expenses consist primarily of costs incurred in connection with the preclinical and clinical development and manufacture of our drug candidates, and include:

- personnel-related expenses, including salaries, bonuses, benefits, stock-based compensation and other related costs for individuals involved in research and development activities;
- external research and development expenses incurred under agreements with CROs as well as investigative sites and consultants that conduct our clinical trials and other scientific development services;
- costs incurred under agreements with CMOs for developing and manufacturing material for our preclinical studies and clinical trials;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- costs related to compliance with regulatory requirements;
- costs of laboratory supplies and acquiring, developing and manufacturing study materials; and

- facilities and other allocated expenses, which include direct and allocated expenses for rent, insurance and other operating costs.

Costs for external development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated financial statements as prepaid or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses and expensed as the related goods are delivered or the services are performed.

A significant portion of our research and development costs have been external costs, which we track on a program-by-program basis after a clinical drug candidate has been identified. Our internal research and development costs are primarily personnel-related costs, internal lab costs and other indirect costs. The majority of our external research and development expenses to date have been incurred in connection with CYT-0851.

We do not allocate employee costs, costs associated with our discovery efforts, and facilities, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We use internal resources and third-party consultants primarily to conduct our research and discovery activities as well as for managing our process development, manufacturing and clinical development activities.

The successful development of our drug candidates is highly uncertain. We plan to substantially increase our research and development expenses for the foreseeable future as we continue our existing clinical trial, initiate future clinical trials for our drug candidates and continue to discover and develop additional drug candidates. Therefore, while we expect our research and development expenses to be higher in 2022 than in 2021, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development and commercialization of our future drug candidates. Our level of costs may be highly variable on a quarterly basis. We are also unable to predict when, if ever, material net cash inflows will commence from the sale of CYT-0851 or potential future drug candidates, if approved. This is due to the numerous risks and uncertainties associated with developing drug candidates, including the uncertainty of:

- the scope, rate of progress and expenses of our ongoing research activities and clinical trials and other research and development activities;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- establishing an appropriate safety profile;
- whether our drug candidates show safety and efficacy in our clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining, maintaining, protecting and enforcing patent and trade secret protection and regulatory exclusivity for our drug candidates;
- commercializing drug candidates, if and when approved, whether alone or in collaboration with others; and
- continued acceptable safety profile of the products following any regulatory approval.

Any changes in the outcome of any of these variables with respect to the development of our drug candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these drug candidates. We may never succeed in achieving regulatory approval for any of our drug candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some drug candidates or focus on others. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that drug candidate.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate and business development and administrative functions.

General and administrative expenses also include professional fees for legal, patent, accounting, auditing, tax and consulting services, insurance costs, and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our general and administrative headcount to support our continued research activities and development of our drug candidates.

Other income

Interest income

Other income includes interest income, which consists of interest earned on cash equivalents that generate interest on a monthly basis.

Results of operations

Comparison of the years ended December 31, 2021 and 2020

The following table summarizes our results of operations:

(in thousands)	Years ended December 31, 2021	2020	Change
Operating expenses:			
Research and development	$ 30,959	$ 16,765	$ 14,194
General and administrative	11,300	4,178	7,122
Total operating expenses	42,259	20,943	21,316
Loss from operations	(42,259)	(20,943)	(21,316)
Other income:			
Other income	133	120	13
Total other income	133	120	13
Net loss	$ (42,126)	$ (20,823)	$ (21,303)

Research and development expenses

The following table summarizes our research and development costs for each of the periods presented:

(in thousands)	Years ended December 31, 2021	2020	Change
Direct research and development expenses by program:			
RAD51-mediated HR inhibitor programs	$ 18,105	$ 9,627	$ 8,478
Unallocated research and development expenses:			
Personnel expenses (including stock-based compensation)	8,285	4,795	3,490
Other expenses	4,569	2,343	2,226
Total research and development expenses	$ 30,959	$ 16,765	$ 14,194

Research and development expenses were $31.0 million for the year ended December 31, 2021, which increased by $14.2 million from $16.8 million for the year ended December 31, 2020. The increase in research and development expenses was primarily attributable to the following:

- a $8.5 million increase in costs related to our RAD51-mediated HR inhibitor programs driven by the continued development of CYT-0851, our lead drug candidate, specifically due to the advancement of our ongoing clinical trial, as well as preclinical costs related to CYT-1853;
- a $3.5 million increase in personnel-related costs, including stock-based compensation expense, primarily due to an increase in headcount; and
- a $2.2 million increase in other research and development operational expenses, including facilities and lab-related costs as well as costs related to our discovery efforts.

General and administrative expenses

General and administrative expenses were $11.3 million for the year ended December 31, 2021, which increased by $7.1 million, from $4.2 million for the year ended December 31, 2020. The increase in general and administrative expenses was primarily attributable to the following:

- a $3.8 million increase in personnel costs, including stock-based compensation expense, primarily due to an increase in headcount; and
- a $3.3 million increase other general and administrative expenses, including professional fees, insurance, facilities, IT services and rent, primarily related to the costs associated with operating as a public company after our initial public offer ("IPO") in June 2021.

Total other income

Total other income was $0.1 million for both years ended December 31, 2021 and 2020 and consists primarily of interest income. The interest income in both periods related to our cash equivalents, which are primarily invested in money market funds.

Liquidity and capital resources

Sources of liquidity

Since our inception, we have not recognized any product revenue and have incurred operating losses and negative cash flows from our operations. We have not yet commercialized any product and we do not expect to generate revenue from sales of any products for several years, if at all.

We have funded our operations primarily with proceeds from the sale of redeemable convertible preferred stock and the sale of common stock in connection with the completion of the IPO. From inception through December 31, 2021, we have raised an aggregate of approximately $141.0 million from the sale of redeemable convertible preferred stock and $136.1 million in net proceeds from the sale of our common stock.

Funding requirements

As of December 31, 2021, we had cash and cash equivalents of $189.7 million. We believe that our existing cash and cash equivalents as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements into 2024. We have based this estimate on assumptions that may prove to be wrong, and we could expend our capital resources sooner than we expect.

We expect to incur significant expenses and operating losses for the foreseeable future as we advance our drug candidates through preclinical and clinical development, seek regulatory approval and pursue commercialization of any approved drug candidates. We expect that our research and development and general and administrative costs will increase in connection with our planned research and development activities. In addition, since the completion of our IPO, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company. If we receive regulatory approval for any of our other drug candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize. We may also require additional capital to pursue in-licenses or acquisitions of other drug candidates.

Because of the numerous risks and uncertainties associated with research, development and commercialization of our drug candidates, we are unable to estimate the exact amount of our working capital requirements. Our future capital requirements will depend on many factors, including:

- the continuation, timing, costs, progress and results of our planned clinical trials of CYT-0851;
- the progress of preclinical development and possible clinical trials of our earlier-stage programs;
- the scope, progress, results and costs of our research programs and preclinical development of any additional drug candidates that we may pursue;
- the development requirements of other drug candidates that we may pursue;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other regulatory authorities;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our drug candidates for which we receive marketing approval;
- the cost of expanding, maintaining, protecting and enforcing our intellectual property portfolio, including filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or any of our drug candidates;
- the extent to which we in-license or acquire rights to other products, drug candidates or technologies;

- the extent to which the impact of COVID-19 or other pandemics may delay the development of our drug candidates;
- our headcount growth and associated costs as we expand our research and development, increase our office space, and establish a commercial infrastructure; and
- the ongoing costs of operating as a public company.

Until such time, if ever, as we can generate substantial product revenue to support our cost structure, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations and other similar arrangements. We are not currently eligible to file a shelf registration statement; however, we believe that shelf registration statements can contribute, when used, to greater financing flexibility. To that end, we plan to file a shelf registration statement on Form S-3 with the SEC once we are eligible to do so. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our shareholders could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common shareholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our drug candidates even if we would otherwise prefer to develop and market such drug candidates ourselves.

