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, 2024

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 001-41989

BOUNDLESS BIO, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization) 10955 Alexandria Way, Suite 100, San Diego, CA (Address of principal executive offices) 83-0751369 (I.R.S. Employer Identification No.)

> 92121 (Zip Code)

Registrant's telephone number, including area code: (858) 766-9912

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 \$	0.0001 per share	BOLD	Nasdaq Global Select Market
Securities registered	pursuant to Section 12(g) of the Act: None		
Indicate by check ma	rk if the registrant is a well-known seasoned issuer, a	as defined in Rule 405 of the	Securities Act. YES □ NO ⊠
Indicate by check ma	rk if the registrant is not required to file reports pursu	uant to Section 13 or 15(d) of	f the Act. YES \Box NO \boxtimes
Indicate by check ma months (or for such shorter pe	rk whether the registrant: (1) has filed all reports req riod that the registrant was required to file such repo	uired to be filed by Section orts), and (2) has been subject	3 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 to such filing requirements for the past 90 days. YES ⊠ NO □
Indicate by check ma this chapter) during the preced	rk whether the registrant has submitted electronically ling 12 months (or for such shorter period that the re	y every Interactive Data File gistrant was required to sub	required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of nit such files). YES \boxtimes $\;$ No \square
Indicate by check ma the definitions of "large accele	rk whether the registrant is a large accelerated filer, a erated filer," "accelerated filer," "smaller reporting c	an accelerated filer, a non-ac ompany," and "emerging gr	celerated filer, smaller reporting company, or an emerging growth company. Se with company" in Rule 12b-2 of the Exchange Act.
Large accelerated filer			Accelerated filer
Non-accelerated filer	X		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.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

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 registrant's common stock held by non-affiliates of the registrant was approximately \$68.4million on the last business day of the registrant's most recently completed second fiscal quarter based on the closing price of \$3.87 per share, which was the closing price of the registrant's common stock as reported on the Nasdaq Global Select Market on such date. Shares of common stock held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant on such date have been excluded from this computation. The determination of affiliate status for this purpose is not necessarily a conclusive determination for other purposes.

The number of shares of registrant's Common Stock outstanding as of March 21, 2025 was 22,300,043.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the registrant's definitive proxy statement for the 2025 annual meeting of stockholders to be filed with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year covered by this report are incorporated by reference into Part III of this report.

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PART I

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND MARKET AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act) and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). All statements other than statements of historical facts contained in this report are forward-looking statements, including statements regarding our future results of operations and financial position, our use of the net proceeds from the initial public offering of our common stock, the sufficiency of our cash position to fund operations and achievement of milestones, including clinical data readouts and regulatory filings, the timing and likelihood of success, plans, and objectives of management for future operations, business strategy, research and development plans, the anticipated timing, costs, design, and conduct of our ongoing and planned clinical trials and preclinical studies for our extrachromosomal DNA (ecDNA) directed therapeutic candidates (ecDTx), ecDNA diagnostic, our other discovery programs, the timing of expected data readouts, the potential safety and therapeutic benefits of our ecDTx, the potential addressable patient populations for our ecDTx, the timing and likelihood of development candidate nominations from our discovery-stage programs, the timing and likelihood of regulatory filings and approvals for our ecDTx, expected regulatory approval pathways for our ecDTx and any ecDNA diagnostic, our ability to commercialize our ecDTx, if approved, the pricing and reimbursement of our ecDTx, if approved, potential competition for our ecDTx, the potential to develop future ecDTx, the potential benefits of strategic collaborations and our intent to enter into any strategic arrangements, our intellectual property and other market exclusivity strategies.

In some cases, you can identify forward-looking statements by terms such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "would," "target," or "will" or the negative of these terms or other similar expressions. Our forward-looking statements are only predictions. We have based our forwardlooking statements largely on our current expectations and projections about future events and financial and other trends that we believe may affect our business, financial condition, and results of operations based upon information available to us as of the date of this report. Such information may be limited or incomplete. Forward-looking statements in this report speak only as of the date of this report and are subject to several risks, uncertainties, and assumptions, including those described in Part I, Item 1, "Business," and Item 1A, "Risk Factors," and Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations." The events and circumstances reflected in our forward-looking statements may not be achieved or occur and our actual results, performance, or achievements could differ materially from those expressed or implied by our forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not place undue reliance on any forwardlooking statement. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances, or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

In addition, statements that "we believe" and similarly qualified statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to rely unduly upon them.

We obtained the industry, market, and competitive position data used in this report from our own internal estimates and research, as well as from independent market research, industry, and general publications and surveys, governmental agencies, and publicly available information in addition to research, surveys, and studies conducted by third parties. The content of these third-party sources, except to the extent specifically set forth in this report, does not constitute a portion of this report and is not incorporated herein. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research, and our industry experience and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

In addition, while we are responsible for all of the disclosure contained in this report and we believe the industry, market, and competitive position data included in this report is reliable and based on reasonable assumptions, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed below under the section titled "Risk Factors Summary" and in Part I, Item 1A, "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

RISK FACTORS SUMMARY

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 factors summary, and other risks that we face, can be found in Part I, Item 1A., "Risk Factors," of this Annual Report on Form 10-K, and should be carefully considered, together with other information in this report and our other filings with the U.S. Securities and Exchange Commission (SEC) before making investment decisions regarding our common stock.

- We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.
- We will require substantial additional financing to finance our operations, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our ecDTx development programs, commercialization efforts or other operations.
- We are early in our development efforts and have only one ecDTx in clinical development. All of our other ecDTx programs are still in the preclinical or discovery stage. If we are unable to successfully develop, obtain regulatory approval, and ultimately commercialize any of our current or future ecDTx, or experience significant delays in doing so, our business will be materially harmed.
- Our approach to treating cancer with oncogene amplifications by developing ecDTx directed against ecDNA is unproven, and we do not know whether we will be able to develop any products of commercial value, or if competing approaches will limit the commercial value of our ecDTx.
- Clinical and preclinical development involves a lengthy and expensive process with uncertain timelines and outcomes, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Our ecDTx may not achieve favorable results in clinical trials or preclinical studies or receive regulatory approval on a timely basis, if at all.
- Any difficulties or delays in the commencement or completion, or the termination or suspension, of our current or planned clinical trials or preclinical studies could result in increased costs to us, delay or limit our ability to generate revenue, or adversely affect our commercial prospects.
- Use of our ecDTx could be associated with side effects, adverse events, or other properties or safety risks, which could delay or preclude regulatory approval, cause us to suspend or discontinue clinical trials, abandon an ecDTx, limit the commercial profile of an approved label, or result in other significant negative consequences that could severely harm our business, financial condition, results of operations, and prospects.
- If we are unable to successfully develop an ecDNA diagnostic to enable patient selection for our ecDTx, or if we experience significant delays in doing so, we may not realize the full commercial potential of our ecDTx.
- We face significant competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If our competitors develop and commercialize their product candidates more rapidly than we do, or their technologies or their product candidates are more effective, safer, or less expensive than our ecDTx, our business and our ability to develop and successfully commercialize ecDTx may be adversely affected.
- We rely on third parties to conduct our clinical trials and preclinical studies, to develop an ecDNA diagnostic, and to manufacture our ecDTx, and these third parties may not perform satisfactorily, which could delay, prevent, or impair our development or commercialization efforts
- If we are unable to obtain, maintain, defend, and enforce patent or other intellectual property protection for our ecDTx, ecDNA diagnostic, or technology, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our ecDTx may be adversely affected.
- The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Item 1. Business.

The terms "we," "us," "our," "our company," "Boundless Bio," "Boundless," or the "Company" refer to Boundless Bio, Inc. unless otherwise stated or the context otherwise requires. All information in this report is based on our fiscal year. Unless otherwise

stated, references to particular years, quarters, months, or periods refer to our fiscal years ending December 31 and the associated quarters, months, and periods of those fiscal years.

Overview

We are a clinical-stage oncology company dedicated to unlocking a new paradigm in cancer therapeutics that addresses the significant unmet need in patients with oncogene amplified tumors by interrogating extrachromosomal DNA (ecDNA), a root cause of oncogene amplification observed in 14 to 17% of cancer patients. Our mission is to be the foremost biopharma company interrogating ecDNA biology to deliver transformative therapies that improve and extend the lives of patients with previously intractable oncogene amplified cancers.

ecDNA are large circular units of nuclear DNA that are a primary mechanism of gene amplification and are detected only in cancer cells, not in healthy cells. Despite tremendous advancements in treating cancer broadly, patients with oncogene amplified cancers generally derive little benefit from existing therapies, such as molecular targeted therapies or immunotherapies, and have worse survival rates than patients without oncogene amplification. Using our proprietary Spyglass platform, we identify targets essential for ecDNA functionality in oncogene amplified cancer cells, then design and develop small molecule drugs called ecDNA-directed therapeutic candidates (ecDTx) to inhibit those targets, with the aim to prevent cancer cells from using amplified oncogenes, which is the approach of traditional targeted therapies, our ecDTx are intended to be synthetic lethal in tumor cells reliant on amplification biology. In the context of drug development, synthetic lethality is a therapeutic approach wherein using a drug to inhibit one target is lethal to cancer cells harboring a specific genetic alteration to a second target, but not lethal to healthy cells that lack the genetic alteration to the second target. Accordingly, our ecDTx are designed to preferentially kill amplification-dependent cancer cells, but not healthy cells. They are engineered to disrupt the underlying cellular machinery that enables functional amplification.

Our lead ecDTx, BBI-355, is a novel, oral, selective inhibitor of checkpoint kinase 1 (CHK1), which manages replication stress associated with gene amplification in cancer cells. BBI-355 demonstrated CHK1 inhibition and tumor regressions in oncogene amplified preclinical cancer models, including those enabled by ecDNA, and is currently being studied in a first-in-human, Phase 1/2 clinical trial in patients with oncogene amplified cancers. We refer to this trial as POTENTIATE (Precision Oncology Trial Evaluating Novel Therapeutic Interrupting Amplifications Tied to ecDNA). We expect to have preliminary clinical proof of concept safety and antitumor activity data of BBI-355 in the second half of 2025. Our next program is directed at a previously undrugged kinesin target that we identified as essential for proper ecDNA segregation and inheritance during cancer cell division. We are advancing our Kinesin program through drug discovery and expect to select a development candidate by mid-2025 and submit an investigational new drug application (IND) in the first half of 2026.

We have been evaluating BBI-825, a novel, oral, selective RNR inhibitor, in the Phase 1/2 STARMAP (<u>Study Treating A</u>cquired <u>R</u>esistance: <u>MAPK</u> Amplifications) clinical trial for patients with solid tumors, including those with BRAF^{V600E} or KRAS^{G12C} mutated colorectal cancer that has developed resistance oncogene amplifications. In December 2024, following an assessment of preliminary pharmacokinetic data from the Part 1 portion of the trial, we made the strategic decision not to continue dose escalation of Part 1 or to proceed into the Part 2 portion of STARMAP trial. To date, BBI-825 has been generally well-tolerated in the STARMAP trial.

To assist in identifying patients that may benefit from our ecDTx, we have developed an ecDNA diagnostic, which we internally call ECHO (ecDNA <u>Harboring Oncogenes</u>), to detect ecDNA in patient tumor samples. This test analyzes the genomic data obtained from routine next-generation sequencing (NGS) of patient tumor samples. ECHO is currently being used as a clinical trial assay to determine ecDNA status of patients enrolled in the BBI-355 POTENTIATE trial.

Our pipeline consists of programs directed against targets critical for functional gene amplifications in cancer. We continue to identify new targets, both novel and previously clinically validated, through our proprietary Spyglass platform. To our knowledge, Spyglass is the only platform in the biopharma industry using ecDNA biology to identify specific druggable targets in oncogene amplified cancers. All of our ecDTx have been discovered internally, and we retain global rights for all of our programs.

We consider ourselves to be the world's leading ecDNA company. To our knowledge, we are the first company developing new cancer medicines directed at ecDNA and the only company to date to bring an ecDTx into the clinic. Our efforts build on the work of our scientific founders and advisors, including Dr. Paul Mischel, who is a globally recognized leader in the ecDNA field, having authored more than 20 peer-reviewed publications on ecDNA and the team leader for the National Institute of Health's (NIH) and Cancer Research United Kingdom's (CRUK) Cancer Grand Challenges team devoted to ecDNA and its role in cancer. Dr. Mischel is the Chairman of our Scientific Advisory Board. We leverage this unique expertise to identify new cancer targets that are synthetic lethal in oncogene amplified cancer cells and to develop new medicines for patients with oncogene amplified cancers.

Our Pipeline and Platform



ecDTx: Therapeutic Candidates **ecHO**: Diagnostic Candidate

Our lead ecDTx, BBI-355, is a novel, oral, selective small molecule CHK1 inhibitor being studied in the ongoing first-in-human, Phase 1/2 POTENTIATE clinical trial in patients with oncogene amplified cancers. CHK1 is a master regulator of cells' response to replication stress (RS). RS is elevated in oncogene amplified cancer cells, including those with ecDNA, and, because of this, represents a key vulnerability of those cells. BBI-355 is designed to exploit the elevated RS in oncogene amplified cancer cells by disrupting proper CHK1 function in regulating RS and thereby facilitating catastrophic RS to preferentially kill cancer cells relative to healthy cells. We believe that our approach differentiates us from other biopharma industry efforts targeting CHK1 or related targets. In addition, BBI-355 is orally administered, which, unlike intravenous (IV) dosing of a CHK1 inhibitor, allows for continuous or chronic intermittent dosing, which we believe is critical for targeting ecDNA biology. BBI-355 showed inhibition of CHK1 in a host of tumor cell lines and demonstrated *in vitro* and *in vivo* single agent tumor growth inhibition or tumor regressions across a range of tumor models representing different oncogene amplifications and tumor types. BBI-355 also demonstrated synergistic tumor growth inhibition or tumor regressions when combined with targeted therapies, both *in vitro* and *in vivo*, across multiple oncogene amplification tumor settings. We expect to have preliminary clinical proof of concept safety and antitumor activity data of BBI-355 from our ongoing POTENTIATE trial in the second half of 2025.

Our next therapeutic program aims to dysregulate ecDNA segregation, which we identified as a unique node of ecDNA vulnerability via our Spyglass platform. Specifically, we are targeting a kinesin involved with the cellular mechanism for segregation of ecDNA and its resulting inheritance into dividing cells. We are advancing our Kinesin program through drug discovery and expect to nominate a development candidate by mid-2025 and submit an IND in the first half of 2026.

We continue to leverage Spyglass to identify and preclinically validate additional targets that span multiple, diverse synthetic lethal nodes in oncogene amplified cancers. In addition to the programs described above, we have preclinically validated multiple additional targets and have initiated ecDTx drug discovery efforts to identify candidates against such targets. We expect to continue to identify and preclinically validate additional cancer targets using our Spyglass platform in the future.

We believe our unique development approach has many potential benefits for patients, including:

- addressing oncogene amplified cancers, a type of cancer without effective treatment options;
- identifying patient populations most likely to benefit from our ecDTx by using a biomarker-driven approach, including our proprietary ecDNA diagnostic; and
- employing a tumor-agnostic development strategy, as appropriate, focusing on oncogene amplified cancers across a broad range of tumor types and amplified oncogene drivers.

Our Strategy

Our mission is to be the foremost biopharma company interrogating ecDNA biology to deliver transformative therapies that improve and extend the lives of patients with previously intractable oncogene amplified cancers. To accomplish this mission, our strategy is to leverage our unique expertise in ecDNA biology and its role in oncogene amplified cancer to pioneer the discovery, development,

and commercialization of novel ecDTx for these patients who are not successfully treated by existing therapeutic options. The principal components of our strategy are to:

- Advance our lead ecDTx, BBI-355, a CHK1 inhibitor, through clinical development and regulatory approval in patients with oncogene amplified cancers, including those enabled by ecDNA. We believe that with the optimized biochemical profile of BBI-355, including its oral route of administration, along with our differentiated precision oncology development strategy and approach to identify patients with oncogene amplifications on ecDNA using our ecDNA diagnostic, we can overcome the historical challenges encountered with prior CHK1 inhibitors. We expect to have preliminary clinical proof of concept safety and antitumor activity data of BBI-355 from our ongoing POTENTIATE trial in the second half of 2025.
- Advance our Kinesin program to identify a development candidate and progress it into IND-enabling studies. Through Spyglass, we have gained a deeper understanding of unique ecDNA segregation mechanisms during cell division and identified a kinesin target essential for ecDNA segregation and inheritance, whose inhibition is synthetic lethal to ecDNA-enabled cancer cells. This program is directed to a kinesin, which is a member of a class of known druggable proteins, but for which there are no approved drugs and to our knowledge no other publicly disclosed drug discovery efforts. We have identified oral, small molecule degraders of this target and expect to nominate a development candidate by mid-2025 and submit an IND in the first half of 2026.
- **Deploy our proprietary ecDNA diagnostic, ECHO, to identify patients most likely to benefit from our ecDTx.** Our ecDNA diagnostic is a software algorithm intended to detect ecDNA in patient tumor samples by analyzing the genomic data of those samples available from routine NGS tests that are commonly used by commercial reference and academic laboratories for profiling patient tumors. Our ecDNA diagnostic is currently being used as a clinical trial assay to determine ecDNA status of patients enrolled in the BBI-355 POTENTIATE trial and we intend to discuss with the FDA whether it will be appropriate or required to enable commercialization of our ecDTx, if approved.
- Leverage Spyglass to continue to identify and preclinically validate additional targets to expand our therapeutic pipeline. We utilize Spyglass to identify targets that exploit cellular vulnerabilities of oncogene amplified cancers. Our target identification efforts to date have revealed multiple distinct nodes of vulnerability within the lifecycle of ecDNA. We continuously incorporate new models, tools, and technologies into our Spyglass platform to identify novel points of synthetic lethality in oncogene amplified cancers. In addition to our programs described above, we have preclinically validated multiple additional targets and have initiated ecDTx drug discovery efforts to identify potential candidates against such targets. We continue to deploy Spyglass to identify and preclinically validate additional targets for future potential ecDTx development opportunities.
- **Opportunistically pursue strategic collaborations to accelerate development timelines and maximize the commercial potential of our ecDTx.** The large number of potential intervention points in the ecDNA life cycle identified by our Spyglass platform has the potential to provide us with more targets, ecDTx, and clinical development strategies than we may be able to pursue on our own. We believe this abundance of potential treatment opportunities may provide an opportunity for potential strategic collaborations involving our targets, our ecDTx, our ecDNA diagnostic test, or our Spyglass platform to maximize the patient benefit and long-term value of our research and development portfolio.

Our History and Team

Our company was founded in 2018 by a leading healthcare investor, ARCH Venture Partners, and the world's leading academic researchers in the burgeoning field of ecDNA. One of our scientific co-founders, Paul Mischel, M.D., Institute Scholar ChEM-H and Vice Chair of Research and Professor for the Department of Pathology at Stanford University, and member of the National Academy of Medicine, is internationally recognized for his expertise in ecDNA and cancer biology. Dr. Mischel serves as the Chairman of our Scientific Advisory Board.

Our other scientific co-founders include:

- Vineet Bafna, Ph.D., Professor of Computer Science & Engineering at the University of California, San Diego; co-founder of Digital Proteomics; current member of our Scientific Advisory Board.
- Howard Chang, M.D., Ph.D., Senior Vice President of Research and Chief Scientific Officer at Amgen, former Director of the Center for Personal Dynamic Regulomes and the Virginia and D.K. Ludwig Professor of Cancer Genomics at Stanford University; co-founder of Accent Therapeutics, Cartography Biosciences, Epinomics, and Orbital Therapeutics; former Howard Hughes Medical Investigator; member of the National Academy of Sciences; current member of our Scientific Advisory Board.