Cash flows

The following table summarizes our cash flows for each of the periods presented:

	Years ended December 31,	
(in thousands)	**2021**	**2020**
Net cash used in operating activities	$ (36,032)	$ (18,539)
Net cash used in investing activities	(1,189)	(850)
Net cash provided by financing activities	216,006	1,427
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 178,785	$ (17,962)

Operating activities

Net cash used in operating activities for the year ended December 31, 2021 was $36.0 million, primarily due to our net loss of $42.1 million, partially offset by non-cash charges of $4.0 million and a net change in our operating assets and liabilities of $2.1 million. The non-cash charges consist of stock-based compensation expense of $3.5 million and depreciation expense of $0.5 million. The net change in our operating assets and liabilities was primarily due to a $4.3 million increase in accrued expenses and a $2.2 million increase in prepaid expense and other current assets.

Net cash used in operating activities for the year ended December 31, 2020 was $18.5 million, primarily due to our net loss of $20.8 million, partially offset by non-cash charges of depreciation expense of $0.4 million, stock-based compensation expense of $0.5 million and changes in operating assets and liabilities, including a $1.0 million increase in our accounts payable, $0.1 million increase in accrued expenses, a $0.1 million increase in deferred rent and $0.2 million decrease in prepaid expenses and other current assets.

Investing activities

Net cash used in investing activities was $1.2 million and $0.9 million for the years ended December 31, 2021 and 2020, respectively, and resulted from our purchases of property and equipment.

Financing activities

Net cash provided by financing activities was $216.0 million for the year ended December 31, 2021, consisting of $136.1 million net proceeds from the issuance of common stock upon our IPO, $79.7 million of net proceeds from the issuance of Series C Preferred Stock in February 2021 and $0.2 million from stock option exercises.

Net cash provided by financing activities was $1.4 million for the year ended December 31, 2020, relating to stock option exercises, including $0.8 million from early exercises of stock options.

Off-balance sheet arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules and regulations.

Contractual obligations and commitments

Lease commitments

Operating lease payments represent our commitments for future minimum rent made under non-cancelable lease for our rental space in Lexington, Massachusetts. The total payments for our operating lease obligations at December 31, 2021 is $3.6 million, of which $0.9 million is due in the next twelve months and the remaining payments are due over the term of the lease. For additional details regarding our lease, see Note 12 to our consolidated financial statements.

Purchase and other obligations

We enter into contracts in the normal course of business with CROs and other third-party vendors for clinical trials and testing and manufacturing services. Most contracts do not contain minimum purchase commitments and are cancellable by us upon written notice. Payments due upon cancellation consist of payments for services provided or expenses incurred, including non-cancelable obligations of our service provided up to one year after the date of cancellation.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make judgments, estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in greater detail in Note 2 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Accrued research and development expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel and vendors to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid balance accordingly.

Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period.

Stock-Based compensation

We account for all share-based compensation awards granted as stock-based compensation expense at fair value. Our share-based payments include stock options and grants of common stock, restricted for vesting conditions. The measurement date for awards is the date of grant, and stock-based compensation costs are recognized as expense over the requisite service period, which is generally the vesting period, on a straight-line basis. Stock-based compensation expense is classified in the accompanying statements of operations based on the function to which the related services are provided. We recognize stock-based compensation expense for the portion of awards that have vested. Forfeitures are recorded as they occur.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected share price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and our expected dividend yield. Since there is limited historical data of our share price on the public market, we determined the volatility for awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected term of our stock options granted to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies.

The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. We have not paid, and do not anticipate paying, dividends on our common shares; therefore, the expected dividend yield is assumed to be zero.

Determination of the fair value of common stock

As there was no public market for our common stock prior to our IPO, the estimated fair value of our common stock prior to the IPO was determined by our board of directors considering the valuations of our company's enterprise value prepared by a third-party valuation firm, and in accordance with the guidance outlined in the American Institute of Certified Public Accountants Technical Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation, or the Practice Aid. These third-party valuations utilized either an option pricing method, or OPM, or a hybrid method, both of which used market approaches to estimate our enterprise value. The market approaches utilized in these valuations were based on the subject company transaction method if our company had completed a recent arm's-length securities transaction, or the guideline public company method if no arm's-length securities transaction was completed near the time that the valuation was performed. The subject company transaction method considers the value based on prior transactions of the subject company, and the guideline public company method relies on analysis of publicly traded companies in the same industry or which have similar operating characteristics to the subject company. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more scenarios is calculated using an OPM. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The estimates of fair value of common stock resulting from each scenario are weighted based on the expected likelihood of each outcome. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each share class. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock.

In addition to considering the results of the third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date prior to the IPO, which may have been a date later than the most recent third-party valuation date, including:

- the prices at which we sold preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development efforts, including the status of preclinical studies and ongoing and planned clinical trials for our RAD51-mediated HR inhibitor programs;
- the lack of liquidity of our equity as a private company;
- our stage of development and business strategy and the material risks related to our business and industry;
- the achievement of enterprise milestones;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- any external market conditions affecting the biotechnology industry, and trends within the biotechnology industry;
- the likelihood of achieving a liquidity event for the holders of our preferred stock and common stock, such as an IPO, or a sale of our company, given prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

There are significant judgments and estimates inherent in these valuations. The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different. Following the IPO, the fair value of our common stock is determined based on the quoted market price of our common stock.

Recent accounting pronouncements

See Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our financial statements.

Emerging growth company status

We are an "emerging growth company," or EGC, under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Section 107 of the JOBS Act provides that an EGC can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as private entities.

As an EGC, we have elected to take advantage of certain exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC:

- we may present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations;
- we may avail ourselves of the exemption from providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act;
- we may avail ourselves of the exemption from complying with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis;
- we may provide reduced disclosure about our executive compensation arrangements; and

- we may not require nonbinding advisory votes on executive compensation or stockholder approval of any golden parachute payments.

We will remain an EGC until the earliest of (i) the last day of the fiscal year following the fifth anniversary of the completion of our IPO, (ii) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more, (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous rolling three-year period or (iv) the date on which we are deemed to be a large accelerated filer under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest rate risk

Our primary exposure to market risk is interest rate sensitivity, which is impacted by changes to the general level of U.S. interest rates, particularly because our cash equivalents are in the form of money market funds that are invested in U.S. Treasury securities. As of December 31, 2021 and 2020, we had cash and cash equivalents of $189.7 million and $10.9 million, respectively. Interest income is sensitive to changes in the general level of interest rates; however, due to the nature of these investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio.

As of December 31, 2021 and 2020, we had no debt outstanding, and therefore we are not subject to interest rate risk related to debt.

Foreign currency exchange risk

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates.

Item 8. Financial Statements and Supplementary Data.

The financial information required by Item 8 is located beginning on page F-1 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rule 13a-15(e) and Rule 15d-(e) under the Exchange Act that are designed to ensure that information required to be disclosed by a company in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Our management has evaluated, with the participation of our principal executive officer and principal financial officer, the effectiveness of our disclosure controls and procedures as of December 31, 2021. Based on that evaluation, our principal executive officer and principal financial officer have concluded that, as of December 31, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

This annual report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the company's registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) during the quarter ended December 31, 2021, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not Applicable.

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2022 Annual Meeting of Stockholders within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Our independent public accounting firm is Ernst & Young LLP, Boston, MA, USA, PCAOB Auditor Firm ID 42.

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(1) Financial Statements

See the Index to Consolidated Financial Statements in the Financial Statements Section beginning on page F-1 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

All financial statement schedules have been omitted as they are not required, not applicable, or the required information is included in the financial statements or notes to the financial statements.