- Ben Cravatt, Ph.D., Professor and Gilula Chair in Biology and Chemistry at The Scripps Research Institute; co-founder of Abide Therapeutics, ActiveX Biosciences, Belharra Therapeutics, and Vividion Therapeutics; recipient of the 2022 Wolf Prize for chemistry; member of the National Academy of Sciences; current member of our Scientific Advisory Board.
- Prashant Mali, Ph.D., Professor of Bioengineering at the University of California, San Diego; co-founder of Navega Therapeutics and Shape Therapeutics.
- Roel Verhaak, Ph.D., Harvey and Kate Cushing Professor in the Department of Neurosurgery at Yale University School of Medicine.

One of our industry co-founders is Jonathan Lim, M.D., Co-founder, CEO, and Chairman of Erasca, Venture Partner at ARCH Venture Partners, and former Co-founder and CEO of Ignyta. Dr. Lim serves as the Chairman of our Board of Directors.

In support of our mission to deliver the world's first ecDTx to patients with oncogene amplified cancers, we have assembled a highly qualified management team with deep experience in precision oncology, drug discovery and development, diagnostic development, company building, capital raising, and strategic partnerships and acquisitions. This team hails from leading oncology-focused organizations such as Ignyta, Loxo Oncology, Sierra Oncology, Halozyme Therapeutics, and Rain Oncology and from leading pharmaceutical companies such as, Genentech/Roche, Eli Lilly, and Merck.

Our management team is led by our President and Chief Executive Officer, Zachary Hornby, who formerly served as Chief Operating Officer and Chief Financial Officer at Ignyta (acquired by Roche/Genentech). At Ignyta, he led the operational team that developed Rozlytrek®, which is globally approved and commercialized for patients with *NTRK*+ solid tumors and *ROS1*+ non-small cell lung cancer. Our Chief Scientific Officer, Chris Hassig, Ph.D., brings over 20 years of oncology research, target discovery, and drug development experience to Boundless Bio. Dr. Hassig was most recently Chief Scientific Officer at Sierra Oncology (acquired by GlaxoSmithKline) where he spearheaded research efforts for the company's pipeline against several oncology and hematology targets. Our Chief Medical Officer, Robert Doebele, M.D., Ph.D., is a medical oncologist and previously served as Chief Medical Officer and Chief Scientific Officer at Rain Oncology, where he led the early and late-stage development of multiple oncology programs using biology-based, tumor-agnostic strategies.

Evolution of Precision Oncology

Cancer is the second leading cause of mortality in the United States, accounting for approximately 1,900,000 new diagnoses and 600,000 deaths on an annual basis. There are many genetic aberrations, including mutations, fusions, and amplifications that lead to the malignant cellular growth that results in cancer.

The first approved precision oncology drugs were predominately directed at the proteins produced by oncogenes hyperactivated by gene mutations or gene fusions. These drugs targeted specific types of receptor tyrosine kinases such as BCR-ABL, HER2, EGFR, ALK, and others. Since 2001, the FDA has approved more than 50 tyrosine kinase inhibitors for the treatment of cancer. This initial class of precision oncology drugs, also known as targeted therapies, generated more than \$30 billion of worldwide sales in 2023. Much of the commercial success of these targeted therapies is due to their capacity to drive deeper and more durable responses than conventional chemotherapy regimens while minimizing unwanted side effects and damage to normal healthy tissues.

An evolution in the understanding of tumor biology coupled with an improved ability to segment subsets of tumors based on genomic alterations has led to the development of new therapies that transcend single tumor or organ-targeted cancers. This improved molecular understanding of cancer resulted in the approval of therapies that address specific genomic features of tumors but are tumor type agnostic; some examples are the TRK inhibitors, including entrectinib and larotrectinib, for the treatment of tumors with *NTRK* gene fusions. This trend for tumor-agnostic indications represented a breakthrough in patient identification, drug development, clinical trial designs, and speed to market approvals, albeit benefiting relatively modest sized patient populations.

Despite these advances of the precision oncology field, treatment resistance is still an unfortunate inevitability in cancer. The predominant resistance mechanisms to targeted therapies are secondary mutations of the treatment target (e.g., *EGFRT790M*, *ALKG1202R*), other means of pathway activation, and oncogene or resistance gene amplifications. The quest to address resistance has given rise to a newer generation of targeted therapies and treatment modalities, mostly directed at secondary mutations and alternative pathways. However, there are still very few approved or investigational therapies in development for patients with gene amplifications.

Significant Unmet Medical Need in Oncogene Amplified Cancers

While progress in treating cancers with other forms of oncogenic driver alterations continues to advance, patients whose cancers harbor oncogene amplifications remain a high unmet medical need. Cancers with gene amplifications are characterized by the abnormal

presence of more than two copies of any gene within the human genome; when more than eight copies of a gene are present, this is often referred to as high copy number gene amplification. Genes whose activating mutation or amplification are associated with cancer are referred to as oncogenes. According to analyses of large cancer patient databases, greater than 25% of all cancer cases involve oncogene amplifications, suggesting that in the U.S. alone the oncogene amplified cancer population may represent more than 400,000 new patients each year across multiple tumor types.

Patients whose tumors harbor oncogene amplification have significantly worse survival compared to the broader cancer population. As seen in the figure below, patients with oncogene amplifications also have significantly worse survival compared to patients with other genetic alterations of the same oncogenes.

Cancer Patients with Oncogene Amplifications Have Worse Survival Than Those with Oncogene Mutations or Fusions



Patients with primary or metastatic cancers with amplifications, point mutations, fusions, or skipping deletions, of these genes: *AR, ALK, ARAF, BRAF, CCND1, CDK4, CDK6, EGFR, ERBB2, FGFR1, FGFR2, FGFR3, FGFR4, HRAS, IDH1, IDH2, KIT, KRAS, MAP2K1, MAP2K2, MAP2K4, MDM2, MET, MYC, NF1, NRAS, NTRK1, NTRK2, NTRK3, PDGFB, PDGFRA, PDGFRB, PIK3CA, RAF1, RET, ROS1*

cBioPortal analysis using MSK-MET (N=14,674 patients) and MSK-IMPACT (N=1,115 patients), p-value =< 0.0001)

A p-value is the probability that the reported result was achieved purely by chance, such that a p-value of less than or equal to 0.05 means that there is a less than or equal to 5% probability that the difference between the control group and the treatment group is purely due to chance. A p-value of 0.05 or less typically represents a statistically significant result. The FDA's evidentiary standard of efficacy when evaluating the results of a clinical trial generally relies on a p-value of less than or equal to 0.05.

Despite the advancements in precision medicine and targeted therapies for these other forms of driver oncogene alterations, as well as immunotherapies for patients whose cancers lack driver oncogenes, both targeted therapies and immunotherapies have proven largely ineffective in oncogene-amplified cancers.

Exami	ples of	Commercial	Targeted	Therapie	s Not Ap	proved for	Oncogene A	mplifications

TARGET	ED THERAPY	TARGET	APPRO	VED		P	NO APPROVAL
palboo ribocio abema	ciclib clib aciclib	CDK4/6	HR+/HER2- bre	ast cancer ————	X	•	Amplification
gefitir afatini erlotir osime	ib b iib rtinib	EGFR	Exon 19 deletion L858R T790M	NSCLC NSCLC NSCLC	×	•	Amplification
erdafi pemig infigra futiba	tinib atinib tinib tinib	FGFR	FGFR3 mutation FGFR2/3 fusion	bladder cancer cholangiocarcinoma	×	►	Amplification
capma tepoti	atinib nib	MET	EXON 14 skipping	NSCLC	X	•	Amplification

Targeted agents that have shown efficacy in patients whose cancers are driven by other oncogene alterations, including point mutations, gene fusions, or skipping deletions, have generally failed to demonstrate robust efficacy in patients whose tumors are driven by oncogene amplification. The lack of approved therapies targeting oncogene amplified tumors exists despite extensive clinical testing of targeted agents in oncogene amplified cancer populations. Clinical studies have shown limited success in treating patients with *EGFR*, *FGFR*, and *CDK4* amplified solid tumors with matching molecular targeted therapies. For example, approved and clinical-stage CDK4/6 inhibitors showed only a collective 2% overall response rate (ORR) in *CDK4* amplified tumors, and FGFR inhibitors showed only a collective 13% ORR in patients with *FGFR* amplified tumors. This unfortunate trend has been observed across several classes of targeted agents when tested in oncogene-amplified tumors. In fact, despite continuous advancement of the precision oncology field, of the more than 200 FDA approved targeted therapies to date, only HER2 inhibitors have ever been approved for oncogene amplified or overexpressed cancer populations.

FGFR Inhibitors Demonstrated Less Clinical Benefit in Patients with FGFR Amplifications Than in Patients with Other FGFR Alterations (Mutations, Fusions)



The presence of oncogene amplification is also associated with a lack of response when patients are treated with immunotherapies, for instance immune checkpoint inhibitors such as pembrolizumab. Furthermore, immune checkpoint inhibitors have been associated with rapid clinical worsening, known as hyper-progression, in patients with oncogene amplified tumors. There is growing evidence that oncogene amplifications could be one of the mechanisms that cancers use to escape immune surveillance or alter the tumor immune environment to avoid being eliminated by the immune system.

Role of extrachromosomal DNA in Oncogene Amplified Cancers

Chromosomal instability and tumor variability, or heterogeneity, account for many failures of targeted therapies in patients with cancer. Oncogene amplification is a consequence of chromosomal instability, arising through either numerical and/or structural alterations in chromosomes including the formation of ecDNA. It has long been recognized that oncogenes can be amplified not only on chromosomes but also on ecDNA. However, the frequency, importance, and specific role of ecDNA in cancer biology has not been well understood until recently. We believe the emerging science of ecDNA, first elucidated by our scientific founders and now the core focus of our Company, brings a new understanding of oncogene amplifications in cancer.

ecDNA are cancer-specific, circular fragments of genomic DNA that often encode full-length genes and regulatory regions such as promoters. ecDNA are physically separate from chromosomes, but still reside in the nucleus, and have unique properties that make them a common cellular mechanism for oncogene amplification. ecDNA often range in size from 2-5 megabase pairs in length and are visible through various forms of microscopy, as seen in the figure below. They have been observed in cancer cells by pathologists for more than 60 years, but until recently their function was unclear.



Microscopy Images of Chromosomes and ecDNA

Low magnification

High magnification

Some of the most common driver oncogenes, such as *EGFR*, *MYC*, *KRAS*, *FGFR*, etc., are found to be amplified on ecDNA and can confer a selective fitness advantage to cancer cells. Oncogenes amplified on ecDNA have several features that distinguish them from amplifications located on chromosomes, including:

- **Overexpression** Genes on ecDNA behave differently from genes on chromosomes because ecDNA are not properly regulated at the epigenetic level. ecDNA have a circular structure that is less tightly compacted compared to chromosomes, allowing easier access to their DNA. The easier access of the DNA to the cellular transcriptional machinery results in highly transcriptionally active genes that are often more actively expressed than genes located on chromosomes.
- *Heterogeneity* ecDNA lack centromeres, a critical regulatory component of chromosomal segregation in cell division. Thus, in contrast to chromosomes, ecDNA can segregate unequally during cell division. This property supports a non-Mendelian inheritance pattern for ecDNA, enabling extreme gene copy number changes in relatively few cell divisions and extensive copy number heterogeneity, thereby driving rapid adaptability and tumor evolution.

These features distinguish oncogene amplification on ecDNA from other forms of oncogenic alterations and uniquely enable amplification dependent tumors to rapidly adapt and evade therapeutics such as targeted therapies.

Circular Shape of ecDNA Enhances Transcriptional Activity, Leading to High Oncogene Expression



Large size: 2 - 5 Mbp Active gene expression

ecDNA Are Inherited via a Non-Mendelian Pattern, Leading to Genomic Heterogeneity



Until recently, the presence of ecDNA in cancer was thought to be a rare event, approximately 1.4% of cancers, and of unclear significance. In 2014, it was demonstrated that ecDNA-enabled gene amplifications are a primary driver of oncogenesis and play a critical role in driving tumor heterogeneity and enabling resistance to targeted therapies. In 2017, it was further demonstrated that ecDNA-enabled gene amplifications were observed in many human cancer types but almost never found in normal cells. More recent publications have shown ecDNA-enabled gene amplifications to be present in 14 to 17% of cancer patients, suggesting an incident population of approximately 750,000 new patients each year in the major addressable markets of the United States, European Union, and Japan, of which approximately 200,000 new patients are in the United States each year. More than half of all cancer cases with high-copy number gene amplification (copy number value >8) have been observed to be in association with ecDNA.

Incident Population of Cancer Patients with ecDNA in the United States, European Union, and Japan is Estimated to be 750,000 Each Year



As seen in the figure below, many of the most aggressive tumor types contain the highest prevalence of ecDNA, including approximately 60% of glioblastomas and approximately 50% of liposarcomas. In fact, based on an analysis of several data sets including The Cancer Genome Atlas (TCGA), Pan-Cancer Analysis of Whole Genomes (PCAWG), and Genomics England (GEL), ecDNA was observed in more than 25% of cases from many different tumor types including: glioblastoma, liposarcoma, esophageal/upper gastrointestinal cancer, ovarian cancer, bladder cancer, lung squamous cancer, head and neck cancer, breast cancer, and gastric cancer.





Analysis of whole genome sequencing data from >3,000 tumor and matched normal samples from donors to TCGA and PCAWG; ~15,000 tumor samples from donors to GEL

Unfortunately, as seen in the figure below, patients whose cancers harbor oncogene amplifications experience significantly shorter survival than cancer patients whose tumors are driven by other molecular alterations, such as mutations or fusions. Due to ecDNA's unique properties in cancer cells, patients with ecDNA-enabled oncogene amplification experience even worse survival. These data strongly indicate that patients with oncogene amplified cancers, including those with ecDNA, are in dire need of a new therapeutic paradigm.





Role of ecDNA in Cancer's Resistance to Therapy

The remarkable genomic plasticity of ecDNA-enabled tumors enables cancers to resist therapies by rapidly adapting their oncogene levels, or by switching their oncogenic drivers all together.

ecDNA's role in enabling resistance to molecular targeted therapies has become better understood through recent preclinical studies. For instance, as seen in the figure below, preclinical studies in a gastric cancer cell line containing FGFR2 amplified on ecDNA demonstrated that cellular resistance to the pan-FGFR inhibitor infigratinib could be driven by oncogene dependency switching from *FGFR2* amplification on ecDNA to a new, rapid amplification of EGFR on ecDNA. Strikingly, this dependency was reversed back to *FGFR2* amplification on ecDNA under EGFR inhibitory pressure via erlotinib. In each case, the initial cell population was sensitive to the respective targeted therapy, resulting in short lived anti-proliferative effects lasting several weeks. Regrowth and resistance to the targeted therapies occurred coincident with switching of the oncogenes amplified on ecDNA.

Dynamic Changes in Average Oncogene Copy Number on ecDNA in Gastric Cancer Cells in Response to Sequential Targeted Therapeutic Pressure



Similarly, mutant oncogenes, such as $BRAF^{V600E}$, $KRAS^{G12C}$, etc., can be amplified on ecDNA as a resistance mechanism to corresponding targeted therapies, such as BRAF or KRAS inhibitors. For example, a mutant $BRAF^{V600E}$ melanoma cell line developed ecDNA-enabled amplification of $BRAF^{V600E}$ after exposure to dual BRAF/MEK inhibitor. This phenomenon has also been documented in clinical cases of melanoma patients treated with an approved BRAF/MEK inhibitor regimen. Relatedly, amplification of $KRAS^{G12C}$ on ecDNA has been reported as a clinical resistance mechanism to the KRAS^{G12C} inhibitor adagrasib and to the KRAS^{G12C} inhibitor sotorasib in combination with EGFR inhibitors; this ecDNA enabled amplification was observed *in vitro* and *in vivo* to confer resistance to both of these clinically validated KRAS^{G12C} inhibitors.

Treatment of Colorectal Cancer Cells with KRAS^{G12C} Inhibitors Generated Resistance via Amplification of *KRASG12C* on ecDNA



In other models, evasion of therapeutic response to the EGFR inhibitor erlotinib was facilitated by rapid loss of the population of *EGFRvIII* amplifications on ecDNA in patient-derived glioblastoma cells, contemporaneous with occurrence of a new cell population containing *MDM2* amplification on ecDNA; this observed effect was consistent with an equivalent lack of response to EGFR inhibitors in *EGFR* amplified cancer patients.

ecDNA can also facilitate resistance to therapeutic classes outside of targeted therapies. ecDNA-enabled resistance to chemotherapy was first demonstrated in a mouse cancer cell line whereby methotrexate treatment led to high amplification of *DHFR* on ecDNA, which was lost upon removal of methotrexate. Similar instances of *DHFR* ecDNA amplification have been recapitulated in multiple human cancer cell lines. Furthermore, amplification of drug efflux pump genes on ecDNA, including the family of ABC transporters, has been observed to facilitate resistance to various chemotherapies and other modalities.

Collectively, these data highlight the striking genomic plasticity and precipitous rise and fall of ecDNA-enabled gene amplification that both drives oncogenesis and enables cancer cells to adapt to various therapeutic pressures, leading to rapid resistance. The rapid adaptability afforded by ecDNA-enabled genomic plasticity, including oncogene switching, helps account for the failure of targeted therapies against oncogene amplification-driven tumors, as well as amplification-driven resistance, resulting in a futile, clinical 'whack-a-mole' phenomenon. We believe a new and differentiated strategy is needed to interfere with the underlying ecDNA biology that engenders tumor adaptability, heterogeneity, and therapeutic resistance.

Our Approach to Treating ecDNA-Enabled Cancer

We aspire to improve clinical outcomes for patients with oncogene amplified cancer by identifying targets essential for the formation and function of ecDNA in cancer cells, then designing and developing drugs to inhibit those targets. As described above, ecDNA contribute to oncogenesis by facilitating high copy number gene amplification and expression and to therapeutic resistance by providing rapid genomic plasticity. While cancer cells can use ecDNA for certain advantages, their reliance on ecDNA can also expose

them to potential vulnerabilities. We use our proprietary Spyglass platform to interrogate ecDNA biology in cancer with the goal of identifying these vulnerabilities in the form of cellular targets that are essential for oncogene amplified tumor cell survival.

We explore the ecDNA lifecycle to identify nodes of synthetic lethality in cancers reliant on amplification biology. In contrast to current precision medicine approaches that focus on targeting proteins that result directly from mutations or fusions of oncogenes such as, *EGFR*, *BRAF*, *ALK*, our precision medicine approach centers on disrupting ecDNA functionality in the cancer cells of patients who are genomically selected based on the presence of ecDNA-enabled oncogene amplification in their tumors. Instead of targeting the specific protein products of the oncogenes encoded by ecDNA, our novel small molecule ecDTx are designed to inhibit cellular machinery proteins that enable ecDNA to function properly, such as those critical for ecDNA formation, expression, replication, repair, and segregation.

We are developing our ecDTx to be administered as single agents and in combination with other therapies. The rationale for a combination approach is based on the observation described above that applying targeted therapy, or other therapeutic pressure, to oncogene amplified cancer cells causes them to respond and adapt via increased reliance on ecDNA. We believe this increased reliance on ecDNA for survival makes the cancer cells more susceptible to our ecDTx. We liken this phenomenon to a cellular vice grip concept as the targeted therapy pushes the surviving cancer cell population to higher reliance on ecDNA, and the ecDTx kills the cancer cells that most rely on ecDNA to survive. Our therapeutic approach is based on the concept of synthetic lethality and uses a strategy to interfere with cancer's ability to employ amplification biology to grow, adapt, and survive.

While targeting ecDNA biology is a novel approach to cancer treatment, our ecDTx drug discovery and development process is rooted in traditional small molecule drug discovery methodology.

Spyglass Platform

We have built our proprietary Spyglass platform to identify specific, druggable targets essential to ecDNA formation and function in cancer cells. To our knowledge, Spyglass is the only platform for identifying ecDNA-enabled vulnerabilities in cancer. We preclinically validate each drug target through our purpose-built validation funnel consisting of multiple oncogene-amplified cancer models. The targets that we identify and preclinically validate represent synthetic lethalities for oncogene amplified tumors.



Spyglass Platform

Spyglass consists of the following elements:

- *Model Systems* A heavily curated library of oncogene amplified cancer model systems, including ecDNA-enabled models, and control models. This library consists of approximately 2,000 well characterized cancer models (*in vitro* and *in vivo*), of which approximately 300 are in-house, including:
 - a panel of ecDNA-enabled models, representing multiple different tumor types, such as colorectal, gastric cancer, and sarcoma and multiple different oncodriver amplifications such as *EGFR*, *FGFR2*, *CDK4*, *KRAS*, and *MYC*;

- a panel of matched control lines of various other states of gene amplification ranging from no amplification to chromosomal forms of amplification;
- the ecDNA-enabled models consist of both "driver oncogene amplified systems" where ecDNA is a primary driver of oncogenesis and "treatment induced resistance systems" where ecDNA becomes the dominant resistance mechanism under therapeutic pressure, such as targeted therapy or chemotherapy; and
- *in vivo* models, including cell derived (CDX) and patient derived (PDX) tumor xenografts.
- *Analytical Tools* A suite of custom-built analytical tools designed to detect, quantify, characterize, monitor, and perturb ecDNA, including:
 - imaging tools for visual detection and monitoring of ecDNA;
 - off-the-shelf sequencing tools coupled to our proprietary analytical methods to detect, quantify, and characterize ecDNA; and
 - whole genome and custom built CRISPR libraries and shRNA to analyze the biology of oncogene and resistance gene amplified cancer cells.
- *Bioinformatics Data* Large databases to understand amplification biology, including:
 - preclinical databases to support target identification, target validation, biological pathway mapping, model library expansion, biomarker discovery, and preliminary indication finding; and
 - clinical databases of cancer patient genomic data and clinical outcome data to validate preclinical findings and help us identify tumor indications representing the largest opportunity and highest unmet need for our novel ecDTx.



Analytical Tools for Model Characterization

WES - whole exome sequencing; SNV - single nucleotide variant; CNV - copy number variation; MSI - microsatellite instability; Indel - insertion and deletion; ECHO - propriety ecDNA diagnostic; ECS - ecDNA solution; RUO - research use only; LP: low-pass; WGS - whole genome sequencing; AA - amplicon architect; SV - structural variation; mFISH - metaphase fluorescence in situ hybridization; iFISH - interphase fluorescence in situ hybridization

Target Identification and Validation

Through Spyglass, we have developed a sophisticated understanding of amplification biology, including ecDNA biology, and key cellular mechanisms that facilitate tumor growth and development of resistance to therapeutic treatments. This understanding has given us new insight on how to disrupt amplification biology and cancer cell growth. Through multiple screening methods, we have identified several potential targets that differ not only by class, but also in the role the target plays in the formation and function of ecDNA in cancer cells.

To complement our target identification approach, we have established a robust target validation funnel through which all our candidate targets must pass before we declare them as targets suitable for initiation of drug discovery efforts. This target validation funnel consists of:

- differential single agent sensitivity in multi cell line panels of matched ecDNA positive (ecDNA+) and ecDNA negative (ecDNA-) cancer cell lines;
- genetic, such as CRISPR, or pharmacologic inhibition of candidate targets in ecDNA-enabled cancer cells *in vitro* and/or *in vivo*;
- phenotypic assessment of ecDNA function in ecDNA-enabled cancer cells in vitro and/or in vivo;
- phenotypic assessment of ecDNA location and distribution in cancer cells;
- synthetic lethality assessment, in combination with various therapeutic classes, in inducible ecDNA assays *in vitro* and/or *in vivo*; and
- *in vivo* assessments performed in multiple CDX and PDX xenograft models representing various cancer types, such as gastric cancer, sarcoma, colorectal cancer, and various oncodriver amplifications, such as *EGFR*, *FGFR2*, *CDK4*, and *MYC*.



Target Identification and Validation Process

The targets that our platform has identified as suitable for drug discovery efforts consist of targets that are either novel, previously clinically validated but lacking approved drugs, or have approved pharmaceutical agents but nonselective to the target. There appears to be a wide range of potential targets whose inhibition impact distinct aspects of the ecDNA life cycle, including enzymatic machinery responsible for segregation, replication, transcription, and repair. Each category of targets may have differentiated benefits in terms of optimal treatment setting, efficacy, tolerability, therapeutic index, and single agent versus combination approach. In addition to targets against which we have initiated drug discovery efforts, we also have multiple additional candidate targets for which we are currently pursuing preclinical target validation efforts. We believe that our ability to identify and pursue ecDNA-essential targets represents a unique capability and a sustainable engine for novel target identification, drug discovery, and value creation.

Our Pipeline of ecDNA-Directed Therapeutic Candidates

We are pioneering a new and differentiated approach to precision medicine focused on developing ecDTx. Our ecDTx are novel, small molecules that target specific biological pathways believed to be essential to ecDNA function in cancer cells. Through Spyglass, we are able to better understand the lifecycle of ecDNA, including ecDNA formation, segregation, maintenance, replication, transcription, and degradation. We have identified several vulnerability nodes of ecDNA biology for therapeutic intervention and are developing novel drug candidates to intercept these nodes. Our drug discovery efforts span multiple ecDNA synthetic lethal targets, including:

- CHK1: a DNA replication checkpoint kinase target that manages the cellular response to RS arising from oncogene amplification on ecDNA; and
- Kinesin: a target essential for ecDNA segregation and inheritance during cell division.

Our diversified ecDTx pipeline currently consists of two small molecule programs against both a novel and a known cancer target. In addition, our Spyglass platform continues to yield new candidate targets for potential future drug discovery efforts.



Our Pipeline and Platform

Our Lead ecDTx: BBI-355 CHK1 Inhibitor

Our lead ecDTx, BBI-355, is a novel, oral, selective small molecule CHK1 inhibitor being studied in the ongoing first-in-human Phase 1/2 POTENTIATE clinical trial in patients with oncogene amplified cancers agnostic to tumor type. In preclinical models, BBI-355 showed inhibition of CHK1 in a host of tumor cell lines. CHK1 is a master regulator of cells' response to RS. RS is elevated in oncogene amplified cancer cells, including those with ecDNA, and, because of this, represents a key vulnerability of those cells. BBI-355 is designed to exploit this elevated RS in oncogene amplified cancer cells by disrupting proper CHK1 function in regulating RS and thereby facilitating catastrophic RS to preferentially kill cancer cells relative to healthy cells. We expect to have preliminary clinical proof of concept safety and antitumor activity data of BBI-355 from the POTENTIATE trial in the second half of 2025.

CHK1 Synthetic Lethality in Oncogene Amplified Cancer

With every mammalian cell division, chromosomes comprised of billions of nucleotides must be precisely copied in coordination with the cell cycle to avoid dysregulated DNA replication or RS, which can lead to DNA damage, mis-segregation of genetic material, and, if unregulated, cell death. RS is characterized by uncoupling of the replicative helicase and DNA polymerase, slowdown of DNA synthesis, and/or replication fork stalling. These result in long stretches of fragile single stranded DNA (ssDNA) that is protected temporarily by binding to phosphorylated RPA protein (pRPA) to allow time for the rest of the cellular RS response to resolve any DNA damage. Low level RS is tolerated by cancer cells through an increased reliance on specific cellular machinery responsible for RS mitigation. In contrast, excessive RS can result in extensive DNA damage and cell death through replication and/or cell division catastrophe. Results from multiple *in vitro* studies suggest that cancer cells with gene amplifications on ecDNA exhibited elevated intrinsic levels of RS and were hypersensitive to further increases in RS, thus providing the rationale to leverage this liability as a therapeutic strategy to treat oncogene amplified cancers.

Circular ecDNA creates abnormally high accessibility of the DNA encoded on the circle, and those DNA remain accessible throughout the cell cycle. Open, accessible DNA is available to the cellular machinery for DNA replication and for RNA transcription.

In healthy cells, these two processes are tightly coordinated so that cells do not replicate and transcribe the same regions of DNA at the same time. When transcription and replication do occur at the same time and place, transcription-replication collisions occur, resulting in stalled replication forks and RS. Consequently, tumor cells that have ecDNA also have colliding transcription and replication and are therefore under a great deal of RS, as detected by high pRPA levels. This elevated RS creates a unique, druggable, cancer-specific vulnerability.



ecDNA- enabled Cancer Cells Demonstrate Elevated Intrinsic Levels of RS

We are seeking to exploit this synthetic lethal relationship to identify druggable targets essential for survival of cells harboring ecDNA. To this end, as seen in the figure below, we conducted a CRISPR kinome screen in cancer cells resistant to the cancer drug methotrexate via amplification of the gene DHFR on ecDNA. In this ecDNA model system, genetic inactivation of the kinase CHK1 (encoded by CHEKI) resulted in enhanced cytotoxicity in ecDNA-enabled cells as compared to ecDNA negative cells, providing evidence of CHK1 as a potential drug target for ecDNA-enabled tumors.

CRISPR Kinome Screen Identified CHK1 (CHEK1) Inhibition as a Top Synthetic Lethality Hit in ecDNA-enabled Methotrexate Resistant (MTX-R) Cancer Cells



CHK1 is cells' master regulator of the RS response. CHK1 protects stalled DNA forks, manages DNA replication origin firing, temporarily arrests the cell cycle to allow time for DNA repair, and orchestrates repair through homologous recombination. As such, as seen in the figure below, CHK1 serves an essential role in managing RS, making it a potential therapeutic target for cancer therapy in tumors with high RS, such as those with ecDNA-enabled oncogene amplifications.

CHK1 is the Cellular Master Regulator of the Response to ecDNA-Induced RS



In our research, both genetic inactivation and pharmacological inhibition of CHK1 using structurally distinct inhibitors resulted in enhanced cytotoxicity to ecDNA-enabled cells compared to cells lacking ecDNA. This synthetic lethal relationship was observed across multiple preclinical models spanning different cancer indications and oncogene amplifications, such as *EGFR*, *FGFR2*, *CDK4*, *MYC*, and *MET*. CHK1 inhibition, both as a single agent and in combination with targeted therapy, resulted in tumor growth inhibition and tumor regressions, which correlated with reduced levels of ecDNA-based gene amplification and protein expression in ecDNAenabled xenograft models.

Historical Challenges with CHK1 Inhibitor Development

CHK1 has been considered a cancer target for many years, and several biopharmaceutical companies have attempted to develop CHK1 inhibitors for cancer. In the past, a major challenge to developing CHK1 inhibitors to treat cancer was difficulty in accurately identifying tumors with high RS or other vulnerabilities that would respond well to this therapeutic approach. Despite strong preclinical data and preliminary evidence of clinical activity for CHK1 inhibition, to date, no development programs have advanced to registration, which we believe is due to lack of adequate predictive biomarker(s) and optimal clinical development strategies. In addition, a range of other challenges have stalled the clinical advancement of prior CHK1 inhibitors. These challenges included suboptimal drug properties, potential compound scaffold-specific safety liabilities, such as potential cardiotoxicities and drug-drug interactions, as well as weak potency or selectivity.

Our Differentiated Approach

Through extensive preclinical studies in oncogene amplified cancer models, we determined what we consider the optimal CHK1 inhibitor profile for targeting oncogene amplified tumors and designed our lead ecDTx, BBI-355, accordingly. We believe that with the optimized biochemical profile of BBI-355, alongside our differentiated precision oncology development strategy, coupled with our approach to identify patients with oncogene amplifications, including those on ecDNA using our ecDNA diagnostic, we can overcome the challenges encountered with prior CHK1 inhibitors. BBI-355 showed picomolar biochemical inhibition of CHK1, low nanomolar activity in a host of tumor cell lines, and substantial antitumor activity in multiple ecDNA-enabled xenograft models representing several tumor types and various driver oncogene amplifications. We are developing BBI-355 for the treatment of oncogene amplified solid tumors, including those with amplifications on ecDNA as detected by our proprietary ecDNA diagnostic.

Properties of BBI-355 observed in preclinical studies are shown below. BBI-355 is a novel, oral, selective small molecule inhibitor of CHK1, and we believe has a predicted low risk of drug-drug interaction and cardiovascular liabilities based on *in vitro* CYP and hERG/cardiomyocyte study results, respectively.

Preclinical Properties of BBI-355 CHK1 Inhibitor

PARAMETER	<u>BBI-355</u>
CHK1 TR-FRET IC ₅₀ nM	0.6
Kinase selectivity	185x CHK2
CHK1 cellular activity (target engagement, CHK1 phosphorylation, HT29) IC ₅₀ nM	16
Cellular activity CellTiter-Glo ecDNA+ COLO320 IC ₅₀ nM	13
CYP inhibition 1A2/2C9/2C19/2D6/3A4 (uM)	>30/>30/>30/22/>30
hERG inhibition (uM); cardiomyocyte assay	2.28; minimal activity @ 10 uM
CEREP/PanLabs profile	No off-target activity, 0/47 hits
PO bioavailability (rat, dog), %F	33-43

BBI-355 In Vitro Preclinical Data

BBI-355 was first characterized extensively *in vitro*. As seen in the figure below, the kinase selectivity of BBI-355 was evaluated in a broad screen, displaying minimal off-target activity and with high selectivity across the kinome.

Kinase Selectivity of BBI-355



Calmodulin-Dependent Protein Kinase (CAMK)

As seen in the figure below, BBI-355 demonstrated broad cytotoxicity against a host of tumor cell lines, with IC50 ranges from approximately 5 nM – 200 nM. Consistent with the enhanced reliance that ecDNA-enabled oncogene amplified cancer cells have on CHK1 due to their intrinsic elevated RS, we have observed increased sensitivity in ecDNA-enabled cancer cell lines over ecDNA negative cancer cell lines. This observation was exemplified using a near isogenic matched cell line pair of colorectal cancer cell lines (COLO320 ecDNA-enabled (+) versus COLO320 ecDNA (-)), wherein BBI-355 was approximately 10-fold more cytotoxic in ecDNA-

enabled cells. Importantly, the potency of cytotoxicity in the ecDNA-enabled cancer cells paralleled the IC50 for cellular biomarkers of RS, including pRPA, pCHK1, and gH2AX.



BBI-355 Demonstrated Increased In Vitro Activity in ecDNA+ Versus ecDNA- Cancer Cells





BBI-355 Single Agent In Vivo Preclinical Data

As seen in the figure below, the antitumor activity of BBI-355 was further exemplified *in vivo* in multiple ecDNA-enabled xenograft models representing several tumor types and various driver oncogene amplifications. Orally administered BBI-355 demonstrated single agent activity, including regressions in several cases, in an ecDNA-enabled *CDK4* amplified osteosarcoma CDX model, ecDNA-enabled *EGFR & MET* amplified NSCLC PDX model, ecDNA-enabled *MYCN* amplified neuroblastoma CDX model, and ecDNA-enabled *FGFR2* amplified gastric cancer PDX model.



BBI-355 dosed for duration unless indicated

BBI-355 Combination In Vivo Preclinical Data

Cancers that harbor amplified oncogenes, such as *EGFR*, *FGFR*, or *CDK4*, typically do not respond well to single agent targeted therapies. We believe this is because ecDNA can facilitate rapid genomic plasticity, leading to resistance to selective therapeutic pressure. We believe this ecDNA-enabled resistance to targeted therapies can be overcome by combining our ecDTx, such as BBI-355, with targeted agents to interrupt the potential for ecDNA to facilitate resistance. We believe that this ecDTx and targeted therapy combination strategy may be effective across multiple different oncogene cargos encoded on the ecDNA and may lead to higher response rates, deeper regressions, and longer duration of responses as compared to single agent targeted therapies.

Preclinically, we have observed that applying targeted therapy pressure to tumors with ecDNA-enabled oncogene amplification induced tumor cells to evade such pressure via ecDNA-based resistance mechanisms, further increasing RS and reliance on CHK1. Accordingly, and consistent with the vice grip analogy described above, BBI-355 demonstrated combination activity when administered alongside targeted therapies in ecDNA-enabled oncogene amplified xenograft models that are generally resistant to treatment with targeted therapies alone.

As an example, in the figure below, oral administration of BBI-355 led to tumor regressions when dosed in combination with the FGFR inhibitor infigratinib in an ecDNA-enabled FGFR2 amplified gastric cancer CDX model. In this model, treatment with single agent infigratinib led to rapid resistance via ecDNA-enabled amplification of FGFR2. Combining BBI-355 with infigratinib inhibited this resistance and induced tumor regressions. Pharmacodynamic (PD) analysis demonstrated that BBI-355 inhibited the expected increase in FGFR2 copy number that would otherwise be caused by single agent infigratinib to confer resistance to infigratinib.

BBI-355 In Vivo Antitumor Activity in Combination with Infigratinib in an ecDNA-enabled FGFR2 Amplified Gastric Cancer CDX Model



The oncogene cargo-agnostic nature of this combination approach is reflected in a second ecDNA-enabled *EGFR* amplified patient-derived gastric cancer xenograft model. In this model, monotherapy treatment with the EGFR inhibitor erlotinib resulted in limited antitumor activity, as seen in the figure below. However, combination with orally administered BBI-355 resulted in statistically significant greater and longer tumor growth inhibition, including regressions in some cases.





As seen in the figure below, oral administration of BBI-355 similarly led to tumor regressions when dosed in combination with the CDK4/6 inhibitor palbociclib in an ecDNA-enabled *CDK4* amplified osteosarcoma CDX model. In this model, treatment with single agent palbociclib led to rapid resistance. Combining BBI-355 with palbociclib inhibited this resistance and induced tumor regressions.

BBI-355 In Vivo Antitumor Activity in Combination with Palbociclib in an ecDNA-enabled CDK4 Amplified Osteosarcoma CDX Model



BBI-355 Clinical Development Plan

Through a comprehensive analysis of the prevalence of ecDNA-enabled gene amplifications alongside clinical outcomes associated with the use of targeted therapies, we have identified specific high unmet need patient populations with oncogene amplified cancers. For our initial targeted indications for clinical development, we are prioritizing cancers with wildtype EGFR amplifications, FGFR1-4 amplifications, or CDK4/6 amplifications.

In May 2023, we enrolled the first patient in our ongoing Phase 1/2 clinical trial of BBI-355 in patients with oncogene amplified cancers. The title of the trial (NCT05827614) is: "An Open-Label, Multicenter, First-in-Human, Dose-Escalation and Dose-Expansion, Phase 1/2 Study of BBI-355 and BBI-355 in Combination with Select Targeted Therapies in Subjects with Locally Advanced or Metastatic Solid Tumors with Oncogene Amplifications." We also call the trial POTENTIATE, for Precision Oncology Trial Evaluating Novel Therapeutic Interrupting Amplifications Tied to ecDNA. We expect to have preliminary proof of concept safety and antitumor activity data of BBI-355 from the POTENTIATE clinical trial in the second half of 2025.

The design of the trial is an open-label, non-randomized, three-part, Phase 1/2 clinical trial to evaluate the safety and tolerability, human PK, PD biomarkers and preliminary antitumor activity, as well as identify the maximum tolerated dose (MTD) and RP2D of BBI-355 administered as a single agent or in combination with select targeted therapies. In the trial, BBI-355 is administered orally every other day (Q2D) or on less frequent dosing schedules to patients with locally advanced or metastatic non-resectable solid tumors harboring oncogene amplifications whose disease has progressed despite all standard therapies or for whom no further standard or clinically acceptable therapy exists. The trial has three parts: Part 1 is a dose escalation of BBI-355 as a single agent and will include a single agent dose expansion cohort at the RP2D in patients with platinum-resistant high-grade serous ovarian cancer or endometrial cancer. Parts 2 and 3 of this trial will be conducted in 3 separate modules, each module testing the combination of BBI-355 with one of the selected targeted therapies, EGFR inhibitor (module 1), pan-FGFR inhibitor (module 2), or CDK4/6 inhibitor (module 3), in patients with cancers harboring amplification of *EGFR*, *FGFR1-4*, or *CDK4/6*, respectively. Notably, patients will be excluded from enrollment in any part of the trial if they harbor other pathogenic driver oncogene alterations, for example *EGFR*, *FGFR3*, *KRAS*, *BRAF* mutations or *ALK*, *NTRK*, *FGFR2*, *RET*, *ROS1* fusions.