(3) Exhibits

Exhibit Number	Description
3.1	Sixth Amended and Restated Certificate of Incorporation of Cyteir Therapeutics, Inc.
3.2	Second Amended and Restated By-laws of Cyteir Therapeutics, Inc.
4.1	Form of Common Stock Certificate
4.2*	Second Amended and Restated Investors' Rights Agreement, by and among Cyteir Therapeutics, Inc. and the investors party thereto, dated as of February 5, 2021
4.3*	Description of the Registrants Securities
10.1	Lease Agreement by and between 128 Spring Street Lexington, LLC and Cyteir Therapeutics, Inc., dated August 8, 2018
10.2	First Amendment to Lease Agreement by and between 128 Spring Street Lexington, LLC and Cyteir Therapeutics, Inc., dated October 15, 2019
10.3	Second Amendment to Lease with 99 Hayden LLC, dated July 1, 2021
10.4	Cyteir Therapeutics, Inc. Amended and Restated 2012 Stock Incentive Plan
10.5	Form of Stock Restriction Agreement under the Cyteir Therapeutics, Inc. 2012 Stock Incentive Plan
10.6	Form of Incentive Stock Option Grant Notice under the Cyteir Therapeutics, Inc. 2012 Stock Incentive Plan
10.7	Form of Non-Qualified Stock Option Grant Notice under the Cyteir Therapeutics, Inc. 2012 Stock Incentive Plan
10.8	Form of Indemnification Agreement between Cyteir Therapeutics, Inc. and its directors and officers
10.9	Amended and Restated Employment Agreement between Cyteir Therapeutics, Inc. and Markus Renschler, M.D., dated May 25, 2021
10.10	Amended and Restated Employment Agreement between Cyteir Therapeutics, Inc. and Andrew Gengos, dated May 25, 2021
10.11	Amended and Restated Employment Agreement between Cyteir Therapeutics, Inc. and Paul Secrist, Ph.D., dated May 25, 2021
10.12	Cyteir Therapeutics, Inc. 2021 Equity Incentive Plan
10.13	Form of Non-Qualified Stock Option Grant Notice for Non-Employee Directors under the Cyteir Therapeutics, Inc. 2021 Equity Incentive Plan
10.14	Form of Incentive Stock Option Grant Notice under the Cyteir Therapeutics, Inc. 2021 Equity Incentive Plan
10.15	Form of Non-Qualified Stock Option Grant Notice under the Cyteir Therapeutics, Inc. 2021 Equity Incentive Plan
10.16	Cyteir Therapeutics, Inc. Employee Stock Purchase Plan
10.17	Cyteir Therapeutics, Inc. Cash Incentive Plan
21.1*	List of Subsidiaries of Cyteir Therapeutics, Inc.
23.1*	Consent of Ernst & Young LLP
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Company Name

Date: By: /s/ Markus Renschler, M.D.

Markus Renschler, M.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Markus Renschler, M.D. **Markus Renschler, M.D.**	President and Chief Executive Officer (Principal Executive Officer)	March 16, 2022
/s/ David Gaiero **David Gaiero**	Vice President, Finance and Treasurer (Principal Financial Officer)	March 16, 2022
/s/ Joseph Zakrzewski **Joseph Zakrzewski**	Chairperson and Director	March 16, 2022
/s/ Racquel Bracken **Racquel Bracken**	Director	March 16, 2022
/s/ Jean George, M.B.A. **Jean George, M.B.A.**	Director	March 16, 2022
/s/ Jeffrey Humphrey, M.D. **Jeffrey Humphrey, M.D.**	Director	March 16, 2022
/s/ Susan Molineaux, Ph.D. **Susan Molineaux, Ph.D.**	Director	March 16, 2022
/s/ Janwillem Naesens, M.Sc., M.B.A. **Janwillem Naesens, M.Sc., M.B.A.**	Director	March 16, 2022
/s/ Timothy Romberger **Timothy Romberger**	Director	March 16, 2022
/s/ Stephen Sands **Stephen Sands**	Director	March 16, 2022
/s/ John Thero **John Thero**	Director	March 16, 2022

Index to consolidated financial statements

Consolidated financial statements for the years ended December 31, 2021 and 2020:

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Cyteir Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Cyteir Therapeutics, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.
Boston, Massachusetts
March 16, 2022

CYTEIR THERAPEUTICS, INC.

Consolidated balance sheets

(in thousands, except share and per share amounts)	Years ended December 31, 2021	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 189,723	$ 10,938
Prepaid expenses and other current assets	3,354	1,193
Total current assets	193,077	12,131
Property and equipment, net	2,055	1,287
Other assets	256	317
Total assets	$ 195,388	$ 13,735
Liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 1,785	$ 1,689
Accrued expenses and other current liabilities	5,726	1,448
Total current liabilities	7,511	3,137
Deferred rent, net of current portion	384	452
Other long term liabilities	201	766
Total liabilities	8,096	4,355
Commitments and contingencies (Note 12)		
Series A redeemable convertible preferred stock, 0 and 5,817,996 shares authorized, issued, and outstanding as of December 31, 2021 and 2020, respectively; liquidation preference of $5,818 as of December 31, 2020	—	5,696
Series B redeemable convertible preferred stock, 0 and 71,199,999 shares authorized as of December 31, 2021 and 2020, respectively; 0 and 55,200,000 shares issued and outstanding as of December 31, 2021 and 2020, respectively; liquidation preference of $55,200 as of December 31, 2020	—	51,715
Series C redeemable convertible preferred stock, 0 shares authorized, issued, and outstanding as of December 31, 2021 and 2020	—	—
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value: 40,000,000 shares authorized as of December 31, 2021; no shares issued and outstanding as of December 31, 2021	—	—
Common stock, $0.001 par value: 280,000,000 and 100,000,000 shares authorized as of December 31, 2021 and 2020, respectively; 35,389,453 and 2,719,721 shares issued as of December 31, 2021 and 2020, respectively; 35,219,834 and 2,044,284 shares outstanding as of December 31, 2021 and 2020, respectively	35	2
Additional paid-in capital	279,310	1,894
Accumulated deficit	(92,053)	(49,927)
Total stockholders' equity (deficit)	187,292	(48,031)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 195,388	$ 13,735

See accompanying notes to consolidated financial statements.

CYTEIR THERAPEUTICS, INC.

Consolidated statements of operations

(in thousands, except share and per share amounts)	Years ended December 31, 2021	2020
Operating expenses:		
Research and development	$ 30,959	$ 16,765
General and administrative	11,300	4,178
Total operating expenses	42,259	20,943
Loss from operations	(42,259)	(20,943)
Other income:		
Other income	133	120
Total other income	133	120
Net loss	$ (42,126)	$ (20,823)
Net loss per share—basic and diluted	$ (2.16)	$ (13.60)
Weighted-average common stock outstanding—basic and diluted	19,499,292	1,530,924

See accompanying notes to consolidated financial statements.

CYTEIR THERAPEUTICS, INC.
Consolidated statements of redeemable convertible preferred stock and stockholders' equity (deficit)

	Redeemable convertible preferred stock										
	Series A		Series B		Series C		Common stock		Additional paid-in	Accumulated	Total stockholders'
(in thousands, except share and per share amounts)	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	capital	deficit	equity (deficit)
Balance at December 31, 2019	5,817,996	$ 5,696	55,200,000	$ 51,715	—	$ —	1,412,954	$ 1	$ 767	$ (29,104)	$ (28,336)
Exercise of common stock options	—	—	—	—	—	—	601,037	1	652	—	653
Vesting of early exercised options	—	—	—	—	—	—	30,293	—	8	—	8
Stock-based compensation expense	—	—	—	—	—	—	—	—	467	—	467
Net loss	—	—	—	—	—	—	—	—	—	(20,823)	(20,823)
Balance at December 31, 2020	5,817,996	$ 5,696	55,200,000	$ 51,715	—	$ —	2,044,284	$ 2	$ 1,894	$ (49,927)	$ (48,031)
Exercise of common stock options	—	—	—	—	—	—	94,714	—	231		231
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $345	—	—	—	—	21,784,885	79,655	—	—	—		—
Initial public offering, net of underwriting discounts, commissions and offering costs		—	—	—	—	—	8,285,644	8	136,112		136,120
Conversion of convertible preferred stock into common stock upon initial public offering	(5,817,996)	(5,696)	(55,200,000)	(51,715)	(21,784,885)	(79,655)	24,290,875	25	137,041		137,066
Vesting of early exercised options	—	—	—	—	—	—	504,317	—	567	—	567
Stock-based compensation expense	—	—	—	—	—	—	—	—	3,465		3,465
Net loss	—	—	—	—	—	—	—	—	—	(42,126)	(42,126)
Balance at December 31, 2021	—	$ —	—	$ —	—	$ —	35,219,834	$ 35	$ 279,310	$ (92,053)	$ 187,292

See accompanying notes to consolidated financial statements

CYTEIR THERAPEUTICS, INC.

Consolidated statements of cash flows

(in thousands)	Years ended December 31, 2021	2020
Cash flows from operating activities:		
Net loss	$ (42,126)	$ (20,823)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	479	351
Stock-based compensation expense	3,465	467
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(2,161)	231
Other assets	61	—
Accounts payable	38	1,027
Accrued expenses and other current liabilities	4,278	78
Other long term liabilities	2	—
Deferred rent	(68)	130
Net cash used in operating activities	(36,032)	(18,539)
Cash flows from investing activities:		
Purchases of property and equipment	(1,189)	(850)
Net cash used in investing activities	(1,189)	(850)
Cash flows from financing activities:		
Proceeds from issuance of preferred stock, net of issuance costs	79,655	—
Proceeds from issuance of common stock upon initial public offering, net of underwriting discounts, commissions and offering costs of $13,022	136,120	—
Proceeds from the early exercise of stock options	—	766
Proceeds from exercise of stock options	231	661
Net cash provided by financing activities	216,006	1,427
Net (decrease) increase in cash, cash equivalents, and restricted cash	178,785	(17,962)
Cash, cash equivalents and restricted cash at beginning of period	11,194	29,156
Cash, cash equivalents and restricted cash at end of period	$ 189,979	$ 11,194
Supplemental disclosure of cash flows		
Deferred financing costs in accounts payable	—	61
Property and equipment purchases still in accounts payable	58	—
Supplemental disclosure of noncash financing activities		
Vesting of early exercised options	567	8
Conversion of preferred stock to common stock upon initial public offering	$ 137,066	$ —

The following table provides a reconciliation of the cash, cash equivalents, and restricted cash balances as of each of the dates shown below:

	Years ended December 31, 2021	2020
Cash and cash equivalents	$ 189,723	$ 10,938
Restricted cash (included in other assets)	256	256
Total cash, cash equivalents, and restricted cash	$ 189,979	$ 11,194

See accompanying notes to consolidated financial statements.

CYTEIR THERAPEUTICS, INC.

Notes to consolidated financial statements

1. Nature of the business

Cyteir Therapeutics, Inc., (the "Company") is a clinical-stage biotechnology company focused on developing and commercializing the next-generation of precision oncology medicines that inhibit DNA damage repair and cause cancer cell death in specific subsets of cancer patients through a therapeutic strategy known as synthetic lethality. The Company's lead program, CYT-0851, was designed to exploit a novel synthetic lethality between overexpression of a family of DNA damaging enzymes called cytidine deaminases, or CD, and functional inhibition of homologous recombination, or HR, a DNA repair pathway critical for the survival of some cancers. The Company is using its expertise in DNA Damage Response biology and a disciplined approach to select targets for other novel, differentiated programs with the aim of building a patient-centric portfolio of effective cancer therapies.

The Company was formed as a Delaware corporation on June 4, 2012, pursuant to the General Corporation Law of the State of Delaware. The Company has a principal office in Lexington, Massachusetts.

Initial Public Offering ("IPO")

On June 22, 2021, the Company completed an IPO in which the Company issued and sold 7,400,000 of its common stock, at a public offering price of $18.00 per share, resulting in gross proceeds of $133.2 million. The Company received $121.6 million in net proceeds after deducting underwriting discounts, commissions and offering costs.

Upon closing of the IPO, all of the then-outstanding shares of convertible preferred stock automatically converted into 24,290,875 shares of common stock at the applicable conversion ratio then in effect. Subsequent to the closing of the IPO, there were no shares of convertible preferred stock outstanding.

On July 1, 2021, the underwriters of the IPO partially exercised their over-allotment option by purchasing an additional 885,644 shares of our common stock at a public offering price of $18.00 per share for gross proceeds of $15.9 million prior to deducting underwriting discounts, commissions, and other offering expenses. The Company received $14.5 million in net proceeds after deducting underwriting discounts, commissions and offering costs. The remainder of the underwriters' over-allotment option expired unexercised.

Reverse Stock Split

On June 11, 2021, the Company effected a 1-for-3.4088 reverse stock split of the Company's common stock and adjusted the ratio at which the Company's preferred stock was convertible into common stock, as well as the number of shares under the 2012 Stock Incentive Plan and the Company's Amended and Restated Certificate of Incorporation, as well as the share amounts of restricted stock grants under the plan and the number of options and exercise prices of options under the plan as a result of the 1-for-3.4088 reverse stock split. All common shares, stock options, and per share information presented in the accompanying consolidated financial statements and notes thereto have been adjusted, where applicable, to reflect the reverse stock split on a retroactive basis for all periods presented. The per share par value and authorized number of shares of the Company's common stock were not adjusted as a result of the split.

Liquidity

The Company has incurred negative cash flows since inception and has funded its operations primarily with proceeds from the sale of redeemable convertible preferred stock and the IPO. As of December 31, 2021, the Company had cash and cash equivalents of $189.7 million and an accumulated deficit of $92.1 million. The Company expects its operating losses and negative operating cash flows to continue into the foreseeable future as it continues to expand its research and development efforts.

The Company expects that its cash and cash equivalents as of December 31, 2021 will be sufficient to fund its operating expenses and capital expenditure requirements for at least twelve months from the date these consolidated financial statements are available to be issued.

The Company will need additional funding to support its planned operating activities. There can be no assurances, however, that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all. If the Company is unable to obtain sufficient funding, it could be required to delay its development efforts, limit activities and reduce research and development costs, which could adversely affect its business prospects.

COVID-19 considerations

The development of the Company's product candidates could be disrupted and materially adversely affected in by a pandemic, epidemic or outbreak of an infectious disease, such as the ongoing COVID-19 pandemic. The ongoing COVID-19 pandemic and the measures taken by the governments of countries affected by it could disrupt the supply chain and the manufacture or shipment of both drug substance and finished drug product for the Company's product candidates for preclinical testing or clinical trials, cause diversion of healthcare resources away from the conduct of preclinical and clinical trial matters to focus on pandemic concerns, limit travel in a manner that interrupts key trial activities, such as trial site initiations and monitoring, delay regulatory filings with regulatory agencies in affected areas or adversely affect the Company's ability to obtain regulatory approvals. These disruptions could also affect other facets of the Company's business, including, but not limited to, the Company's ability to recruit employees from outside of the United States, the ability of the Company's CROs to conduct clinical trials and preclinical studies in countries outside of the United States, the Company's ability to import materials from outside of the United States, including raw materials required to manufacture its drug candidates, the Company's ability to export materials to its CROs and other third-parties located outside of the United States, the Company's ability to identify suitable clinical sites or open those sites for enrollment due to competing business needs, the Company's ability to enroll patients due to their fear of coming into medical facilities and their perceived risk of becoming infected at such facilities, and the Company's ability to monitor the clinical data generated at its clinical sites, required for completion of clinical trials.