In Part 1 of the trial, patients with amplification of driver oncogenes, as determined by standard NGS testing, are eligible for enrollment. The goal of Part 1 is to evaluate the safety, tolerability, PK and PD of single agent BBI-355, to determine the RP2D and MTD of BBI-355, and to evaluate preliminary single agent antitumor activity in patients with oncogene amplifications. Single agent BBI-355 will be further tested in a dose expansion cohort at the RP2D in platinum-resistant high-grade serous ovarian cancer or endometrial cancer patients with oncogene amplifications.

In Part 2 of the trial, patients with amplification of driver oncogenes of interest, *EGFR*, *FGFR1-4*, or *CDK4/CDK6*, as determined by standard NGS testing, will be enrolled in the corresponding module. The goal of Part 2 is to evaluate safety, tolerability, PK, and PD, as well as the RP2D and MTD, and to evaluate preliminary antitumor activity of BBI-355 in combination with the respective targeted therapy inhibitor studied in each module, that is the EGFR inhibitor erlotinib (module 1), pan-FGFR inhibitor futibatinib (module 2), or CDK4/CDK6 inhibitor abemaciclib (module 3).

In Part 3 of the trial, patients with amplification of oncogenes of interest, *EGFR*, *FGFR1-4*, or *CDK4/CDK6*, including those enabled by ecDNA as determined by testing with our ecDNA diagnostic clinical trial assay (see "Our Precision Medicine Approach" below), will be enrolled. The goal of Part 3 is to further evaluate combination antitumor activity at the combination RP2D.

We have entered into clinical trial collaboration and supply agreements with each of Taiho Oncology and Eli Lilly providing for no-cost supply of futibatinib and abemaciclib, respectively, for use in the applicable modules of Parts 2 and 3 of this trial. These agreements also provide for the sharing of certain clinical trial data but have no financial obligations and terminate upon conclusion of the trial.

It is anticipated that approximately 250 to 350 patients will be enrolled in total in this trial. Should any cohort of the trial demonstrate compelling signs of clinical antitumor activity, along with acceptable safety and tolerability, we would seek to engage with the FDA and other global regulatory bodies to discuss potential registrational paths, including the designs of any additional clinical trials we may need to conduct to support potential registrations for BBI-355. We may also consider expanding this trial with additional matched targeted agent and oncogene amplification cohorts based on our ongoing research and the dynamic clinical therapeutic landscape.



High-Grade Serous Ovarian Carcinoma (HGSOC) Bayesian Optimal Interval (BOIN)

Preliminary Results from Part 1 of the POTENTIATE trial

Preliminary data from the ongoing POTENTIATE trial as of the dates noted below have been obtained from 22 subjects enrolled across six dosing cohorts in Part 1 of the trial. Subjects have been treated or are ongoing on an oral Q2D dosing regimen in escalating dose cohorts of 20 mg (N=3), 40 mg (N=4), 60 mg (N=3), and 80 mg (N=4), and on an oral 2 days on and 5 days off weekly dosing regimen (20N/50FF) at 80 mg (N=5) and 120 mg (N=3).

Phase 1 Preliminary PK, PD, and Antitumor Activity Data

Preliminary PK data analysis as of February 21, 2024, revealed good oral bioavailability of BBI-355 across the dosing range, including a dose proportional increase of Cmax and AUC values, with some inter-subject variability. The average half-life of BBI-355 was approximately 40 hours, and average drug accumulation was approximately 2 to 3-fold from day 1 to steady state. Average PK exposures at the 40 mg, 60 mg, and 80 mg Q2D doses achieved or exceeded the minimum PK concentration required for tumor regression in certain rodent cancer xenograft models.

BBI-355 Preliminary Multi-Dose Fitted Human PK Data



A clinical PD assay measuring pCHK1 by immunohistochemistry (IHC) showed CHK1 target engagement in skin punch biopsies across the dosing range as well as in tumor tissue of one patient who consented to serial tumor biopsy.





As for preliminary clinical antitumor activity as of February 21, 2024, stable disease (per RECIST 1.1 criteria) was observed in five of eighteen RECIST evaluable subjects, including regression of target lesions by approximately 20% in a patient with metastatic breast cancer harboring oncogene amplifications who had been a subject in the POTENTIATE trial for approximately six months and is continuing in the trial.

Phase 1 Safety and Tolerability Data

Preliminary clinical safety data as of the data cut-off date of March 4, 2024, showed that, BBI-355 was generally well-tolerated at the first three dose levels (20 mg, 40 mg, 60 mg) administered Q2D, without any dose-limiting toxicities (DLTs) or drug-related serious adverse events (SAEs). At the 80 mg Q2D dose level, DLTs, specifically Grade 4 platelet count decrease and neutrophil count decrease, occurred in two of four subjects, and this dose level was determined to exceed the target toxicity rate. Therefore, 60 mg was determined to be the MTD with this dosing regimen.

BBI-355 was also evaluated on a 2ON/5OFF dosing regimen. Preliminary clinical safety data in this dosing regimen, showed that, as of the data cut-off date of March 4, 2024, BBI-355 was generally well tolerated at the first dose level (80mg), with one DLT, specifically, administration of less than 70% of the intended dose in the DLT evaluation period due to an adverse event of Grade 4 neutrophil count decrease, in one out of five subjects at this dose level. At the 120 mg 2ON/5OFF dose level, DLTs occurred in two of three subjects, specifically one subject experienced a Grade 4 platelet count decrease and a second subject experienced an administration of less than 70% of the intended dose in the DLT evaluation period following Grade 4 neutrophil count decrease, and therefore this dose level was determined to exceed the target toxicity rate or MTD.

We may consider evaluating other dose levels or dosing schedules to further inform the single agent RP2D and dosing schedule before proceeding to Part 1 dose expansion in platinum-resistant high-grade serous ovarian cancer or endometrial cancer. We anticipate that in the enrolled subjects continuing in the trial as well as those we may enroll in potential future dose escalation cohorts, we may observe toxicities that are novel or on-target class effects for CHK1 inhibitors, which may also constitute DLTs and/or drug-related SAEs.

The following safety information is as of the data cut-off date of March 4, 2024. The most common reported drug-related adverse events (i.e., number of subjects with a specific adverse event) and across all dosing cohorts were neutrophil count decrease or neutropenia (N=4), fatigue (N=4), nausea (N=4), platelet count decrease (N=3), lymphocyte count decrease (N=3), white blood cell count decrease (N=3), diarrhea (N=3), vomiting (N=2), urinary frequency (N=2), headache (N=2), anorexia or loss of appetite (N=2), and dry skin (N=2). Two subjects experienced drug-related SAEs; a Grade 4 platelet count decrease and Grade 4 neutrophil count decrease in one subject, while the other subject experienced Grade 3 anemia leading to hospitalization. All observed hematologic toxicities were asymptomatic, are considered an on-target class effect for CHK1 inhibitors, and have been reported for several other clinical stage CHK1/2 inhibitors.

Based on the totality of the clinical safety, PK, PD, and antitumor activity observed, the POTENTIATE trial advanced into Part 2 of the study. We expect to have preliminary clinical proof of concept safety and antitumor activity data of BBI-355 in the second half of 2025.

Addressable Patient Populations for BBI-355

We estimate that BBI-355, if approved for the combination indications we are targeting in the POTENTIATE trial, could address an initial potential U.S. patient population of approximately 30,000 new patients per year with *EGFR*, *FGFR1-4*, or *CDK4/6*, on ecDNA across a broad range of tumor types. Beyond the United States, we estimate that BBI-355, if approved for such indications, could address approximately 40,000 such patients in the European Union and over 10,000 such patients in Japan, representing a total potential addressable patient population of 80,000 new patients annually in the United States, European Union, and Japan. Our goal is to achieve a tumor agnostic label for BBI-355 in combination with targeted therapies (e.g., an EGFR inhibitor, a pan-FGFR inhibitor, and a CDK4/6 inhibitor) for patients with EGFR, FGFR1-4, or CDK4/6 amplifications. Guided by our ecDNA diagnostic test, we are evaluating basket trial cohorts of each of these indications and treatment settings.

- **EGFR Amplified Tumor Types** Using U.S. SEER incidence data by tumor type and adjusting for ecDNA prevalence, we estimate a potential patient population of approximately 5,000 new patients annually in the United States alone for *EGFR* amplifications. This estimate includes patients with esophageal and gastric cancer, head and neck squamous cell carcinoma, non-small cell lung cancer (NSCLC) squamous cell carcinoma, and other tumor types that exhibit *EGFR* driver oncogene amplifications on ecDNA, with the potential to expand to glioblastoma, which has high ecDNA prevalence.
- *FGFR1-4 Amplified Tumor Types* The potential *FGFR1-4* amplified patient population, including early and late stage metastatic, represents up to approximately 18,000 new patients annually in the United States alone. This population includes patients with breast cancer, NSCLC squamous cell carcinoma, esophageal and gastric cancer, bladder cancer, and other tumor types that exhibit *FGFR1-4* driver oncogene amplifications on ecDNA.
- **CDK4/6** Amplified Tumor Types The potential CDK4/6 amplified patient population, including early and late stage metastatic, represents approximately 6,000 new patients annually in the United States alone. This population includes patients with liposarcoma, NSCLC squamous cell carcinoma, esophageal and gastric cancer, and other tumor types that exhibit CDK4/6 driver oncogene amplifications on ecDNA, with the potential to expand to glioblastoma.

We also estimate that BBI-355, if approved for the monotherapy indications we are targeting in the POTENTIATE trial, could address a total potential patient population of approximately 65,000 new patients per year with high-grade serous ovarian cancer or endometrial cancer, each with oncogene amplification, in the United States, European Union, and Japan.

In addition to the gene amplified cancer types described above, we are currently conducting preclinical studies of BBI-355 in *MDM2* amplified cancers, *MET* amplified cancers, *AR* amplified metastatic castration-resistant prostate cancer (mCRPC), and $BRAF^{V600E}$ metastatic colorectal cancers (mCRC). In the future, we intend to pursue additional gene amplified tumor settings as well. Clinical success in one or more of these indications could expand the potential addressable patient population for BBI-355.

Initial Indications for BBI-355 May Represent a Total Addressable Population of 145,000 New Patients in the United States, the European Union, and Japan Each Year



Central Nervous System (CNS) Penetrant CHK1 Inhibitor Program: BBI-098

In addition to BBI-355, we have also identified a second CHK1 inhibitor candidate with a differentiated profile from BBI-355. This novel ecDTx compound, BBI-098, is orally available, selective, has shown picomolar biochemical inhibition of CHK1, and has demonstrated CNS penetrance in preclinical models. We have nominated BBI-098 as a development candidate and have completed non-Good Laboratory Practice (non-GLP) dose range finding toxicology studies. We are currently conducting *in vivo* studies in multiple glioblastoma pharmacology models. If those studies are successful and we are able to demonstrate clinical activity of CHK1 inhibition in ecDNA-bearing cancers with our BBI-355 ecDTx, then we may advance BBI-098 into GLP toxicology studies and formulation development to pursue ecDNA-bearing oncology CNS indications such as glioblastoma or brain metastases. Properties of BBI-098 observed in preclinical studies are shown below.

PARAMETER	<u>BBI-098</u>			
CHK1 biochemical inhibition (TR-FRET) IC ₅₀ nM	0.7			
Kinase selectivity	>200x CHK2			
CHK1 cellular activity (target engagement, CHK1 phosphorylation, HT29) IC ₅₀ nM	15			
Cellular activity CellTiter-Glo COLO320 ecDNA+ IC ₅₀ nM	20			
CYP inhibition 1A2/2C9/2C19/2D6/3A4 (uM)	>50/48/>50/4.9/50			
hERG inhibition (uM); cardiomyocyte assay	2.7; minimal activity @ 10 uM			
CEREP/PanLabs profile	No off-target activity, 0/47 hits			
PO bioavailability (dog, rat), %F	22-64			
CNS penetration Brain:plasma AUC - mouse, rat	2.1, 1.9			
Brain Kp _{uu} (unbound partition coefficient)- mouse, rat	0.35, 0.19			

Preclinical Properties of BBI-098 CNS Penetrant CHK1 Inhibitor

Our Kinesin Program

Our next ecDTx program is directed against a novel member of a class of druggable proteins, the kinesins. This ecDTx target has no approved drugs and, to our knowledge, no other publicly disclosed drug discovery efforts. This kinesin is involved with ecDNA segregation during cellular division and targeting it leverages the fact that ecDNA, unlike chromosomes, lack centromeres.

The cell has evolved numerous redundant mechanisms governing the interactions of chromosomes with the mitotic spindle, the highly coordinated network of factors that separates chromosomes equally into daughter cells during cell division. The primary and essential attachment point for chromosomes to the mitotic spindle is via the centromere, although additional non-essential factors can assist in shepherding chromosomes independently of the centromere. Whereas these centromere-independent segregation factors are non-essential to chromosome segregation, they may be required for ecDNA due to ecDNA's lack of centromeres. Consistent with this hypothesis, when certain proteins are genetically deactivated, it can result in abnormal ecDNA segregation during cell division. As shown below, in certain cancer cell lines genetic deactivation of certain proteins can lead to aggregation and eventual loss of ecDNA that is statistically significant. This defect in the segregation process during cell division is directly correlated with significant cytotoxicity in certain ecDNA-enabled tumor cells while demonstrating minimal impact on non-cancerous cells, where such targets may be non-essential.

Genetic Inhibition of Novel Kinesin Target Was Associated with (1) Abnormal ecDNA Segregation, (2) Depleted ecDNA Levels, and (3) Cytotoxicity in Tumor Cells



Through Spyglass, we identified a novel kinesin essential for ecDNA segregation during cellular division. We preclinically validated this target *in vitro* by demonstrating that genetic inactivation was associated with statistically significant differential sensitivity (and reduction of ecDNA levels) in multiple ecDNA tumor cell lines compared to non-ecDNA-bearing tumor cell lines. We also preclinically validated this target *in vivo* in multiple tumor models by demonstrating that treatment with our selective degraders led to statistically significant tumor growth inhibition and reduction in oncogene copy number in concert with the degradation of the kinesin target. The therapeutic potential of targeting this kinesin may extend beyond ecDNA-driven cancers, given that tumor cells with other forms of chromosomal instability (CIN) have also demonstrated sensitivity to inactivation of this kinesin in cellular cytotoxicity assays. We have generated orally available nanomolar degraders against this target and are currently advancing our Kinesin program through lead optimization and expect to select a development candidate by mid-2025 and submit an IND in the first half of 2026.

Ongoing Discovery Efforts for Future Programs

In addition to our programs described above, we continue to leverage Spyglass to identify and preclinically validate additional targets. These candidate targets span multiple, diverse nodes, including those leveraging ecDNA, in oncogene amplified cancers. We have preclinically validated multiple additional targets and have initiated ecDTx drug discovery efforts to identify inhibitors against such targets. We expect to continue to identify and preclinically validate additional ecDNA targets and, more broadly, targets associated with oncogene and resistance gene amplification, using our Spyglass platform in the future.

Our Precision Medicine Approach – ecDNA Diagnostic Test

Precision medicine aims to identify and treat patients with specific biomarkers to maximize the likelihood of therapeutic benefit while minimizing side effects. We developed an ecDNA diagnostic test, internally called ECHO, to detect ecDNA in patient tumor specimens and identify patients most likely to benefit from our ecDTx. Our ecDNA diagnostic is a proprietary software algorithm designed to detect the presence of ecDNA by analyzing genomic data in the form of raw data output format files, such as FASTQ or binary sequence alignment map files, generated from routine clinical NGS assays that are commonly used by commercial reference

laboratories and academic laboratories to profile patient tumor samples. Our ecDNA diagnostic is currently being used as a clinical trial assay to determine ecDNA status of patients enrolled in the BBI-355 POTENTIATE trial. To our knowledge, this is the first and only ecDNA diagnostic in clinical use. As data from our clinical studies mature, we intend to discuss with the FDA whether the ecDNA diagnostic will be appropriate or required to enable commercialization of certain of our ecDTx, if approved.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid evolution of technologies and understanding of disease etiology, intense development and commercial competition, and a strong emphasis on intellectual property. We believe that our approach, strategy, scientific capabilities, know-how, and experience, particularly in the fields of ecDNA and precision oncology, provide us with competitive advantages. Nonetheless, we expect substantial competition from multiple sources, including major biopharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions, governmental agencies, and public and private research institutions worldwide. Many of our competitors, either alone or through collaborations, have or will have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies may be or may become interested in developing ecDNA-directed therapeutic candidates and may rapidly develop programs that compete with ours by studying ecDNA at scale in the context of oncogene amplified cancer. Even if they do not advance programs with the same mechanism(s) of action as ours, these companies could develop products or product candidates that are competitive with ours or that have a superior product profile and may do so at a rapid pace. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license, or commercialize products before or more successfully than we do.

We face competition from segments of the pharmaceutical, biotechnology, and other related markets that pursue the development of precision oncology therapies for patients with genetically defined cancers. In addition, we may face competition from companies developing product candidates that are based on synthetic lethality in cancer.

Furthermore, we also face competition more broadly across the oncology market for cost-effective and reimbursable cancer treatments. The most common methods of treating patients with cancer are surgery, radiation, and drug therapy, including chemotherapy, hormone therapy, biologic therapy, such as monoclonal and bispecific antibodies, antibody-drug conjugates, radiopharmaceuticals, immunotherapy, cell-based therapy, and targeted therapy, or a combination of any such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our ecDTx, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our ecDTx may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our ecDTx that we successfully introduce to the market may pose challenges. In addition, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

For BBI-355, Acrivon Therapeutics, Esperas Pharma, Sumitomo Pharma, and PharmaEngine have CHK1 inhibitors in clinical development. BenevolentAI, Fosun Pharma, and Impact Therapeutics have publicly disclosed preclinical-stage CHK1 inhibitors.

For our pipeline of ecDTx programs, potential competition includes established companies as well as emerging biotechnology companies that launch programs against any of the targets we are pursuing. However, we are not aware of any companies with ecDNA-directed therapeutic programs in clinical development and a patient selection strategy for ecDNA-enabled oncogene amplification. We are currently aware of one early-stage private company that is focused on research in ecDNA, Econic Biosciences.

We could see a reduction or elimination in our potential 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, are less expensive, or have more favorable commercial labeling than our ecDTx, regardless of whether they target ecDNA as a mechanism of action. 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 our ecDTx, if approved, are likely to be their efficacy, safety, route of administration, convenience, price, level of generic competition, and availability of reimbursement from government and other third-party payors.

Intellectual Property

We strive to protect the intellectual property and proprietary technology that we consider important to our business through a variety of methods. We seek to obtain domestic and international patent protection and endeavor to promptly file patent applications for new commercially valuable inventions as they arise to expand our intellectual property portfolio. We also rely on proprietary know-how and trade secrets to protect certain innovations that may be important to our business and to benefit from their confidential status.

As of March 27, 2025, our intellectual property portfolio included 25 patent families solely owned by us, which include 3 pending US provisional applications, 14 pending US non-provisional patent applications, 4 issued US patents, pending applications in Australia, Brazil, Canada, China, Eurasia, Europe, India, Israel, Japan, Korea, Mexico, Singapore, South Africa and Taiwan, as well as 7 pending applications filed pursuant to the Patent Cooperation Treaty (PCT).

We continually assess and refine our intellectual property strategy as we discover and validate new ecDNA targets, develop new ecDTx product candidates, and make improvements to our Spyglass platform and our ecDNA diagnostic test. To that end, we are prepared to file additional patent applications as appropriate to support our intellectual property strategy, or where we seek to adapt to competition or seize business opportunities.