The COVID-19 pandemic and mitigation measures also may have an adverse impact on global economic conditions, which could adversely impact the Company's business, financial condition or results of operations. Additionally, the COVID-19 pandemic has resulted in significant financial market volatility and uncertainty. A continuation or worsening of the levels of market disruption and volatility as a result of the COVID-19 pandemic could have an adverse effect on the Company's ability to access capital and on the market price of its common stock. The Company cannot presently predict the scope and severity of any potential business shutdowns or disruptions, but if the Company or any of the third parties on whom it relies on or with whom it conducts business, were to experience shutdowns or other business disruptions, the Company's ability to conduct business in the manner and on the timelines presently planned could be materially and adversely impacted.

2. Summary of significant accounting policies

Basis of presentation and consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP"). The consolidated financial statements include Cyteir Securities Corporation, which was incorporated as a Massachusetts Security Corporation. All intercompany accounts, transactions and balances have been eliminated in consolidation.

Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Changes in estimates and assumptions are reflected in reported results in the period in which they become known. Actual results could differ from those estimates.

Segment information

Operating segments are defined as components of an enterprise for which separate and discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company has one operating segment. The Company's focus is the research and development of small molecule therapeutics that target DNA repair in cancer. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources. All of the Company's long-lived assets are held in the United States.

Cash and cash equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include standard checking accounts and amounts held in money market funds.

Restricted cash

Cash accounts with any type of restriction are classified as restricted cash. The Company has restricted cash deposits with a bank, which serve as collateral for a letter of credit issued to the landlord of the Company's leased facility for a security deposit. The Company classified this amount as restricted cash in the accompanying consolidated balance sheets within non-current assets as of December 31, 2021 and 2020.

Concentration of credit risk and off-balance sheet risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents, and restricted cash. The Company may maintain deposits in federally insured financial institutions and limits its exposure to cash risk by keeping amounts in each institution under the federally insured limits and by placing its cash with high credit quality financial institutions, further the Company has not experienced any losses on these deposits. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimize its exposure to concentration of credit risk. The Company has no financial instruments with off-balance-sheet risk of loss and has not experienced any losses on such accounts.

The Company is dependent on third-party contract research organizations ("CROs") and contract manufacturing organizations ("CMOs") with whom they do business. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements of active pharmaceutical ingredients and formulated drugs in order to perform research and development activities in its programs. The Company also relies on a limited number of third-party contract research organizations to perform research and development activities on its behalf. These programs could be adversely affected by significant interruption from these providers.

Comprehensive loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2021 and 2020, there was no difference between net loss and comprehensive loss.

Property and equipment, net

Property and equipment are stated at cost, less accumulated depreciation. Costs of major additions and betterments are capitalized. Maintenance and repairs which do not improve or extend the life of the respective assets are charged to expense as incurred. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which range from five to seven years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. When an item is sold or retired, the costs and related accumulated depreciation are eliminated, and the resulting gain or loss, if any, is credited or charged to the consolidated statements of operations. Property and equipment to be disposed of are carried at fair value less costs to sell. The estimated useful lives of the Company's property and equipment are as follows:

	Estimated useful life (in years)
Laboratory equipment and computer equipment	5 years
Furniture	5-7 years
Leasehold improvements	Lesser of asset useful life or lease term

Impairment of long-lived assets

The Company accounts for long-lived assets in accordance with ASC Topic 360, *Property, Plant, and Equipment* ("ASC 360"). ASC 360 requires companies to: (i) recognize an impairment loss only if the carrying amount of a long-lived asset is not recoverable based on its undiscounted future cash flows and (ii) measure an impairment loss as the difference between the carrying amount and the fair value of the asset.

The Company tests long-lived assets to be held and used, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of assets or asset groups may not be fully recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written down to their fair values. The Company has not recognized any impairment losses during the years ended December 31, 2021 and 2020.

Fair value measurements

ASC Topic 820, Fair Value Measurement ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes among the following:

Level 1—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. The Company has no assets or liabilities classified as Level 3 on its consolidated balance sheets as of December 31, 2021 and 2020.

Financial instruments consist of cash and cash equivalents, restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses and other current liabilities. These financial instruments are stated at their respective historical carrying amounts, which approximate fair value due to their short-term nature.

Deferred financing costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred financing costs until such financings are closed. After consummation of the equity financing, these costs are presented in the consolidated balance sheets as a direct reduction from the carrying amount of the respective equity instrument issued. Should an in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statements of operations. No amounts were recorded as of December 31, 2021. As of December 31, 2020, the Company recorded deferred financing costs of $0.1 million, presented within other assets on the consolidated balance sheets.

Deferred rent

Deferred rent consists of rent escalation payment terms, tenant improvement allowances, and other incentives received from landlords related to the Company's operating leases. Rent escalation represents the difference between actual operating lease payments due and straight-line rent expense, which is recorded by the Company over the term of the lease. Tenant improvement allowances and other incentives are recorded as deferred rent and amortized as a reduction of periodic rent expense, over the term of the lease.

Research and development costs

Research and development costs are charged to expense as incurred. Research and development costs are comprised of costs incurred in performing research and development activities, including personnel-related costs, stock-based compensation, facilities, research-related overhead, clinical trial costs, contracted services, research-related manufacturing, license fees and other external costs. The Company accounts for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the services have been performed or when the goods have been received.

Accrued research and development expenses

The Company has entered into various research and development contracts. The payments under these contracts are recorded as research and development expenses as incurred. The Company records accrued liabilities for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes the progress of the research and development activities, including the phase or completion of events, invoices received and contracted costs. Significant judgements and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent costs

All patent-related costs incurred in connection with filing and prosecuting patent applications such as direct application fees, and legal and consulting expenses are expensed as incurred due to the uncertainty about the recovery of the expenditure. Patent-related costs are classified as general and administrative expenses within the Company's consolidated statements of operations.

Redeemable convertible preferred stock

The Company has classified redeemable convertible preferred stock ("preferred stock") as temporary equity in the accompanying consolidated balance sheets due to terms that allow for redemption of the shares upon certain events that are outside of the Company's control. The Company did not have any preferred stock outstanding as of December 31, 2021. The Company did not accrete the carrying values of the preferred stock to the redemption values since the occurrence of these events was not considered probable as of December 31, 2020.

Stock-based compensation

The Company accounts for all share-based payment awards granted to employees and non-employees as stock-based compensation expense at fair value. The Company's share-based payments include stock options and grants of common stock, including common stock subject to vesting. The measurement date for employee awards is the date of grant, and stock-based compensation costs are recognized as expense over the employees' requisite service period, which is the vesting period, on a straight-line basis. Prior to the adoption of Accounting Standards Update ("ASU") No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU No. 2018-07") on January 1, 2020, the measurement date for non-employee awards was generally the date the services were completed, resulting in financial reporting period adjustments to stock-based compensation during the vesting terms for changes in the fair value of the awards. Since the adoption of ASU 2018-07, the measurement date for non-employee awards is the date of grant without changes in the fair value of the award. There was no material impact as a result of adopting this new standard. Stock-based compensation costs for non-employees are recognized as expense over the vesting period on a straight-line basis. Stock-based compensation expense is classified in the accompanying consolidated statements of operations based on the function to which the related services are provided. Forfeitures are recorded as they occur.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Since there is limited historical data of the Company's share price on the public market, the Company estimates its expected stock volatility based on the historical volatility of a publicly traded set of representative companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

Net loss per share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted-average number of common shares outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Net loss per share attributable to common stockholders is calculated using the two-class method, which is an earnings allocation formula that determines net loss per share for the holders of the Company's common shares and participating securities. The Company's preferred stock contained participation rights in any dividend paid by the Company and was deemed to be a participating security. Net loss attributable to common stockholders is allocated to each share on an as-converted basis as if all of the earnings for the period had been distributed. The participating securities did not include a contractual obligation to share in losses of the Company and are not included in the calculation of net loss per share in the periods in which a net loss is recorded.

In June 2021, upon the closing of the IPO, all outstanding shares of the Company's preferred stock automatically converted into shares of the Company's common stock. Prior to this conversion, the Company calculated diluted net loss per share using the more dilutive of (a) the two-class method or (b) the if-converted method. The Company allocated earnings first to preferred stockholders based on dividend rights and then to common and preferred stockholders based on ownership interests. The weighted-average number of common shares included in the computation of diluted net loss gives effect to all potentially dilutive common equivalent shares, including outstanding stock options and preferred stock.

Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders generally the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2021 and 2020.

Income taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or the Company's tax returns. Under this method, deferred tax assets and liabilities are determined based on the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements by prescribing a "more likely than not" threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. There are no unrecognized tax benefits included in the Company's consolidated balance sheet as of December 31, 2021 and 2020. The Company's policy is to recognize interest and penalties related to income tax matters in income tax expense. The Company has not recognized interest or penalties in its Statements of Operations since inception.

Recently issued accounting pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB"), or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the impact of recently issued standards that are not yet effective will not have a material impact on the Company's consolidated financial statements upon adoption. Under the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"), the Company meets the definition of an emerging growth company and has elected the extended transition period for complying with certain new or revised accounting standards pursuant to Section 107(b) of the JOBS Act.

Recently Adopted Accounting Pronouncements

In August 2018, the FASB issued ASU No. 2018-13, *Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement*, which modifies certain disclosure requirements on fair value measurements. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other

amendments should be applied retrospectively to all periods presented upon their effective date. The Company adopted ASU 2018-13 as of January 1, 2021. The adoption of ASU 2018-13 had no impact on the Company's consolidated financial statements and accompanying notes.

Recently issued accounting pronouncements not yet adopted

In February 2016, the FASB issued ASU 2016-02, *Leases* (Topic 842) to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the consolidated balance sheets for all leases and disclosing key information about leasing arrangements. This ASU was originally proposed to be effective for annual reporting periods after December 15, 2019, however, in July 2019, the FASB delayed the effective date to January 2021 and ASU 2020-05 delayed the effective date to January 2022. The Company is currently evaluating the impact that this standard will have on its consolidated financial statements and related disclosures.

In December 2019, the FASB issued Accounting Standards Update No. 2019-12 (ASU 2019-12) *Simplifying the Accounting for Income Tax*. The standard contains several provisions that reduce financial statement complexity including removing the exception to the incremental approach for intra-period tax expense allocation when a company has a loss from continuing operations and income from other items not included in continuing operations. The new guidance is effective for the year beginning January 1, 2022 with optional adoption prior to the effective date. The Company does not expect that the new standard will have a material impact to the Company's consolidated financial statements.

3. Fair value measurement

The following tables present information about the Company's financial assets measured at fair value on a recurring basis (in thousands):

	December 31, 2021			
Assets	**Total**	**Quoted prices in active markets for identical assets (level 1)**	**Significant other observable inputs (level 2)**	**Significant other observable inputs (level 3)**
Cash equivalents:				
Money market funds	$ 189,488	$ 189,488	$ —	$ —
Total assets	$ 189,488	$ 189,488	$ —	$ —

	December 31, 2020			
Assets	**Total**	**Quoted prices in active markets for identical assets (level 1)**	**Significant other observable inputs (level 2)**	**Significant other observable inputs (level 3)**
Cash equivalents:				
Money market funds	$ 10,472	$ 10,472	$ —	$ —
Total assets	$ 10,472	$ 10,472	$ —	$ —

During the years ended December 31, 2021 and 2020, there were no transfers between levels. The fair values of the Company's cash equivalents, consisting of its money market funds, are based on quoted market prices in active markets without any valuation adjustment.

The Company uses the carrying amounts of its restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses and other current liabilities to approximate their fair value due to the short-term nature of these amounts.

4. Prepaid expenses and other current assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2021	2020
Prepaid research and development expenses	$ 1,549	$ 871
Prepaid insurance	1,397	19
Payroll tax credit	38	63
Prepaid other	370	240
Total	$ 3,354	$ 1,193

5. Property and equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2021	2020
Laboratory and computer equipment	$ 1,541	$ 694
Leasehold improvements	1,668	1,268
Total property and equipment	3,209	1,962
Less: accumulated depreciation and amortization	(1,154)	(675)
Property and equipment, net	$ 2,055	$ 1,287

Depreciation and amortization expense related to property and equipment for the years ended December 31, 2021 and 2020 was $0.5 million and $0.4 million, respectively.

6. Accrued expenses and other current liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2021	2020
Accrued research and development expenses	$ 3,448	$ 193
Accrued bonuses	1,660	854
Accrued other	618	401
Total accrued expenses and other current liabilities	$ 5,726	$ 1,448

7. Redeemable convertible preferred stock

The Company issued Series A redeemable convertible preferred stock (“Series A Preferred Stock”), Series B redeemable convertible preferred stock ("Series B Preferred Stock), and Series C redeemable preferred stock ("Series C Preferred Stock). Upon issuance of each class of convertible preferred stock, the Company assessed the embedded conversion and liquidation features of the shares and determined that such features did not require the Company to separately account for these features. The Company also concluded that no beneficial conversion feature existed on the issuance date of each class of convertible preferred stock.

In February 2021, the Company completed the sale of an aggregate of 21,784,885 shares of the Series C preferred stock at a purchase price of $3.67 per share for an aggregate purchase price of $79,999,980.

On June 22, 2021, upon closing of the Company's IPO, all of the then-outstanding shares of preferred stock automatically converted into 24,290,875 shares of common stock. There were no outstanding shares of preferred stock at December 31, 2021.

As of December 31, 2020, Preferred stock consisted of the following (in thousands, except share amounts):

	December 31, 2020				
	Preferred stock authorized	Preferred stock issued and outstanding	Carrying value	Liquidation preference	Common stock issuable upon conversion
Series A Preferred Stock	5,817,996	5,817,996	$ 5,696	$ 5,818	1,706,998
Series B Preferred Stock	71,199,999	55,200,000	51,715	55,200	16,195,656
Total	77,017,995	61,017,996	$ 57,411	$ 61,018	17,902,654

Significant terms of the Series A Preferred Stock and Series B Preferred Stock (collectively, "Preferred Stock") were as follows:

Voting

The holder of each share of Preferred Stock was entitled to one vote for each share of common stock into which it would convert and to vote with the common stock on all matters. As long as a minimum number of Series A Preferred Stock and Series B Preferred Stock was outstanding, the holders of the Series A Preferred Stock and Series B Preferred Stock were entitled to elect three directors and the approval of certain actions requires a majority of the Preferred Stockholders.

Conversion

As of December 31, 2020, the shares of Preferred Stock were convertible into shares of common stock, at the conversion price in effect at the time of such conversion, which was initially one-for-one subject to adjustment for certain potential non-dilutive transactions. The conversion could be initiated by the holder at any time or was mandatory (a) at any time upon the written consent of the holders of a majority of the outstanding shares of the Preferred Stock or (b) immediately upon the closing of a qualified public offering of gross proceeds to the Company of at least $50,000,000. In the event that any holder of shares of Series B Preferred Stock did not purchase the full amount of such holder's preferred stock tranche obligation, then each share of Series B Preferred Stock held by such holder automatically converted into shares of common stock at a ratio of 1/10th of the applicable conversion ratio. As all tranche obligations were completed as of July 2019, this conversion feature expired unexercised.