We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may own or license in the future, nor can we be sure that any patents we may own or license in the future will be useful in protecting our technology. Please see "Risk Factors—Risks Related to Our Intellectual Property" for additional information on the risks associated with our intellectual property strategy and portfolio.

Intellectual Property Relating to Our CHK1 Program

With regard to our CHK1 program including our BBI-355 and BBI-098 product candidates, as of March 27, 2025, we owned 10 patent families, including 3 pending US non-provisional patent applications, 2 issued US patents, pending applications in Australia, Brazil, Canada, China, Eurasia, Europe, India, Israel, Japan, Korea, Mexico, Singapore, South Africa and Taiwan, as well as 5 pending applications filed pursuant to the Patent Cooperation Treaty (PCT). These patent rights relate to compositions of matter, as well as methods of treating diseases using CHK1 inhibitors. We expect these patents and patents issued from these applications, if any, to expire in 2041-2045 without accounting for any patent term adjustment or extension that may be available.

Intellectual Property Relating to Our Precision Medicine Program

With regard to our precision medicine program, we have developed a proprietary ecDNA diagnostic to detect ecDNA based on the data outputs from NGS tests routinely used to profile patient tumor samples. As of March 27, 2025, we owned 1 patent family related to methods of detecting ecDNA signatures in cancers that is currently pending in the US, China, Europe, and Japan. Additionally, we own 1 pending US non-provisional patent application related to our ecDNA diagnostic. We expect patents issued from these applications, if any, to expire in 2041-2044 without accounting for any patent term adjustment or extension that may be available. We also protect the intellectual property related to ecDNA detection as a trade secret.

Scope and Duration of Intellectual Property Protection

The term of individual patents depends upon the laws of the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent. Under certain circumstances, the term of US patents may be adjusted for delays encountered during prosecution that are caused by the USPTO. Additionally, the term of a patent as it specifically relates to an FDA regulated product may be extended. For example, for drugs that are regulated by the FDA under the Hatch-Waxman Act, the FDA is permitted to extend the exclusivity term that covers such drug for up to five years beyond the normal expiration date of the patent, depending on the timing of the issuance of the patent, the IND filing, the NDA filing and the approval date, and provided that the term of the patent does not extend beyond 14 years from the NDA approval date. In the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. We intend to seek patent term extensions to any of our issued patents in jurisdictions where these are available; however, there is no guarantee that the applicable authorities, including the USPTO and FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of oncology therapy has emerged in the US. The patent situation

outside of the US is even more uncertain. Changes in the patent laws and rules, either by legislation, judicial decisions, or regulatory interpretation in the US and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights, and more generally could affect the value of our intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, importing, or otherwise commercializing any of our patented inventions, either directly or indirectly, will depend in part on our success in obtaining, defending, and enforcing patent claims that cover our technology, inventions, and improvements. We cannot be sure that patents will be granted with respect to any of our patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our patents that may be granted to us in the future will be commercially useful in protecting our product candidates and the methods used to manufacture them.

The area of patent and other intellectual property rights in the biopharmaceutical industry is an evolving one with many risks and uncertainties, and third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology. Our patents that may issue in the future may be challenged, narrowed, circumvented, or invalidated, which could limit our ability to stop competitors from marketing related product candidates. In addition, our competitors may independently develop similar technologies, and the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. For these and other reasons, we may have competition for our product candidates. Moreover, because of the extensive time required for development, testing, and regulatory review of a potential product, it is possible that before any product candidate can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any protection afforded by the patent. For this and other risks related to our proprietary technology, inventions, improvements, and product candidates, please see the section titled "Risk Factors—Risks Related to Our Intellectual Property."

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our confidential and proprietary information as trade secrets, including through contractual means with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our technology as trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors to execute confidentiality agreements under the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In many cases our agreements with consultants, outside scientific collaborators, sponsored researchers, and other advisors require them to assign or grant us licenses to inventions they invent as a result of the work or services they render under such agreements or grant us an option to negotiate a license to use such inventions. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, and we may not be able to obtain adequate remedies for such breaches.

We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. To the extent that our employees, contractors, consultants, collaborators, and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in relation to the resulting know-how or inventions. We seek trademark protection in the United States and in certain other jurisdictions where available and when we deem appropriate. We currently have registrations for our "Boundless Bio" mark in the United States as well as in certain foreign jurisdictions, including the European Union. We have registrations for our "UNBOUND BY CONVENTION, BOUND TO SAVE LIVES" mark in the United States. We have also filed a trademark application in the United States for registration of our "ECHO" mark, and we have registrations for our "ECHO" mark in certain foreign jurisdictions, including the European Union. For more information, please see the section titled "Risk Factors—Risks Related to Our Intellectual Property."

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our ecDTx for preclinical and clinical testing, as well as for commercial manufacture if any of our ecDTx obtain marketing approval. We work with our current manufacturers to ensure that we will be able to scale up our manufacturing capabilities to support our clinical plans. We also plan to continue to evaluate additional manufacturers to build redundancies into our supply chain. In addition, we rely on third parties to package, label, store, and distribute our ecDTx, and we intend to rely on third parties for our commercial products if marketing approval is obtained. We believe that this strategy allows us to maintain
a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment, and personnel while also enabling us to focus our expertise and resources on the design and development of our ecDTx.

Commercialization

We intend to retain significant development and commercial rights to our ecDTx and, if marketing approval is obtained, to commercialize our ecDTx on our own, or potentially with a partner, in the United States and other regions. We currently have no sales, marketing, or commercial product distribution capabilities. We intend to build the necessary infrastructure and capabilities over time for the United States, and potentially other regions, following further advancement of our ecDTx. Clinical data, the size of the addressable patient population, the size of the commercial infrastructure, and manufacturing needs may all influence or alter our commercialization plans.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and post-approval activities of drug and biological product candidates, such as those we are developing.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and its implementing regulations. Drugs are also subject to other federal, state, and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations require the expenditure of substantial time and financial resources. The process required by the FDA before a new drug may be marketed in the United States generally involves the following:

- completion of nonclinical or preclinical laboratory tests, animal studies and formulation studies, with certain studies conducted in accordance with Good Laboratory Practice (GLP) regulations, and other applicable regulations;
- submission to the FDA of an Investigational New Drug Application (IND), which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (IRB) or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice regulations (GCPs) to evaluate the safety and efficacy of the product candidate for its intended use;
- submission to the FDA of an NDA after completion of all pivotal trials;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice requirements (cGMPs) to assure that the facilities, methods, and controls are adequate to preserve the drug's identity, strength, quality, and purity;
- satisfactory completion of potential inspection of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Once a product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, and formulation, as well as animal studies. An IND sponsor must submit, among other things, the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of an IND. An IND is a request for allowance from the FDA to administer an investigational drug product to humans. An IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the trial includes an efficacy evaluation. Some preclinical testing may continue even 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, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about ongoing or proposed clinical trials or non-compliance with specific FDA requirements, and in such case, the trials may not begin or

continue until the FDA notifies the sponsor that the hold has been lifted. FDA may also place a trial on a partial clinical hold. A partial clinical hold is a delay or suspension of only part of the clinical work requested or ongoing under the IND. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation (or full investigation in the case of a partial clinical hold) may only begin or resume after the FDA has notified the sponsor that the investigation may proceed.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs, which include, among other things, the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials must be conducted under protocols detailing, among other things, the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and a separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure. The sponsor must report to the FDA any suspected adverse reaction that is both serious and unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

Furthermore, an independent IRB at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the trial until completed and otherwise comply with IRB regulations. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. There are also requirements governing the registration of certain clinical trials and reporting of ongoing clinical studies and clinical trial results to public registries, including clinicaltrials.gov.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition, and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness, identify any adverse effects, and determine maximal dosage.
- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance and appropriate dosage.
- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide substantial evidence of efficacy, purity, and potency, 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 product candidate and provide an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

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

U.S. Review and Approval Process

The results of product development, preclinical and other non-clinical studies, and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, the Pediatric Research Equity Act (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, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness, or safety, purity, and potency of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is deemed safe and effective, or safe, pure, and potent. The sponsor may request or the FDA may grant a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current, or fails to submit a request for approval of a pediatric formulation.

Once an NDA has been submitted, the FDA conducts a preliminary review of the application within the first 60 days after submission, before accepting it for filing, to determine whether it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality, and purity. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of an NDA for a new molecular entity to complete a standard review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted.

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, that reviews, evaluates, and provides recommendations 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 will typically inspect the facility or facilities where the product is manufactured to assure compliance with cGMPs. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCPs. After the FDA evaluates an NDA and conducts any required inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter (CRL). An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A CRL indicates that the review cycle for the application is complete, and the application will not be approved in its present form. A CRL usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, including additional clinical trials or other significant and time-consuming requirements related to clinical trials, nonclinical studies, or manufacturing. If a CRL is issued, the sponsor must resubmit the NDA addressing all of the deficiencies identified in the letter or withdraw the application. Even if such data and information are submitted, the FDA may decide that the resubmitted NDA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require that contraindications, warnings or precautions be included in the product's labeling; require that post-approval studies be conducted to further assess the drug's safety or effectiveness; require testing and surveillance programs to monitor the safety of the commercialized product; or impose other conditions, including distribution restrictions or other risk management mechanisms, including a risk evaluation and mitigation strategy (REMS) to assure safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS, which could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA will not approve the NDA without an approved REMS, if required. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products.

Orphan Drug Designation

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 a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

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 orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. However, competitors, may receive approval of different products for the disease or condition for which the orphan product has exclusivity or obtain approval for the same product but for a different disease or condition for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of a competing product for seven years if a competitor obtains approval of the "same drug," as defined by the FDA, or if the active moiety of the product candidate is determined to be contained within the competitor's product for the same disease or condition. In addition, if an orphan designated product receives marketing approval for a disease or condition broader than what is designated, it may not be entitled to orphan exclusivity.

Expedited Development and Review Programs

The FDA has a number of programs intended to expedite the development or review of a marketing application for an investigational drug. For example, the fast track designation program is intended to expedite or facilitate the process for developing and reviewing product candidates that meet certain criteria. Specifically, investigational drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. The sponsor of a fast track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the application may be eligible for priority review. With regard to a fast track product candidate, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

An NDA may also be eligible for priority review if the product candidate is designed to treat a serious condition and, if approved, would provide a significant improvement in safety or efficacy compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an NDA designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, depending on the design of the applicable clinical trials, a product candidate may be eligible for accelerated approval. Specifically, drugs intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that 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. As a condition of approval, the FDA generally requires that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled confirmatory clinical trials and may require that such confirmatory trials be underway prior to granting accelerated approval. Drugs receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required confirmatory trials in a timely manner or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition of accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast track designation, breakthrough therapy designation, priority review, and accelerated approval do not change the standards for approval but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time for FDA review or approval will not be shortened.

Post-Approval Requirements

Any drug manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications, or additional labeling claims, are subject to further FDA review and approval. There also are continuing, annual program fees for any marketed products.

Drug manufacturers and other entities 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 cGMP requirements, which impose certain procedural and documentation requirements upon NDA holders and their third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain compliance with cGMPs and other aspects of regulatory compliance.

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

In addition, the FDA closely regulates the marketing, labeling, advertising, and promotion of drug products. A sponsor can only make those claims relating to safety and efficacy that are approved by the FDA 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. Failure to

comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe legally-available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Marketing Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent data 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 accept for review an abbreviated new drug application (ANDA), or an NDA submitted under Section 505(b)(2) (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 FDCA alternatively provides three years of non-patent 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 based on 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, all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to an existing period of regulatory exclusivity or available patent term if a sponsor conducts clinical trials in children in response to a "written request" from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials, and the FDA's grant of pediatric exclusivity does not require the FDA to approve labeling containing information on pediatric use based on the studies conducted.

FDA Regulation of Companion Diagnostics

We believe that certain of our ecDTx may require an in vitro diagnostic to identify appropriate patient populations for investigation and/or use of our ecDTx. These diagnostics, often referred to as companion diagnostics, are regulated as medical devices. In the United States, the FDCA 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 applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval (PMA). Most companion diagnostics for oncology product candidates, such as those we are developing, utilize the PMA pathway.

If use of a companion diagnostic is deemed essential to the safe and effective use of a drug product, then the FDA generally will require approval or clearance of the diagnostic contemporaneously with the approval of the therapeutic product. In August 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance, for novel product candidates, a companion diagnostic device and its corresponding drug candidate should be approved or cleared contemporaneously by FDA for the use indicated in the therapeutic product labeling. The guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device may be considered a significant risk device under the FDA's Investigational Device Exemption (IDE) regulations. In which case, the sponsor of the diagnostic device will be required to submit and obtain approval of an IDE application and subsequently comply with the IDE regulations. However, according to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of applicable IDE regulations and the IND regulations. The guidance provides that, depending on the details of the study plan and degree of risk posed to subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE.

The FDA has generally required companion diagnostics intended to select the patients who will respond to cancer treatment to obtain approval of a PMA for that diagnostic simultaneously with approval of the therapeutic. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing, and labeling. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation (QSR), which currently imposes elaborate testing, control, documentation, and other quality assurance requirements.

If the FDA's evaluation of the PMA application is favorable, the FDA may issue an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny 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. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If and when the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale, and distribution. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained, or problems are identified following initial marketing.

After a device is commercialized, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which currently cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging, and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Other Healthcare Laws

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal and state anti-kickback, fraud and abuse, false claims, pricing reporting, and physician payment transparency laws and regulations regarding drug pricing and payments or other transfers of value made to physicians and other licensed healthcare professionals as well as similar foreign laws in the jurisdictions outside the United States. Violation of any of such laws or any other governmental regulations that apply may result in significant penalties, including, without limitation, administrative civil and criminal penalties, damages, disgorgement fines, additional reporting requirements and oversight obligations, contractual damages, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and/ or imprisonment.

Coverage and Reimbursement

Successful sales of our ecDTx in the U.S. market, if approved, will depend, in part, on the extent to which our ecDTx will be covered and eligible for adequate reimbursement by third-party payors, including government health programs, such as Medicare and Medicaid, and private health insurance (including managed care plans). Patients generally rely on such third-party payors to reimburse all or part of the costs associated with their prescriptions and therefore adequate coverage and reimbursement from such third-party payors are critical to new and ongoing product acceptance. Coverage and reimbursement policies for drug products can differ significantly from payor to payor as there is no uniform policy of coverage and reimbursement for drug products among third-party payors in the United States. Even if coverage is provided, the approved reimbursement amount may not be adequate to support pricing sufficient to realize a return on our investment. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time consuming and costly. Further, third-party payors are increasingly reducing reimbursements for medical drugs and services and implementing measures to control utilization of drugs such as requiring prior authorization or step therapy for coverage, among other things. For products administered under the supervision of a physician or other healthcare professional, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product

is used or delivered may not be available, which may impact physician utilization. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures, and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic drugs. Adoption or expansion of price controls and cost-containment measures could further limit our net revenue and results. Decreases in third-party payor reimbursement for our drug candidates, if approved, or a decision by third-party payors to not cover our drug candidates could have a material adverse effect on our sales, results of operations, and financial condition.

General regulatory cost control measures may also affect reimbursement for our products. If we obtain approval to market a drug candidate in the United States, we may be subject to spending reductions affecting Medicare, Medicaid, or other publicly funded or subsidized health programs and/or any significant taxes or fees.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, CMS, an agency within the DHHS, determines whether and to what extent a new medicine will be covered and reimbursed under Medicare, and private payors tend to follow Medicare policies to a substantial degree. Factors payors frequently consider in determining reimbursement are whether the product is: (a) a covered benefit under its health plan; (b) safe, effective, and medically necessary; (c) appropriate for the specific patient; (d) cost-effective; and (e) neither experimental nor investigational.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any current or future programs to promote the importation of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot provide any assurances that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, whether the level of reimbursement will be adequate. Further, reimbursement for drugs by government healthcare programs may be reduced by mandatory discounts or rebates required by such programs. Certain government healthcare programs impose ceiling prices on products of participating manufacturers.

U.S. Healthcare Reform

The U.S. government, state legislatures, and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price-controls, restrictions on reimbursement, and requirements for substitution of generic products for branded prescription drugs.

For example, in March 2010, the Affordable Care Act (ACA) was enacted in the United States and substantially changed the way healthcare is financed by both the government and private insurers. The ACA contains provisions that may reduce the profitability of drug products. Among other things, the ACA established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; extended manufacturers' Medicaid rebate liability to covered outpatient drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; expanded eligibility criteria for Medicaid programs; expanded the entities eligible for discounts under the 340B drug pricing program; and increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program. Since its enactment, there have been executive, judicial, and Congressional challenges to certain aspects of the ACA. In June 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in force in its current form.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. Enacted in August 2011, the Budget Control Act of 2011 includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, unless additional Congressional action is taken. Enacted in January 2013, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to providers from three to five years. Further, enacted in March 2021, the American Rescue Plan Act of 2021 eliminated the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries, presidential executive orders and proposed and enacted federal and state legislation and regulations designed to, among other things, reduce the cost of prescription drugs under Medicare, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

Most significantly, in August 2022, the Inflation Reduction Act of 2022 (IRA) was enacted. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the ACA in 2010. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare, with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); redesigns the Medicare Part D benefit (beginning in 2024); and replaces the Part D coverage gap discount program with a new manufacturer discounting program (which began in 2025). CMS has published the negotiated prices for the initial ten drugs, which will first be effective in 2026, and has published the list of the subsequent 15 drugs that will be subject to negotiation. The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented, although the Medicare drug price negotiation program is currently subject to legal challenges. The impact of the IRA on the pharmaceutical industry cannot yet be fully determined but is likely to be significant.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure, drug price reporting and other transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some states have enacted legislation creating so-called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain drugs in these states. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products, and which suppliers will be included in their prescription drug and other healthcare programs.

Existing healthcare reform measures, as well as the implementation of additional cost containment measures or other reforms, may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates, if approved. These new laws and the regulations and policies implementing them, as well as other healthcare-related measures that may be adopted in the future, could materially reduce our ability to develop and commercialize our product candidates, if approved.

Data Privacy and Security Laws

Numerous state, federal, and foreign laws, regulations and standards govern the collection, use, access to, confidentiality, and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Human Capital

As of March 21, 2025, we had 64 employees, all of whom are full-time employees. Of these employees, 47 employees are engaged in research and development and 17 are engaged in finance, legal, business development, and general management and administration. A total of 20 of these employees have M.D. or Ph.D. degrees. 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 resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing, and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain, and motivate selected employees, consultants, and directors through the granting of stock-based compensation awards. We value our employees and regularly benchmark total rewards we provide, such as short and long-term compensation, 401(k) contributions, health, welfare, and quality of life benefits, paid time off, and personal leave, against our industry peers to ensure we remain competitive and attractive to potential new hires.

Corporate Information

We were originally founded as a Delaware corporation on April 10, 2018, under the name Pretzel Therapeutics, Inc. On July 8, 2019, we changed our name to Boundless Bio, Inc.

We use our trademarks in this report as well as trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this report appear without the ® and TM symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

Available Information

Our website address is www.boundlessbio.com. The investor relations portion of our website is located at https://investors.boundlessbio.com. We make available free of charge on the investor relations portion of our website under "Financials – SEC Filings" certain reports and other information we file with or furnish to the SEC, including our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, our directors' and officers' Section 16 reports, and any amendments to those reports, as soon as reasonably practicable after we electronically file such materials with, or furnish them to, the SEC. They are also available for free on the SEC's website at www.sec.gov.

We intend to use the investor relations portion of our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD. Investors should monitor such website, in addition to following our press releases, SEC filings and public conference calls and webcasts. Information relating to our corporate governance is also included in the investor relations portion of our website. The information found on or accessible through our website and the SEC website is not incorporated into, and is not considered part of, this report. We have included these website addresses as inactive textual references only.

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, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes included elsewhere in this Annual Report on Form 10-K and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before making a decision to purchase or sell shares of our common stock. If any of the following risks are realized, our business, financial condition, results of operations, and prospects could be materially and adversely affected. In that event, the trading price of our common stock could decline, and you could lose all or part of your investment. The risks described below are not the only ones we face, and additional risks and uncertainties not known to us or that we currently believe to be immaterial may also impair our business, financial condition, results of operations and prospects.

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

We have a limited operating history, have incurred significant operating losses since our inception, and expect to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a clinical-stage oncology company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2018, have no products approved for commercial sale, and have not generated any revenue from the sale of our products. To date, we have focused primarily on organizing and staffing our company, business planning, raising capital, building our proprietary Spyglass platform, discovering our ecDTx, developing our ecDNA diagnostic, establishing our intellectual property portfolio, conducting research, preclinical studies and clinical trials, establishing arrangements with third parties for the manufacture of our ecDTx and supply of related raw materials, and providing general and administrative support for these operations. Our scientific approach to the discovery and development of ecDTx, including our use of the Spyglass platform, is unproven, and we do not know whether we will be able to develop or obtain regulatory approval for any products of commercial value. We have only one ecDTx, BBI-355, in early clinical trials, successfully developed and validated a diagnostic test, obtained regulatory approvals, manufactured products at commercial scale, or arranged for a third party to do so on our behalf, or conducted sales or marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing biopharmaceutical products.

We have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future. We do not have any products approved for sale and have not generated any revenue since our inception. If we are unable to successfully develop, obtain requisite approval for and commercialize our ecDTx, we may never generate revenue. Our net losses were \$65.4 million and \$49.4 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of \$201.5 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. All of our ecDTx will require substantial additional development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as we continue our development of, seek regulatory approval for, and potentially commercialize any of our ecDTx and seek to discover and develop additional ecDTx, as well as operate as a public company.

To become and remain profitable, we must succeed in discovering, developing, obtaining regulatory approvals for, and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials and preclinical studies of our ecDTx, discovering additional ecDTx, obtaining regulatory approval for these ecDTx and, if required, our ecDNA diagnostic, and manufacturing, marketing, and selling any products for which we may obtain regulatory approval. We are in only the preliminary stages of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve profitability. In addition, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable may have an adverse effect on the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our ecDTx pipeline, achieve our strategic objectives, or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will require substantial additional capital to finance our operations, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce, or terminate our ecDTx development programs, commercialization efforts or other operations.

The development of our ecDTx, including conducting preclinical studies and clinical trials, is a very time-consuming, capitalintensive, and uncertain process. Our operations have consumed substantial amounts of cash since inception. We expect our expenses to substantially increase in connection with our ongoing activities, particularly as we conduct our ongoing and planned clinical trials and preclinical studies and potentially seek regulatory approval for our current ecDTx and any future ecDTx we may develop. If we obtain regulatory approval for any of our ecDTx, we also expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution. Because the outcome of any clinical trial or preclinical study is highly uncertain, we cannot reasonably estimate the actual amount of capital necessary to successfully complete the development and commercialization of our ecDTx. Furthermore, we will continue to incur additional costs associated with operating as a public company.

Based on our current operating plan, we believe that our existing cash, cash equivalents, and short-term investments will be sufficient to fund our operations into 2027. We have based our belief in this regard on assumptions that may prove to be wrong, and we could expend our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Our existing capital is not sufficient to complete development of our ecDTx, or any future ecDTx, and we will require substantial capital in order to advance our ecDTx and any future ecDTx through clinical trials, regulatory approval, and commercialization. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Our ability to raise additional funds may be adversely impacted by global economic conditions, disruptions to, and volatility in, the credit and financial markets in the United States, inflation, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce, or eliminate our research and development programs or any future commercialization efforts, or even cease operations. We expect to finance our cash needs through public or private equity or debt financings or other capital sources, including potential collaborations, licenses, and other similar arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our ecDTx.

Our future capital requirements will depend on many factors, including, but not limited to:

• the initiation, type, number, scope, progress, expansions, results, costs, and timing of clinical trials and preclinical studies of our ecDTx that we are pursuing or may choose to pursue in the future, including the costs of any third-party products used as combination agents in our clinical trials;

- the costs and timing of manufacturing for our ecDTx, including commercial manufacturing at sufficient scale, if any ecDTx is approved;
- the costs and timing of developing ecDNA diagnostics, if required, and the outcome of their regulatory review;
- the costs, timing, and outcome of regulatory meetings and reviews of our ecDTx;
- the costs of obtaining, maintaining, enforcing, and protecting our patents and other intellectual property and proprietary rights;
- the costs associated with hiring additional personnel and consultants as our clinical and preclinical activities increase;
- the costs and timing of establishing or securing sales and marketing capabilities if any ecDTx is approved;
- our ability to achieve sufficient market acceptance, coverage, and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- patients' willingness to pay out-of-pocket for any approved products in the absence of coverage and/or adequate reimbursement from third-party payors;
- the terms and timing of establishing and maintaining collaborations, licenses, and other similar arrangements; and
- costs associated with any products or technologies that we may in-license or acquire.

Conducting clinical trials and preclinical studies and discovering potential ecDTx is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and commercialize our ecDTx. In addition, our ecDTx, if approved, may not achieve commercial success. Our commercial revenue, if any, will initially be derived from sales of products that we do not expect to be commercially available for many years, if at all.

Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all, including as a result of financial and credit market deterioration or instability, market-wide liquidity shortages, geopolitical events, or otherwise.

Raising additional capital may cause dilution to our stockholders, restrict our operations, or require us to relinquish rights to our technologies or ecDTx.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, including potential collaborations, licenses, and other similar arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred 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. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

If we raise additional funds through future collaborations, licenses, and other similar arrangements, we may be required to relinquish valuable rights to our future revenue streams, ecDTx, research programs, ecDNA diagnostic, intellectual property, or proprietary technology, or grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed or on terms acceptable to us, we would be required to delay, limit, reduce, or terminate our product development or future commercialization efforts, or grant rights to develop and market ecDTx that we might otherwise prefer to develop and market ourselves, or on less favorable terms than we would otherwise choose.

Risks Related to the Discovery, Development, and Regulatory Approval of Our ecDTx

We are early in our development efforts and have only one ecDTx in clinical development. All of our other ecDTx programs are still in the preclinical or discovery stage. If we are unable to successfully develop, obtain regulatory approval, and ultimately commercialize any of our current or future ecDTx, or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts and have only one ecDTx, BBI-355, in early clinical development. All of our other ecDTx programs are still in the preclinical or discovery stage. We have invested substantially all of our efforts to date in developing our ecDTx, developing our ecDNA diagnostic as a potential patient selection tool, identifying other targets for therapeutic pursuit, and continuing

to develop our proprietary Spyglass platform. We will need to progress BBI-355 through first-in-human clinical trials and progress our other ecDTx programs through additional preclinical studies to enable us to submit INDs to the FDA and receive allowance from the FDA to proceed with initiating their clinical development. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our ecDTx. The success of our ecDTx will depend on several factors, including the following:

- successful initiation and enrollment of clinical trials, and timely completion of clinical trials and preclinical studies with favorable results;
- allowance to proceed with clinical trials for our ecDTx under INDs by the FDA, or under similar regulatory submissions by comparable foreign regulatory authorities;
- the frequency and severity of adverse events observed in clinical trials and preclinical studies;
- maintaining and establishing relationships with contract research organizations (CROs) and clinical sites for the clinical development of our ecDTx, and ability of such CROs and clinical sites to comply with clinical trial protocols, Good Clinical Practice requirements (GCPs) and other applicable requirements;
- demonstrating the safety and efficacy of our ecDTx to the satisfaction of applicable regulatory authorities, including by establishing a safety database of a size satisfactory to regulatory authorities;
- successful development, validation, and regulatory approval of companion diagnostic tests for use in patient selection with our ecDTx, if required;
- receipt of regulatory approvals from applicable regulatory authorities, including approvals of new drug applications (NDAs), from the FDA and maintaining such approvals;
- maintaining relationships with our third-party manufacturers and their ability to comply with current Good Manufacturing Practice requirements (cGMPs) as well as making arrangements with our third-party manufacturers for, or establishing our own, commercial manufacturing capabilities at a cost and scale sufficient to support commercialization;
- establishing sales, marketing, and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- obtaining, maintaining, protecting, and enforcing any patent and trade secret protection, patent term extensions (if applicable) and/or regulatory exclusivity for our ecDTx;
- maintaining an acceptable safety profile of our products following regulatory approval, if any;
- maintaining and growing an organization of people who can develop and commercialize our products; and
- acceptance of our products, if approved, by patients, the medical community, and third-party payors.

If we are unable to develop, obtain regulatory approval for, or, if approved, successfully commercialize our ecDTx, or if we experience delays as a result of any of the above factors or otherwise, our business would be materially harmed.

Our approach to treating cancer with oncogene amplifications by developing ecDTx directed against ecDNA is unproven, and we do not know whether we will be able to develop any products of commercial value, or if competing approaches will limit the commercial value of our ecDTx.

The success of our business depends primarily upon our ability to discover, develop, and commercialize products based on our scientific approach, which is focused on developing therapies that are directed against ecDNA in oncogene amplified cancers, a novel and unproven approach. While we have had favorable preclinical study results for certain of our ecDTx programs, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any of our ecDTx in clinical trials or in obtaining regulatory approvals from the FDA or other regulatory authorities or in commercializing such ecDTx. For example, as discussed above, in December 2024, we made the strategic decision not to continue dose escalation of Part 1 or to proceed into the Part 2 portion of the STARMAP trial following an assessment of preliminary pharmacokinetic data from the Part 1 portion of the trial. Currently, we have only one ecDTx. BBI-355, in early clinical development, and, as an organization, we have not completed any clinical trials for any of our ecDTx. Our research methodology and scientific approach in using our Spyglass platform may be unsuccessful in identifying and discovering additional ecDTx, and, even if successful, we may not be able to submit INDs and have such INDs allowed to proceed to enable us to commence clinical trials on the timelines we expect, if at all. Any ecDTx we do discover may be shown to have harmful side effects or may have other characteristics that may necessitate additional clinical testing or make the ecDTx unmarketable or unlikely to receive regulatory approval. In particular, developing therapies that are directed against ecDNA in oncogene amplified cancers is a novel approach that may have unexpected consequences, including adverse events that preclude successful development and approval

of our ecDTx. Further, because our current ecDTx and all of our discovery programs are ecDNA based, adverse developments with respect to one of our programs may have a significant adverse impact on the actual or perceived likelihood of success and value of our other programs.

In addition, the biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies. Our future success will depend in part on our ability to maintain a competitive position with our scientific approach. If we fail to stay at the forefront of technological change in utilizing our approach to create and develop ecDTx and, if required, diagnostic tests, we may be unable to compete effectively. Our competitors may render our approach obsolete or limit the commercial value of our products or ecDTx by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our approach. By contrast, adverse developments with respect to other companies that attempt to use a similar approach to our approach may adversely impact the actual or perceived value and potential of our ecDTx.

If any of these events occur, we may be forced to delay, modify, or abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Clinical and preclinical development involves a lengthy and expensive process with uncertain timelines and outcomes, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Our ecDTx may not achieve favorable results in clinical trials or preclinical studies or receive regulatory approval on a timely basis, if at all.

Clinical and preclinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. We cannot guarantee that any clinical trials or preclinical studies will be conducted as planned, including whether we are able to meet expected timeframes for data readouts, or completed on schedule, if at all, and failure can occur at any time during the trial or study process. Despite promising preclinical or clinical results, any ecDTx can unexpectedly fail at any stage of clinical or preclinical development. The historical failure rate for product candidates in our industry is high, particularly in the earlier stages of development. For example, in December 2024, we made the strategic decision not to continue dose escalation of Part 1 or to proceed into the Part 2 portion of the STARMAP trial following an assessment of preliminary pharmacokinetic data from the Part 1 portion of the trial. The results from preclinical studies or clinical trials of an ecDTx or of a competitor's product candidates in the same class may not predict the results of later clinical trials of our ecDTx, and interim, topline, or preliminary results of a clinical trial are not necessarily indicative of final results. ecDTx in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials. It is not uncommon to observe results in clinical trials that are unexpected based on preclinical studies and early clinical trials, and many product candidates fail in clinical trials despite very promising early results. If unexpected observations or toxicities are observed in these studies, or in future IND-enabling studies for any of our other ecDTx development programs, such results may delay or prevent the initiation of clinical trials for such ecDTx programs.

Moreover, preclinical and clinical data may be susceptible to varying interpretations and analyses. A number of companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies. Such setbacks have occurred and may occur for many reasons, including, but not limited to: clinical sites and investigators may deviate from clinical trial protocols, whether due to lack of training or otherwise, and we may fail to detect any such deviations in a timely manner; patients may fail to adhere to any required clinical trial procedures, including any requirements for post-treatment follow-up; our ecDTx may fail to demonstrate effectiveness or safety in certain patient subpopulations, which has not been observed in earlier trials due to limited sample size, lack of analysis, or otherwise; or our clinical trials may not adequately represent the patient populations we intend to treat, whether due to limitations in our trial designs or otherwise, such as where one patient subgroup is overrepresented in the clinical trial. There can be no assurance that we will not suffer similar setbacks despite the data we observed in earlier or ongoing studies. Based upon negative or inconclusive results, we or any future collaborator may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, which would cause us to incur additional operating expenses and delays and may not be sufficient to support regulatory approval on a timely basis or at all.

As a result, we cannot be certain that our ongoing or planned clinical trials and preclinical studies will be successful. Any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our ecDTx in those and other indications, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Any difficulties or delays in the commencement or completion, or the termination or suspension, of our current or planned clinical trials or preclinical studies could result in increased costs to us, delay or limit our ability to generate revenue, or adversely affect our commercial prospects.

Before obtaining marketing approval from regulatory authorities for the sale of our ecDTx, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the ecDTx in humans. Before we can initiate clinical trials for our preclinical ecDTx, we

must submit the results of preclinical studies to the FDA or comparable foreign regulatory authorities along with other information, including information about ecDTx chemistry, manufacturing, and controls, and our proposed clinical trial protocol, as part of an IND or similar regulatory submission. The FDA or comparable foreign regulatory authorities may require us to conduct additional preclinical studies for any ecDTx before it allows us to initiate clinical trials under any IND or similar regulatory submission, which may lead to delays and increase the costs of our preclinical ecDTx programs. Moreover, even if we commence clinical trials, issues may arise that could cause regulatory authorities to suspend or terminate such clinical trials. Any such delays in the commencement or completion, or the termination or suspension, of our ongoing and planned clinical trials or preclinical studies for our current and any future ecDTx could significantly affect our product development timelines and product development costs.

We do not know whether our planned clinical trials and preclinical studies will begin on time or if our ongoing or future trials or studies will be completed on schedule, if at all. The commencement, data readouts, and completion of clinical trials and preclinical studies can be delayed for a number of reasons, including delays related to:

- inability to obtain animals or materials to initiate and generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- obtaining allowance from regulatory authorities to commence a trial or reaching a consensus with regulatory authorities on trial design;
- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in identifying, recruiting, and training suitable clinical investigators;
- obtaining approval from one or more institutional review boards (IRBs) or ethics committees (ECs) at clinical trial sites;
- IRBs/ECs refusing to approve, suspending, or terminating the trial at an investigational site, precluding enrollment of additional patients, or withdrawing their approval of the trial;
- changes or amendments to the clinical trial protocol;
- clinical sites deviating from the trial protocol or dropping out of a trial;
- failure by our CROs to perform in accordance with GCP requirements or applicable regulatory requirements or guidelines in other countries;
- obtaining raw materials for manufacturing sufficient quantities of our ecDTx or obtaining sufficient quantities of combination therapies or other materials needed for use in clinical trials and preclinical studies;
- patients failing to enroll or remain in our trials at the rate we expect, or failing to return for post-treatment follow-up, including patients failing to remain in our trials due to movement restrictions, health reasons, or otherwise resulting from any future public health concerns;
- patients choosing alternative treatments for the indications for which we are developing our ecDTx, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trials or preclinical studies or costs being greater than we anticipate;
- patients experiencing severe or serious unexpected drug-related adverse effects;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies that could be considered similar to our ecDTx;
- selection of clinical endpoints that require prolonged periods of clinical observation or extended analysis of the resulting data;
- transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization (CMO), delays or failure by our CMOs or us to make any necessary changes to such manufacturing process, or failure of our CMOs to produce clinical trial materials in accordance with cGMP regulations or other applicable requirements; and
- third parties being unwilling or unable to satisfy their contractual obligations to us in a timely manner.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities' legal requirements, regulations, or guidelines, and are subject to oversight by these governmental agencies and ECs or IRBs at the medical institutions where the clinical trials are conducted. We could also encounter delays if a clinical trial is suspended or terminated by us, by ECs or IRBs of

the institutions in which such trials are being conducted, by a data safety monitoring board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with GCP and other regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations, or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to ECs or IRBs for reexamination, which may impact the costs, timing, or successful completion of a clinical trial.

Further, in the future we may conduct clinical trials in foreign countries, and this will present additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocols as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, and political and economic risks, including war, relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or a comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of regulatory approval of one or more of our ecDTx.

In addition, many of the factors that cause, or lead to, the termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of an ecDTx. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our ecDTx. In such cases, our competitors may be able to bring products to market before we do, and the commercial viability of our ecDTx could be significantly reduced. Any of these occurrences may harm our business, financial condition, results of operations, and prospects.

We may find it difficult to enroll patients in our clinical trials. If we encounter difficulties or delays enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Successful and timely completion of clinical trials will require that we identify and enroll a specified number of patients for each of our clinical trials. We may not be able to initiate or continue clinical trials for our ecDTx if we are unable to identify 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. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and characteristics of the patient population, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the risk that enrolled patients will not complete a clinical trial, our ability to recruit clinical trial investigators with the appropriate competencies and experience, and competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the ecDTx being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating as well as any product candidates under development. We will be required to identify and enroll a sufficient number of patients for each of our clinical trials and monitor such patients adequately during and after treatment. Potential patients for any planned clinical trials may not be adequately diagnosed or identified with the diseases that we are targeting, which could adversely impact the outcomes of our trials and could have safety concerns for the potential patients. Potential patients for any planned clinical trials may not meet the entry criteria for such trials.

In particular, because our ecDTx are focused on patients with tumors harboring oncogene amplifications on ecDNA, our ability to enroll eligible patients may be limited or take more time than we anticipate, due to the frequency of the biomarker we are seeking to target, or our ability to effectively identify such biomarker. We also may encounter difficulties in identifying and enrolling patients with the proper tumor characteristics or stage of disease appropriate for our planned clinical trials and monitoring such patients adequately during and after treatment. Additionally, other pharmaceutical companies targeting these same types of cancer are recruiting clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow-up periods. The eligibility criteria of our clinical trials, once established, may further limit the pool of available trial patients. If patients are unwilling or unable to participate in our trials for any reason, including the existence of concurrent clinical trials for similar target populations, the availability of approved therapies, or the fact that enrolling in our trials may prevent patients from taking a different product, or we otherwise have difficulty enrolling a sufficient number of patients, the timeline for recruiting patients, conducting trials, and obtaining regulatory approval of our ecDTx may be delayed. Additionally, because our clinical trials are in patients

with relapsed/refractory cancer, the patients are typically in the late stages of their disease and may experience disease progression independent from our ecDTx, making them unevaluable for purposes of the clinical trial and requiring additional patient enrollment. Our inability to enroll a sufficient number of patients for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

In addition, we rely on, and will continue to rely on, CROs and clinical trial sites to ensure proper and timely enrollment of our clinical trials. Though we have entered into agreements governing their services, we have limited influence over their actual performance. We cannot assure you that our assumptions used in determining expected clinical trial timelines are correct, or that we will not experience delays or difficulties in enrollment, or be required by the FDA or other regulatory authorities to increase our enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

Use of our ecDTx could be associated with side effects, adverse events, or other properties or safety risks, which could delay or preclude regulatory approval, cause us to suspend or discontinue clinical trials, abandon an ecDTx, limit the commercial profile of an approved label, or result in other significant negative consequences that could severely harm our business, financial condition, results of operations, and prospects.