Dividends

The holders of the Preferred Stock were entitled to receive dividends at the rate of 8% of the applicable original issue price per annum, as potentially adjusted for certain non-dilutive transactions. Dividends would accrue whether or not declared, would not be cumulative or compounded and would be payable only when, as and if declared by the Board of Directors (the "Board") and in preference and in priority to any dividends on common stock. There were no dividends declared by the Board.

Liquidation preference

In the event of any liquidation, dissolution, or winding up of the Company ("Liquidation Event"), the holders of Preferred Stock were entitled to receive prior and in preference to the holders of common stock, an amount equal to an amount per share equal to the greater of the original issue price, as potentially adjusted for certain non-dilutive transactions, plus all declared and unpaid dividends on the Preferred Stock or the price per share that would be received if the Preferred Stock were converted to common stock. If the assets and funds available to be distributed to all holders of Preferred Stock were insufficient to permit the payment, in full, of any of the liquidation preferences, then the entire assets and funds legally available for distribution to holders of the Preferred Stock would be distributed ratably among the holders of Preferred Stock, acting as a single class, at the time outstanding, ratably in proportion to the full amounts to which they would otherwise be respectively entitled.

After the payment of the full liquidation preference of the Preferred Stock as set forth above, the remaining assets of the Company legally available for distribution in such Liquidation event would be distributed ratably to the holders of shares of common stock.

Redemption

The Company has determined that all series of preferred stock were redeemable, based on the Certificate of Incorporation that states upon the occurrence of a deemed liquidation event, the holders of preferred stock were entitled to receive cash or other assets.

8. Common stock

The voting, dividend and liquidation rights of the holders of the Company's common stock were subject to and qualified by the rights, powers and preferences of the holders of the preferred stock as set forth above.

The holders of the common stock are entitled to one vote for each share of common stock held submitted to a vote of stockholders, and there are not any cumulative voting rights. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

As of December 31, 2021 and 2020, the Company has reserved the following shares of common stock for the potential conversion of outstanding preferred stock and exercise of stock options:

	December 31,	
	2021	2020
Preferred Stock, as converted	—	17,902,654
Options to purchase common stock	2,778,963	1,293,212
Remaining shares reserved for future issuance	5,670,560	148,035
Total	8,449,523	19,343,901

9. Stock-based compensation

2012 stock incentive plan

The 2012 Stock Incentive Plan (the "2012 Plan") provides for the issuance of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards and other stock awards. Recipients of stock options or stock appreciate rights shall be eligible to purchase shares of the Company's common stock at an exercise price equal to the estimated fair market value of such stock on the date of grant. The exercise price may be less than fair market value if the stock award is granted pursuant to an assumption or substitution for another stock award in the event of a merger or sale of the Company. The maximum term of options granted under the 2012 Plan is ten years, and stock options typically vest over a four-year period. The Board may assign vesting terms to the stock option grants as deemed appropriate. The Company also has the right of refusal to purchase any proposed disposition of shares issued under the 2012 Plan. The 2012 Plan allows for early exercise of all stock option grants if authorized by the Board at the time of grant. The shares of common stock issued from the early exercise of stock options are restricted and vest over time. The Company has the option to repurchase any unvested shares at the original purchase price upon any voluntary or involuntary termination. At the discretion of the Board, unvested shares held by employees may accelerate vesting in the event of a change of control of the Company unless assumed or substituted by the acquirer or surviving entity. The 2012 Plan, as amended, provides for the issuance of up to 6,941,421 shares of common stock as of December 31, 2021, of which 2,732,632 shares of common stock remained available for future grant under the 2012 Plan upon the effectiveness of the 2021 Equity Incentive Plan (the "2021 Plan") and were made available for future issuance under the 2021 Plan.

2021 Equity Incentive Plan

In June 2021, the Company's board of directors adopted, and in June 2021 the Company's stockholders approved, the 2021 Plan, which became effective immediately prior to the effectiveness of the registration statement for the initial public offering. The 2021 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. Upon effectiveness of the 2021 Plan, the number of shares of common stock reserved for issuance under the 2021 Plan was 5,932,632, which represents 3,200,000 shares along with 2,732,632 shares of common stock reserved for issuance under the 2012 Plan that remained available for grant under the 2012 Plan immediately prior to the effectiveness of the 2021 Plan. Shares of our common stock subject to outstanding awards granted under the 2012 Plan that expire unexercised or are terminated, surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right will become available for issuance under the 2021 Plan. The 2021 Plan includes an "evergreen" provision, which provides for an annual increase to

be added on January 1st of each year beginning in 2022 and continuing through and including 2031 by the lesser of (i) 5% of the number of shares of Stock outstanding as of such date and (ii) an amount determined by the board of directors. Upon adoption of the 2021 Plan, the Company ceased the grant of additional awards under the 2012 Plan.

At December 31, 2021, 5,670,560 shares of common stock remained available for future grant under the 2021 Plan.

2021 Employee Stock Purchase Plan

In June 2021, the Company's board of directors adopted, and the Company's stockholders approved, the 2021 Employee Stock Purchase Plan (the "ESPP"), which became effective immediately prior to the effectiveness of the registration statement for the initial public offering. The ESPP is administered by the Company's board of directors or by a committee appointed by the board of directors. The ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 300,000 shares of common stock. The number of shares of common stock reserved for issuance under the ESPP will automatically increase on January 1st of each year beginning in 2022 and continuing through and including 2031 by the least of (i) 1% of the number of shares of Stock outstanding as of such date, (ii) 600,000 shares of Stock and (iii) the number of shares of Stock determined by the Board on or prior to such date for such year, up to a maximum of 6,300,000 shares in the aggregate.

As of December 31, 2021, no shares were issued under the ESPP.

Early exercise of unvested stock options

Shares purchased by employees pursuant to the early exercise of stock options are not deemed, for accounting purposes, to be outstanding shares until those shares vest according to their respective vesting schedules. Cash received from employee exercises of unvested options is included in long-term liabilities on the consolidated balance sheets. Amounts recorded are reclassified to common stock and additional paid-in capital as the shares vest. As of December 31, 2021 and 2020, there were 169,919 and 675,070 unvested shares related to early exercises of stock options, respectively.

Stock option valuation

The assumptions that the Company used in the Black Scholes option-pricing model to determine the grant date fair value of stock options granted were as follows:

	December 31,	
	2021	2020
Risk-free interest rate range%-%	0.75%-1.35%	0.36%-1.20%
Dividend yield%	0.0%	0.0%
Expected life of options (years)	5.5-6.1	5.5-6.5
Volatility rate range%-%	93.6%-97.1%	88.8%-94.6%

The following table summarizes the Company's stock option activity under the 2012 and 2021 Plan:

	Number of shares	Weighted average exercise price	Weighted average remaining contractual term (in years)	Aggregate intrinsic value (in thousands)
Outstanding as of December 31, 2020	1,293,021	$ 1.23	9.03	$ 567
Granted	1,650,548	9.02		
Exercised	(94,714)	2.48		
Forfeited or cancelled	(69,892)	1.91		
Outstanding as of December 31, 2021	2,778,963	$ 5.80	8.76	$ 17,102
Options vested and exercisable as of December 31, 2021	549,877	$ 3.89	8.28	$ 4,149

As of December 31, 2021, there was $9.3 million of unrecognized stock-based compensation expense related to the share-based compensation arrangements under the 2012 and 2021 Plans. The Company expects to recognize this amount over a weighted-average period of 2.2 years.