As is the case with oncology drugs generally, it is likely that there may be side effects and adverse events associated with use of our ecDTx. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of expected or unexpected side effects or unexpected characteristics. Undesirable side effects caused by our ecDTx when used alone or in combination with approved or investigational drugs could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label, or lead to the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition, results of operations, and prospects significantly.

Moreover, if our ecDTx are associated with undesirable side effects in clinical trials or demonstrate characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the ecDTx if approved. Unacceptable enhancement of certain toxicities may be seen when our ecDTx are combined with standard of care therapies, or when they are used as single agents. We may also be required to modify our development and clinical trial plans based on findings in our ongoing clinical trials. Many compounds that initially showed promise in early-stage testing for treating cancer have later been found to cause side effects that prevented further development of the compounds.

It is possible that as we test our ecDTx in larger, longer, and more extensive clinical trials, including with different dosing regimens, or as the use of these ecDTx becomes more widespread following any regulatory approval, more illnesses, injuries, discomforts, and other adverse events than were observed in earlier trials, as well as new conditions that did not occur or went undetected in previous trials, may be discovered. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition, and prospects significantly.

In addition, we plan to study our ecDTx in combination with other therapies, which may exacerbate adverse events associated with such ecDTx. Patients treated with our ecDTx may also be undergoing surgical, radiation, and/or chemotherapy treatments, which can cause side effects or adverse events that are unrelated to our ecDTx but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. For example, we expect that some of the patients enrolled in our clinical trials will die or experience major clinical events either during the course of our clinical trials or after participating in such trials.

In addition, if one or more of our ecDTx receives regulatory approval, and we or others later identify undesirable side effects caused by such product, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend, or limit approvals of such product, or seek an injunction against its manufacture or distribution;
- we may be required to recall a product or change the way such product is administered to patients;
- regulatory authorities may require additional warnings on the label, such as a "black box" warning or a contraindication;
- we may be required to implement a Risk Evaluation and Mitigation Strategy (REMS) or create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product is distributed or administered, conduct additional clinical trials, change the labeling of a product, or conduct additional post-marketing studies or surveillance;

- we could be sued and held liable for harm caused to patients;
- sales of the product may decrease significantly or the product could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular ecDTx, if approved, and could significantly harm our business, results of operations, and prospects.

As an organization, we have never completed any clinical trials and may be unable to do so for any of our ecDTx.

We are early in our development efforts for our ecDTx, have never completed any clinical trials, and we will need to successfully complete our ongoing and later-stage and pivotal clinical trials in order to obtain FDA or comparable foreign regulatory approval to market our ecDTx. Carrying out later-stage clinical trials and the submission of a successful NDA is a complicated process. We are currently conducting our first Phase 1/2 clinical trial for BBI-355. We have not yet completed any clinical trials for our other ecDTx or development programs. We have limited experience as a company in preparing and submitting marketing applications and have not previously submitted an NDA or other comparable foreign regulatory submission for any ecDTx. In addition, as a company, we have had limited interactions with the FDA and no interaction with other comparable foreign regulatory authorities and cannot be certain how many additional clinical trials of our ecDTx will be required or how such trials should be designed. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to submission and regulatory approval of any of our ecDTx. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of ecDTx that we develop. Failure to commence or complete, or delays in, our planned clinical trials could prevent us from or delay us in submitting marketing applications, including NDAs, for and commercializing our ecDTx.

If we are unable to successfully develop an ecDNA diagnostic to enable patient selection for our ecDTx, or if we experience significant delays in doing so, we may not realize the full commercial potential of our ecDTx.

A key component of our strategy is our ability to identify patients with tumors harboring oncogene amplifications on ecDNA from genomic data obtained through next generation sequencing of patient tumor samples. Identification of these patients will require the development and use of an ecDNA diagnostic assay. We developed our ecDNA diagnostic as a clinical trial assay for use during our Phase 1/2 POTENTIATE clinical trial of BBI-355 using a third-party *in vitro* diagnostic company. We may continue to work with this company on this, and/or other ecDNA diagnostic assays in the future, or we may choose to work with other third-party diagnostic developers. We may have difficulty in maintaining our relationship with our current third-party diagnostic developer or establishing or maintaining relationships with other third-party diagnostic development companies in the future, and we may face competition from other companies in establishing these relationships.

There are also several risks associated with the development of an ecDNA diagnostic assay. We may not be able to identify predictive biomarkers to identify patients whose tumors harbor oncogene amplifications on ecDNA. We may not be able to validate an ecDNA diagnostic and the related biomarkers or their functional relevance clinically. Potential biomarkers, even if validated preclinically, may not be functionally validated in human clinical trials. Any failure by us or our third-party diagnostic developer to successfully develop or obtain marketing authorization for an ecDNA diagnostic assay, or any delays in doing so, may harm the commercial prospects of our ecDTx.

We intend to develop our ecDTx in combination with other therapies, which exposes us to additional risks.

We intend to develop our current and any future ecDTx for use in combination with one or more currently approved cancer therapies. Even if any ecDTx we develop was to receive regulatory 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 ecDTx or that safety, efficacy, manufacturing, or supply issues could arise with these existing therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our ecDTx for use in combination with other drugs or biologics or for indications other than cancer. Developing combination therapies using approved therapeutics, as we plan to do for our ecDTx, also exposes us to additional clinical risks, such as the requirement that we demonstrate the safety and efficacy of each active component of any combination regimen we may develop.

If the FDA or similar foreign regulatory authorities revoke the approval of combination agents, or if safety, efficacy, manufacturing, or supply issues arise with the drugs we choose to evaluate in combination with our ecDTx, we may be unable to obtain approval of or market our ecDTx for combination therapy regimens.

Additionally, if the third-party providers of therapies or therapies in development used in combination with our ecDTx are unable to produce sufficient quantities for clinical trials or for commercialization of our ecDTx, or if the cost of combination therapies are

prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations, and prospects.

We may expend our limited resources to pursue a particular ecDTx or a particular indication for an ecDTx and fail to capitalize on ecDTx 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 specific ecDTx, development programs, and indications. As a result, we may forgo or delay pursuit of opportunities with other ecDTx that could have had greater commercial potential. Our resource allocation and other decisions may cause us to fail to identify and capitalize on viable potential ecDTx or additional indications for our ecDTx or other profitable market opportunities. Our spending on current and future research and development programs and ecDTx for specific indications may not yield any commercially viable ecDTx. For example, in December 2024, we made the strategic decision not to continue dose escalation of Part 1 or to proceed into the Part 2 portion of the STARMAP trial following an assessment of preliminary pharmacokinetic data from the Part 1 portion of the trial. If we do not accurately evaluate the commercial potential or target market for a particular indication or ecDTx, we may relinquish valuable rights to that ecDTx through collaborations, licenses, and other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such ecDTx.

We may in the future conduct certain of our clinical trials for our ecDTx outside of the United States. However, the FDA and other foreign equivalents may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.

We may in the future conduct one or more of our clinical trials for our ecDTx outside the United States. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for regulatory approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless the data are applicable to the United States population and United States medical practice; the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and the data may be considered valid without the need for an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, if the relevant study was not conducted pursuant to an IND, the FDA will not accept the data as support for a marketing application unless the study was conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar requirements for clinical data gathered outside of their respective jurisdictions. There can be no assurance the FDA will accept data from clinical trials conducted outside of the United States. If the FDA does not accept data from our clinical trials of our ecDTx, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay or permanently halt our development of our ecDTx.

Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment, and storage requirements;
- inconsistent standards for reporting and evaluating clinical data and adverse events;
- diminished protection of intellectual property in some countries; and
- public health concerns or political instability, civil unrest, war, or similar events that may jeopardize our ability to commence, conduct, or complete a clinical trial and evaluate resulting data.

Interim, topline, and preliminary data from our clinical trials and preclinical studies 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 publicly disclose interim, topline, or preliminary data from our clinical trials and preclinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, topline, or preliminary results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated.

Topline and preliminary data also remain subject to audit and verification procedures that may result, in the final data being materially different from the topline or preliminary data we previously published. As a result, topline and preliminary data should be viewed with caution until the final data are available. Interim data from clinical trials that we may complete are further 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. Adverse differences between interim, topline, or preliminary data and final data could significantly harm our business prospects.

In addition, others, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular ecDTx or product and our company in general. Moreover, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, ecDTx or our business. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our ecDTx may be harmed, which could harm our business, operating results, prospects, or financial condition.

Changes in methods of ecDTx manufacturing or formulation may result in additional costs or delay.

As our ecDTx progress through clinical trials to regulatory approval and commercialization, it is common that various aspects of the ecDTx development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize safety, efficacy, yield, and manufacturing batch size, minimize costs, and achieve consistent quality and results. There can be no assurance that this or any other future manufacturing or formulation changes will achieve their intended objectives. These changes and any future changes we may make to our ecDTx may also cause such candidates to perform differently and affect the results of future clinical trials conducted with the altered materials. Such changes or related unfavorable clinical trial results could delay initiation or completion of additional clinical trials, require the conduct of bridging studies or clinical trials or the repetition of one or more studies or clinical trials, increase development costs, delay or prevent potential regulatory approval, and jeopardize our ability to commercialize our ecDTx, if approved, and generate revenue.

If we are required by the FDA or comparable foreign regulatory authority to obtain approval of a companion diagnostic test, such as our investigational ecDNA diagnostic, in connection with approval of any of our ecDTx, and we do not obtain, or face delays in obtaining, FDA or foreign approval of such companion diagnostic, we will not be able to commercialize our ecDTx, and our ability to generate revenue will be materially impaired.

We are currently working with a third party to develop an ecDNA diagnostic assay to identify patients with tumors harboring oncogene amplifications on ecDNA. We believe an ecDNA diagnostic will be helpful in identifying patients that may benefit from certain of our ecDTx, including BBI-355. If the FDA believes that the safe and effective use of any of our ecDTx depends on an *in vitro* diagnostic, such as our investigational ecDNA diagnostic, then it may require approval or clearance of that diagnostic as a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. If an ecDNA diagnostic, or an alternative companion diagnostic is not commercially available in this situation, we may be required to complete the development of an ecDNA diagnostic or obtain an alternative companion diagnostic that would be subject to regulatory approval requirements. The process of obtaining or creating such diagnostics is time-consuming and costly.

Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical devices by the FDA and comparable foreign regulatory authorities, and the FDA has generally required premarket approval of companion diagnostics for cancer therapies. As such, we expect we may need to obtain approval for any ecDNA diagnostic we may develop for use with our ecDTx. The approval or clearance of a companion diagnostic as part of the therapeutic product's further labeling limits the use of the therapeutic product to only those patients who express the specific characteristic that the companion diagnostic was developed to detect.

If the FDA or a comparable foreign regulatory authority requires approval or clearance of a companion diagnostic for any of our ecDTx, whether before, simultaneously with, or after the ecDTx obtains regulatory approval, we and/or third-party developers may encounter difficulties in developing and obtaining approval or clearance for these companion diagnostics. Any delay or failure by us or third-party developers to develop or obtain regulatory approval or clearance of a companion diagnostic could delay or prevent approval or continued marketing of the relevant ecDTx. We or our third-party developers may also experience delays in developing a sustainable, reproducible, and scalable manufacturing process for the companion diagnostic or in transferring that process to commercial partners or

negotiating insurance reimbursement plans, all of which may prevent us from completing our clinical trials or commercializing our ecDTx, if approved, on a timely or profitable basis, if at all.

We may attempt to secure approval from the FDA through the use of the accelerated approval pathway. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary regulatory approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw any accelerated approval we have obtained.

We may in the future seek an accelerated approval for one or more of our ecDTx. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit.

The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such confirmatory studies fail to confirm the drug's clinical benefit or are not completed in a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. In addition, the Food and Drug Omnibus Reform Act of 2022, among other things, provided the FDA with statutory authority to mitigate potential risks to patients from continued marketing of ineffective drugs previously granted accelerated approval and additional oversight over confirmatory trials. Under these provisions, the FDA may, among other things, require a sponsor of a product seeking accelerated approval to have a confirmatory trial underway prior to such approval being granted.

Prior to seeking approval for any of our ecDTx, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or obtain any other form of expedited development, review, or approval. Furthermore, if we decide to submit an application for accelerated approval for our ecDTx, there can be no assurance that such submission or application will be accepted or that any expedited development, review, or approval will be granted on a timely basis, or at all. The FDA could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review, or approval for our ecDTx would result in a longer time period to commercialization of such ecDTx, if any, could increase the cost of development of such ecDTx, and could harm our competitive position in the marketplace.

Disruptions at the FDA, the SEC, and other government agencies including due to funding shortages, changes in leadership, changes in policy, significant personnel turnover, or global health concerns, could delay or hinder clinical and preclinical development and potential marketing approval of our ecDTx and our ability to raise capital.

Twice in the past decade, the previous appropriations legislation deadline was reached and Congress failed to pass a new appropriations bill or continuing resolution to temporarily extend funding, resulting in U.S. government shutdowns that caused federal agencies to halt non-essential operations. Political polarization among lawmakers may lead to a higher frequency and longer duration of government shutdowns in the future. A federal government shutdown could prevent or delay staff at federal agencies from performing key functions that may adversely affect our business. In addition, considerable uncertainty exists regarding how federal government policy and budget decisions will unfold, including the regulatory and spending priorities of the current U.S. presidential administration and Congress, and what challenges potential policy changes and budget reductions will present for us and our industry generally. The new current U.S. presidential administration may institute significant changes to certain federal regulatory agencies including the FDA and SEC, including reductions in funding levels or restructuring of such agencies that could adversely impact us.

For example, the ability of the FDA to review and approve new product applications or take action with respect to other regulatory matters can be affected by a variety of factors, including funding levels, ability to accept the payment of user fees, ability to hire and retain key personnel, and statutory, regulatory and policy changes. Government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. For example, the current U.S. presidential administration has issued certain policies and executive orders directed towards reducing the employee headcount and costs associated with U.S. administrative agencies, including the FDA, and it remains unclear the degree to which these efforts may limit or

otherwise adversely affect the FDA's ability to conduct routine activities. Disruptions at the FDA may delay meetings and other communications with agency staff necessary to progress development of our product candidates and may slow the time necessary for acceptance, review, and approval of applications to commence clinical studies or to market a new product in the U.S.

In addition, disruptions at the SEC could prevent or delay SEC staff from performing key functions, including, for example, granting acceleration requests for registration statements, declaring registration statements or amendments thereto effective and providing interpretive guidance or no-action letters. If a federal government shutdown halts non-essential SEC operations for an extended period, it may negatively impact our ability to raise additional capital through registered offerings of our securities. If a prolonged U.S. government shutdown or other event or condition occurs that prevents or significantly delays the FDA, SEC or other regulatory agencies from hiring and retaining personnel and conducting their regular activities, or if an agency is restructured or experiences significant reduction in funding, leadership changes or employee turnover, it could significantly impact the ability of these agencies to timely review and process our regulatory submissions and may impede our access to additional capital needed to maintain or expand our operations or to complete important acquisitions or other transactions, which could have a material adverse effect on our business.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our clinical trials and preclinical studies. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements, or meet expected deadlines, our ecDTx development programs and our ability to seek or obtain regulatory approval for or commercialize our ecDTx may be delayed.

We are dependent on third parties to conduct our clinical trials and preclinical studies. Specifically, we rely on, and intend to continue to rely on, medical institutions, clinical investigators, CROs, and consultants to conduct our preclinical studies and clinical trials in accordance with our clinical protocols and regulatory requirements. These CROs, investigators, and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. While we have and will have agreements governing the activities of our third-party contractors, we have limited influence over their actual performance. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory, and scientific standards and requirements, and our reliance on our CROs and other third parties does not relieve us of our regulatory responsibilities. In addition, we and our CROs are required to comply with Good Laboratory Practice (GLP) requirements for certain preclinical studies, as well as GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for clinical trials of all of our ecDTx. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators, and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GLP or GCP or other requirements, the clinical data generated in our preclinical studies or clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional preclinical studies or clinical trials before approving our marketing applications, if ever. Further, our clinical trials must be conducted with products produced in accordance with cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

There is no guarantee that any of our CROs, investigators, or other third parties will devote adequate time and resources to such trials or studies or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols, or meet regulatory requirements, or otherwise perform in a substandard manner, our clinical trials may be extended, delayed, or terminated. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other development activities that could harm our competitive position.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach and under other specified circumstances. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties on commercially reasonable terms, in a timely manner or at all. Switching or adding additional CROs, investigators, and other third parties involves additional cost and requires our management's 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. Though we work to carefully manage our relationships with our CROs, investigators and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

We rely on third parties for the manufacture of our ecDTx for clinical and preclinical development and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our ecDTx

or products or such quantities at an acceptable cost, which could delay, prevent, or impair, our development or commercialization efforts.

We do not own or operate manufacturing facilities and have no plans to develop our own clinical or commercial-scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture of our ecDTx and related raw materials for clinical and preclinical development, as well as for commercial manufacture if any of our ecDTx receive regulatory approval. The facilities used by third-party manufacturers to manufacture our ecDTx must be approved for the manufacture of our ecDTx by the FDA and any comparable foreign regulatory authority pursuant to inspections that will be conducted after we submit an NDA to the FDA or any comparable submission to a foreign regulatory authority. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements for manufacture of products. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or any comparable foreign regulatory authority, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance, and qualified personnel. If the FDA or any comparable foreign regulatory authority does not approve these facilities for the manufacture of our ecDTx or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for, or market our ecDTx, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of ecDTx or products, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our ecDTx.

Our or a third party's failure to execute on our manufacturing requirements on commercially reasonable terms, in a timely manner and in compliance with cGMP or other regulatory requirements could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of our ecDTx;
- delay in submitting regulatory applications, or receiving regulatory approvals, for our ecDTx;
- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease development or to recall batches of our ecDTx; and
- in the event of approval to market and commercialize our ecDTx, an inability to meet commercial demands for our ecDTx.

In addition, we do not have any long-term commitments or supply agreements with our third-party manufacturers. We may be unable to establish any long-term supply agreements with third-party manufacturers or to do so on acceptable terms or at all, which increases the risk of failing to timely obtain sufficient quantities of our ecDTx or such quantities at an acceptable cost. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of the manufacturing agreement by the third party;
- failure to manufacture our product according to our specifications;
- failure to obtain adequate raw materials and other materials required for manufacturing;
- failure to manufacture our product according to our schedule or at all;
- failure to successfully scale up manufacturing capacity, if required;
- misappropriation of our proprietary information, including our trade secrets and know-how; and
- termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Our ecDTx and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or regulatory approval, and any related remedial measures may be costly or time consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of our ecDTx. If our existing or future third-party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all.

In addition, our current and anticipated future dependence upon others for the manufacture of our ecDTx or products may adversely affect our future profit margins and our ability to commercialize any products that receive regulatory approval on a timely and competitive basis.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor or other third party will discover them or that our trade secrets will be misappropriated or disclosed.

Because we currently rely on third parties for the development of a diagnostic and to manufacture our ecDTx and to perform quality testing, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements, and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements, or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors or other third parties, are intentionally or inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets and despite our efforts to protect our trade secrets, a competitor's or other third party's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure of such technology or information would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may seek to enter into collaborations, licenses, and other similar arrangements and may not be successful in doing so, and even if we are, we may relinquish valuable rights and may not realize the benefits of such relationships.