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value

of the common stock as of the end of the reporting period. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The weighted-average grant date fair value of the Company's stock options granted during the years ended December 31, 2021 and 2020 was $6.87 and $0.94, respectively.

The total fair value of options vested during the years ended December 31, 2021 and 2020, was $2.1 million and $0.4 million, respectively.

Stock-based compensation expense

Stock-based compensation expense included in the Company's consolidated statements of operations is as follows (in thousands):

	December 31,	
	2021	2020
Research and development	$ 1,154	$ 174
General and administrative	2,311	293
Total stock-based compensation expense	$ 3,465	$ 467

10. Income taxes

Loss before provision for income taxes was as follows (in thousands):

	December 31,	
	2021	2020
United States	$ (42,129)	$ (20,800)
Total	$ (42,129)	$ (20,800)

No current or deferred provisions for income taxes were recorded as of December 31, 2021 and 2020, respectively due to losses incurred in both periods.

The following reconciles the differences between income taxes computed at the federal statutory rate and the provision for income taxes:

	December 31,	
	2021	2020
Federal statutory income tax rate	21.0%	21.0%
State taxes	6.8%	6.9%
Valuation allowance	(29.5)%	(31.5)%
Tax Credits	2.5%	3.0%
Stock Based Compensation	(0.4)%	(0.5)%
Other	(0.4)%	1.1%
Total	—%	—%

Certain amounts in prior year's financial statements have been reclassified to conform to the current presentation. The reclassifications had no effect on the reported net loss.

Deferred tax assets and liabilities reflect the net tax effects of net operating loss ("NOL") and tax credit carryforwards and temporary differences between the carrying amount of assets and liabilities for financial reporting and the amounts used for tax purposes. Significant components of the Company's deferred tax assets and liabilities were as follows (in thousands):

	December 31, 2021	December 31, 2020
Deferred tax assets:		
Net operating loss carryforwards	$ 24,239	$ 13,496
Tax credits carryforward	3,163	1,708
Deferred rent	24	10
Accrued expenses	454	233
Stock-based compensation	402	22
Total deferred tax assets	28,282	15,469
Valuation allowance	(27,413)	(14,983)
Deferred tax assets	$ 869	$ 486
Deferred tax liabilities:		
Depreciation	$ (433)	$ (213)
Prepaid expenses	(396)	(273)
Stock-based compensation	(40)	—
Total deferred tax liabilities	(869)	(486)
Net deferred tax assets	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2021 and 2020. Management reevaluates the positive and negative evidence at each reporting period. Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2021 and 2020 related primarily to the increase in net operating loss carryforwards and Research and Development credits and were as follows (in thousands):

	December 31, 2021	December 31, 2020
Valuation allowance at beginning of year	$ 14,983	$ 8,426
Increases recorded to income tax provision	12,430	6,557
Valuation allowance at end of year	$ 27,413	$ 14,983

As of December 31, 2021, the Company had federal net operating loss carryforwards of approximately $89.4 million, including $84.9 million of which may be available to offset future income tax liabilities indefinitely, while $4.6 million of carryforwards that were in existence as of December 31, 2017 may offset future income tax liabilities up through 2037. The Company had state net operating loss carryforwards of approximately $86.5 million to offset future state taxable income which will expire at various time through 2041. The Company also had U.S Federal research and development tax credit carryforwards of $2.8 million available to offset future U.S. federal income taxes. As of December 31, 2021, the Company had state tax credit carryforwards of $1.1 million which expire at various times through 2035 and may be used to offset future state taxable income.

The Company's NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

The Company has not completed a study to assess whether a change of ownership has occurred, or whether there have been multiple ownership changes since its formation, due to the significant cost and complexity associated with such a study. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development

credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has not, as of yet, conducted a study of research and development credit carryforwards. Such a study, once undertaken by the Company, may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheet or statement of operations if an adjustment is required.

The Company accounts for Uncertainty in Income Taxes under the provisions of ASC 740 which defines the thresholds for recognizing the benefits of tax return positions in the financial statements as "more likely than not" to be sustained by the taxing authority. The tax benefit is measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement. As of December 31, 2021 and 2020, the Company has recorded $0.6 million and $0.3 million respectively, in unrecognized tax benefits.

The Company's policy is to recognize both interest and penalties related to unrecognized tax benefits as a component of income tax expense. As of December 31, 2021, and 2020, respectively, there were no interest or penalties associated with unrecognized tax benefits. The following is a reconciliation of the total amount of unrecognized tax benefits (in thousands):

	December 31,	
	2021	2020
Unrecognized benefit at beginning of year	$ 315	$ 138
Additions/reductions for tax positions related to the current year	267	177
Unrecognized benefit at end of year	$ 582	$ 315

The federal and state income tax returns are generally subject to examinations for the tax years ended December 31, 2018 through December 31, 2020. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period. The Company files income tax returns in the U.S. federal and various state jurisdictions. There are currently no federal or state audits in process.

11. Net loss per share

The Company's potentially dilutive securities, which include preferred stock and stock options, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following shares from the computation of diluted net loss per share attributable to common stockholders as of December 31, 2021 and 2020 because including them would have had an anti-dilutive effect:

	December 31,	
	2021	2020
Series A Preferred Stock	—	1,706,998
Series B Preferred Stock	—	16,195,656
Series C Preferred Stock	—	—
Options to purchase common stock	2,778,963	1,293,212
Unvested shares from early exercises	169,619	675,070

12. Commitments and contingencies

Lease commitments

On November 1, 2018, the Company entered into a lease agreement (the "lease") for office space for a term of 5 years and the Company has the option to extend the term for one additional 3 year period. The Company received a tenant improvement allowance of $70 per square foot, which is being amortized as a reduction in rent expense over the lease term. The Company was also required to provide an initial security deposit in the form of a letter of credit, which is secured by cash on deposit of $0.1 million, which is recorded as restricted cash on the consolidated balance sheets. Rent expense,

recognized on a straight-line basis over the term of the lease, for the years ended December 31, 2021 and 2020 was $0.6 million and $0.5 million, respectively.

On October 15, 2019, the Company entered into the First Amendment to the Lease (the "1st Amendment") for additional office space at 128 Spring Street in Lexington, Massachusetts. The term of the 1st Amendment began on February 16, 2020 and runs co-terminus with the existing lease through October 31, 2023. The Company also has the same option to extend the term of the 1st Amendment for one additional 3 year period. The Company received a tenant improvement allowance of $60 per square foot. which is being amortized as a reduction in rent expense over the lease term. The Company was required to increase its total security deposit to $0.3 million as of the commencement date of the 1st Amendment.

On July 1, 2021, the Company entered into a Second Amendment (the "2nd Amendment") to the Lease with 99 Hayden LLC, successor-in-interest to 128 Spring Street Lexington, which covers certain laboratory and office space at Ledgemont Technology Center at 99 Hayden Avenue, Lexington, Massachusetts (the "Premises"). The 2nd Amendment expands the space leased by the Company at the Premises by approximately 5,531 square feet to a total of 20,167 rentable square feet for an additional two years and two months, commencing on October 31, 2023 and expiring on December 31, 2025.

The future minimum payments required under the lease as of December 31, 2021 are as follows (in thousands):

Year Ending December 31,		
2022	$	899
2023		913
2024		881
2025		907
	$	3,600

Legal proceedings

From time to time, in the ordinary course of business, the Company is subject to litigation and regulatory examinations as well as information gathering requests, inquiries and investigations. As of December 31, 2021, there were no matters which would have a material impact on the Company's financial results.

13. Employee benefit plans

The Company has a 401(k) retirement plan for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) plan within statutory and 401(k) plan limits. The Company has made no matching contributions during the years ended December 31, 2021 and 2020.