We may seek to enter into collaborations, joint ventures, licenses, and other similar arrangements for the development or commercialization of our ecDTx, if approved, due to capital costs required to develop or commercialize the ecDTx or manufacturing constraints. We may not be successful in our efforts to establish or maintain such collaborations for our ecDTx because our research and development pipeline may be insufficient, our ecDTx may be deemed to be at too early of a stage of development for collaborative effort, or third parties may not view our ecDTx as having the requisite potential to demonstrate safety and efficacy or significant commercial opportunity. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process can be time-consuming and complex. Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us. For example, we may need to relinquish valuable rights to our future revenue streams, research programs, intellectual property, ecDTx or ecDNA diagnostic, or grant licenses on terms that may not be favorable to us, as part of any such arrangement, and such arrangements may restrict us from entering into additional agreements with other potential collaborators. In addition, if we enter into such collaborations, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our ecDTx. Our ability to generate revenue from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot be certain that, following a collaboration, license, or strategic transaction, we will achieve an economic benefit that justifies such transaction, and such transaction may not yield additional development or ecDTx for our pipeline. Furthermore, we may not be able to maintain such collaborations if, for example, the development or approval of an ecDTx is delayed, the safety of an ecDTx is questioned, or the sales of an approved ecDTx are unsatisfactory.

In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of our ecDTx, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we enter into in the future, or any delay in entering into collaborations related to our ecDTx, could delay the development and commercialization of our ecDTx, if approved, and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Commercialization of Our ecDTx

Even if we receive regulatory approval for any ecDTx, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense.

Any regulatory approvals that we may receive for our ecDTx will require the submission of reports to regulatory authorities, subject us to surveillance to monitor the safety and efficacy of the product, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions, or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS as a condition of approval of our ecDTx, which could include requirements for 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.

In addition, if the FDA or a comparable foreign regulatory authority approves our ecDTx, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, and recordkeeping for our products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCP requirements for any clinical trials that we conduct post-approval. Manufacturers of approved products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. Failure to comply with regulatory requirements or later discovery of previously unknown problems with our products, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, may result in, 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;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- fines, restitutions, disgorgement of profits or revenue, warning letters, untitled letters, adverse publicity requirements, or holds on clinical trials;
- refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications submitted by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our products; and
- injunctions and the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our ecDTx and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be promulgated that could prevent, limit, or delay marketing authorization of any ecDTx. We also 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 be subject to enforcement action and we may not achieve or sustain profitability.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as our ecDTx, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive regulatory approval for an ecDTx, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The government has also required companies to enter into consent decrees or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our ecDTx, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

The commercial success of our ecDTx will depend upon the degree of market acceptance of such ecDTx by physicians, patients, healthcare payors, and others in the medical community.

Our ecDTx may not be commercially successful. Even if any of our ecDTx receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors, or the medical community. The commercial success of any of our current or future ecDTx will depend significantly on the broad adoption and use of the resulting product by these individuals and organizations for approved indications. The degree of market acceptance of our products will depend on a number of factors, including:

- demonstration of clinical efficacy and safety, including as compared to any more-established products;
- the indications for which our ecDTx are approved;
- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;
- acceptance of a new drug for the relevant indication by healthcare providers and their patients;

- the pricing and cost-effectiveness of our products, as well as the cost of treatment with our products in relation to alternative treatments and therapies;
- our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government healthcare programs, including Medicare and Medicaid, private health insurers, and other third-party payors;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement;
- any restrictions on the use of our products, and the prevalence and severity of any adverse effects;
- potential product liability claims;
- the timing of market introduction of our products as well as availability, safety, and efficacy of competitive drugs;
- the effectiveness of our or any potential future collaborators' sales and marketing strategies; and
- unfavorable publicity relating to the product.

If any ecDTx is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors, or patients, we may not generate sufficient revenue from that product and may not become or remain profitable. Our efforts to educate the medical community and third-party payors regarding the benefits of our products may require significant resources and may never be successful.

The successful commercialization of our ecDTx, if approved, will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels, and favorable pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our ecDTx could limit our ability to market those products and decrease our ability to generate revenue.

The availability of coverage and the adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers, and other third-party payors are essential for most patients to be able to afford prescription medications such as our ecDTx, if approved. Our ability to achieve coverage and adequate levels of reimbursement for our ecDTx by third-party payors will have a material effect on our ability to successfully commercialize our ecDTx. Accordingly, we will need to successfully implement a coverage and reimbursement strategy for any approved ecDTx. Even if we obtain coverage for a given ecDTx by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Reimbursement for drugs by government healthcare programs may be reduced by mandatory discounts or rebates required by such programs. Certain government healthcare programs impose ceiling prices on products of participating manufacturers.

Third-party payors increasingly are challenging prices charged for biopharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available. It is possible that a third-party payor may consider our ecDTx as substitutable and offer to reimburse patients only for the less expensive product. Even if we are successful in demonstrating improved efficacy or improved convenience of administration with our ecDTx, pricing of existing drugs may limit the amount we will be able to charge for our ecDTx. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are not adequate to enable us to realize an appropriate return on our investment in ecDTx development. If reimbursement is not available or is available only at inadequate levels, we may not be able to successfully commercialize our ecDTx and may not be able to obtain a satisfactory financial return on ecDTx that we may develop. In addition, in the event that we develop companion diagnostic tests for use with our ecDTx, once approved, such companion diagnostic tests will require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical product. Similar challenges to obtaining coverage and reimbursement applicable to pharmaceutical products will apply to companion diagnostic tests.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid, play an important role in determining the extent to which new drugs will be covered. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our products.

Obtaining and maintaining reimbursement status is time-consuming, costly, and uncertain. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. However, 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 time consuming and costly and may require us to provide scientific and clinical support for the use of our ecDTx to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Reimbursement practices are also subject to rules and regulations that may change frequently, and, in some cases, at short notice.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our ecDTx, if approved in these jurisdictions. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our ecDTx. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our ecDTx. We expect to experience pricing pressures in connection with the sale of any of our ecDTx due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. There is increasing downward pressure on healthcare costs in general, and prescription drugs, surgical procedures, and other treatments in particular. As a result, increasingly high barriers are being erected to the entry of new products. See the section titled "Risk Factors—Risks Related to Our Business Operations and Industry—Current and future healthcare reform legislation or regulation may increase the difficulty and cost for us to obtain coverage for and commercialize our ecDTx and may adversely affect the prices we may set" for additional related information.

We face significant competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If our competitors develop and commercialize their product candidates more rapidly than we do, or their technologies or their product candidates are more effective, safer, or less expensive than our ecDTx, our business and our ability to develop and successfully commercialize ecDTx may be adversely affected.

The biopharmaceutical industry is characterized by rapid advancing technologies, intense competition, and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing, or may develop products or product candidates competitive with our ecDTx. Any ecDTx that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under develop ecDTx. In particular, there is intense competition in the oncology field. Our competitors include larger and better-funded pharmaceutical, biotechnological, and therapeutics companies. Moreover, we may also compete with universities and other research institutions that may be active in oncology research and could be in direct competition with us. We also compete with these organizations to recruit management, scientists, and clinical development personnel, and our inability to compete successfully could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, enrolling patients for clinical trials, and identifying and in-licensing intellectual property related to new ecDTx, as well as entering into collaborations, joint ventures, license agreements, and other similar arrangements. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

If any of our ecDTx are approved, they will compete with surgery, radiation, and drug therapy, including chemotherapy, hormone therapy, biologic therapy, such as monoclonal and bispecific antibodies, antibody-drug conjugates, radiopharmaceuticals, immunotherapy, cell-based therapy, and targeted therapy, or a combination of any such methods, either approved or under development, that are intended to treat the same indications that we are targeting or may target, including through approaches that may prove to be more effective, have fewer side effects, be less costly to manufacture, be more convenient to administer, or have other advantages over our ecDTx. There are numerous companies developing precision oncology medicines with which we may compete. In addition to competing with other therapies targeting similar indications, there are numerous other companies and academic institutions focused on similar targets as our ecDTx and/or different scientific approaches to treating the same indications. We face competition from such companies in seeking any future potential collaborations to partner our ecDTx, as well as potentially competing commercially for any approved products.

Specifically, for BBI-355, Acrivon Therapeutics, Esperas Pharma, Sumitomo Pharma, and PharmaEngine have CHK1 inhibitors in clinical development. BenevolentAI, Fosun Pharma, and Impact Therapeutics have publicly disclosed preclinical stage CHK1 inhibitors. For our pipeline of ecDTx programs, potential competition includes established companies as well as emerging biotechnology companies that may launch programs against similar targets; however, we are not aware of any companies with ecDNA-directed therapeutic programs in clinical development or a patient selection strategy for ecDNA-enabled oncogene amplification. We are aware of one early-stage private company that is focused on research in ecDNA, Econic Biosciences.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales, and supply resources or experience than we do. If we successfully obtain approval for any ecDTx, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered, and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing, and sales capabilities, price, reimbursement coverage, and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive, or marketed and sold more effectively than any products we may develop. Competitive products may make any ecDTx we develop obsolete or noncompetitive before we recover the expense of developing and commercializing it. If we are unable to compete effectively, our opportunity to generate revenue from the sale of any ecDTx we may develop, if approved, could be adversely affected.

The market opportunities for our ecDTx may be limited to patients who are ineligible for or have failed prior treatments and may be small or different from our estimates.

Cancer therapies are defined by lines of therapy as well as by treatment-naïve or previously-treated status. Often the initial approval for a new therapy is in later lines and subsequent approval in an earlier line may not be feasible. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, including surgery, radiation therapy, targeted therapy, immunotherapy, chemotherapy, hormone therapy, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of additional chemotherapy, radiation, antibody drugs, tumor targeted small molecules, or a combination of these. Third line therapies can include antibody and small molecule targeted therapies, more invasive forms of surgery, and new technologies. In markets with approved therapies, there is no guarantee that our ecDTx, even if approved, would be approved for second line or first line therapy. This could limit our potential market opportunity. In addition, we may have to conduct additional clinical trials prior to gaining approval for second line or first line therapy.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive later stage therapy and who have the potential to benefit from treatment with our ecDTx, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, publicly available clinical molecular reports, patient foundations, or market research, and may prove to be incorrect. Further, new trials or information may change the estimated incidence or prevalence of these cancers. Further, specific to our biomarker-driven strategy, data analytics and information from databases that we rely on for identifying or validating some of our biomarker-target relationships may not accurately reflect potential patient populations or may be based on incorrect methodology. As ecDNA in oncogene amplified cancers is a new and novel approach, this heightens the risk that our estimates of the eligible patient population may not be accurate. The number of patients in the United States and other major markets and elsewhere 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. Further, even if we obtain significant market share for our ecDTx, because some of our potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may need to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate product revenue.

We have no internal sales, marketing, or distribution capabilities, nor have we ever commercialized a product. If any of our ecDTx ultimately receives regulatory approval, we must build a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming, or collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We have no prior experience as a company with the marketing, sale, or distribution of biopharmaceutical products, and there are significant risks involved in the building and managing of a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities would adversely impact the commercialization of these products. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing, and distribution functions on acceptable financial terms, or at all. In addition, our ecDTx revenue and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell, and distribute any ecDTx that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our ecDTx effectively. If we are not successful in commercializing our ecDTx, either on our own or through arrangements with one or more third parties, we may not be able to generate any future ecDTx revenue and we would incur significant additional losses.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future growth may depend, in part, on our ability to develop and commercialize our ecDTx in foreign markets. We are not permitted to market or promote any of our ecDTx before we receive regulatory approval from applicable regulatory authorities in foreign markets, and we may never receive such regulatory approvals for any of our ecDTx. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements regarding safety and efficacy and governing, among other things, clinical trials, commercial sales, pricing, and distribution of our ecDTx. Approval procedures may be more onerous than those in the United States and may require that we conduct additional preclinical studies or clinical trials. If we obtain regulatory approval of our ecDTx and ultimately commercialize our ecDTx in foreign markets, we would be subject to additional risks and uncertainties, including:

- different regulatory requirements for approval of drugs in foreign countries;
- reduced protection for intellectual property rights;
- the existence of additional third-party patent rights of potential relevance to our business;
- compliance with export control and import laws and regulations and unexpected changes in tariffs, trade barriers, and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing, and insurance regimes;
- workforce uncertainty in countries where labor unrest is common;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, public health pandemics or epidemics, or natural disasters including earthquakes, typhoons, floods, and fires.

Risks Related to Our Business Operations and Industry

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to:

- the timing and cost of, and level of investment in, research, development, regulatory approval, and commercialization activities relating to our ecDTx, which may change from time to time, including the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- the timing and success or failure of preclinical studies or clinical trials for our ecDTx or competing products, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- coverage and reimbursement policies with respect to our ecDTx, if approved, and potential future drugs that compete with our ecDTx;
- the cost of manufacturing our ecDTx, which may vary depending on the quantity of production and the terms of our agreements with third-party manufacturers;
- expenditures that we may incur to acquire, develop, or commercialize additional ecDTx and technologies;
- the level of demand for any approved ecDTx, which may vary significantly and be difficult to predict;
- our ability to establish and maintain collaborations, licensing, or other arrangements;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the timing and amount of any milestone, royalty, or other payments payable by us or due to us under any collaboration, licensing, or other similar agreement.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

Our success is dependent on our ability to attract and retain highly qualified management and other clinical and scientific personnel.

Our success depends in part on our continued ability to attract, recruit, retain, manage, and motivate highly qualified management, clinical, and scientific personnel, and we face significant competition for experienced personnel. We are highly dependent upon our senior management, as well as our senior scientists and other members of our management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, initiation or completion of our clinical trials and preclinical studies, regulatory approvals, or the commercialization of our ecDTx. Although we have executed employment agreements or offer letters with each member of our senior management team, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected. For example, the employment of our former Chief Financial Officer, Chief Medical Officer, and Chief Business Officer with us terminated in October 2024, December 2024, and January 2025, respectively. We do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

In addition, employment candidates and existing employees often consider the value of the stock awards they receive in connection with their employment. If the perceived benefits of our stock awards decline, either due to the trading price of our stock or for other reasons, it may harm our ability to recruit and retain highly skilled employees. Our ability to retain highly skilled employees may be negatively impacted by any significant appreciation or depreciation in our stock price relative to the exercise price of outstanding stock options.

We will need to expand and effectively manage our managerial, operational, financial, and other resources in order to successfully pursue our clinical development and commercialization efforts. We may not be successful in maintaining our unique company culture and continuing to attract or retain qualified management, clinical, and scientific personnel in the future due to the intense competition for qualified personnel among biopharmaceutical, biotechnology, and other businesses. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, integrate, retain, and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital, and our ability to implement our business strategy.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As of March 21, 2025, we had 64 full-time employees. As we continue development and pursue the potential commercialization of our ecDTx, we will need to expand our financial, development, regulatory, manufacturing, information technology, marketing, and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers, and other third parties, and we may not be successful in doing so. Our future financial performance and our ability to develop and commercialize our ecDTx and to compete effectively will depend, in part, on our ability to manage any future growth effectively.

We are subject to various U.S. federal, state, and foreign healthcare laws and regulations, which could increase compliance costs, and our failure to comply with these laws and regulations could harm our reputation, subject us to significant fines and liability, or otherwise adversely affect our business.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers expose us to broadly applicable foreign, federal, and state fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell, and distribute any products for which we obtain regulatory approval. Such laws include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving, or providing any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, in return for, either the referral of an individual or the purchase, lease, or order, or arranging for or recommending the purchase, lease, or order of any good, facility, item, 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 does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;
- the federal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making or causing to be made a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items, or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare & Medicaid Services (CMS), information related to payments and other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants, and certified nurse-midwives), and teaching hospitals and other healthcare providers, as well as ownership and investment interests held by such healthcare professionals and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-

party payors, including private insurers; some state laws require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; some state laws that require biopharmaceutical companies to report information on the pricing of certain drug products; and some state and local laws that require the registration or pharmaceutical sales representatives.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare and privacy laws and regulations will involve ongoing substantial costs. It is possible that governmental authorities will conclude that our business practices, including certain consulting agreements and advisory board agreements we have entered into with physicians who are paid, in part, in the form of stock or stock options, may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Due to the breadth of these laws, the narrowness of statutory exceptions and regulatory safe harbors available, and the range of interpretations to which they are subject, it is possible that some of our current or future practices might be challenged under one or more of these laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including civil, criminal, and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government-funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. Defending against any such actions can be costly and time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business are found not to be in compliance with applicable laws or regulations, they may be subject to significant criminal, civil, or administrative sanctions, including exclusions from government-funded healthcare programs.

Current and future healthcare reform legislation or regulation may increase the difficulty and cost for us to obtain coverage for and commercialize our ecDTx and may adversely affect the prices we may set.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures, that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any ecDTx for which we obtain regulatory approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare.

For example, in March 2010, the Affordable Care Act (ACA) was enacted in the United States and substantially changed the way healthcare is financed by both the government and private insurers. The ACA contains provisions that may reduce the profitability of drug products. Among other things, the ACA established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; extended manufacturers' Medicaid rebate liability to covered outpatient drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; expanded eligibility criteria for Medicaid programs; expanded the entities eligible for discounts under the 340B drug pricing program; and increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program. Since its enactment, there have been executive, judicial, and Congressional challenges to certain aspects of the ACA. In June 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in force in its current form.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. Enacted in August 2011, the Budget Control Act of 2011 includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2032, unless additional Congressional action is taken. Enacted in January 2013, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to providers from three to five years. Further, enacted in March 2021, the American Rescue Plan Act of 2021 eliminated the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100% of a drug's average manufacturer price.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries, presidential executive orders and proposed and enacted federal and state legislation and regulations designed to, among other things, reduce the cost of prescription drugs under Medicare, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. Most significantly, in August 2022, the Inflation Reduction Act of 2022 (IRA) was enacted. This statute marks the most significant action by Congress with

respect to the pharmaceutical industry since adoption of the ACA in 2010. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare, with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); redesigns the Medicare Part D benefit (beginning in 2024); and replaces the Part D coverage gap discount program with a new manufacturer discounting program (which began in 2025). CMS has published the negotiated prices for the initial ten drugs, which will first be effective in 2026, and has published the list of the subsequent 15 drugs that will be subject to negotiation. The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented, although the Medicare drug price negotiation program is currently subject to legal challenges. The impact of the IRA on the pharmaceutical industry cannot yet be fully determined but is likely to be significant. Additional drug pricing proposals could appear in future legislation.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure, drug price reporting and other transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some states have enacted legislation creating so-called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain drugs in these states. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition, and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our ecDTx, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition, and prospects.

We expect that these existing laws and other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies, and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our ecDTx, if approved.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit, delay, or cease commercialization of our ecDTx.

We face an inherent risk of product liability as a result of the clinical trials of our ecDTx and will face an even greater risk if we commercialize our ecDTx, if approved. For example, we may be sued if our ecDTx allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing, or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the ecDTx, negligence, strict liability, and a breach of warranties. Claims may be brought against us by clinical trial participants, patients or others using, administering, or selling products that may be approved in the future. Claims could also be asserted under state consumer protection acts.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit, delay, or cease the commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our ecDTx;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of our management's time and our resources;
- substantial monetary awards to trial participants or product recipients;
- product recalls, withdrawals, or labeling, marketing, or promotional restrictions;
- significant negative financial impact;
- the inability to commercialize our ecDTx; and
- a decline in our stock price.

We currently hold approximately \$10.0 million in product liability insurance coverage in the aggregate. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our ecDTx. Insurance coverage is increasingly expensive. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our ecDTx. Although we will maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our insurance policies are expensive and protect us from only some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include property, general liability, employee benefits liability, business automobile, workers' compensation, products/clinical trial liability, cyber liability, clinical trials, and directors' and officers', and employment practices insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. No assurance can be given that an insurance carrier will not seek to cancel or deny coverage after a claim has occurred. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

We and our service providers may be subject to a variety of data protection, privacy, and security obligations, including laws, regulations, standards, and contractual provisions, which could increase compliance costs, and our actual or perceived failure to comply with such laws and obligations could subject us to potentially significant liability, fines, or penalties and otherwise harm our business.

We and our service providers maintain a large quantity of sensitive information, including confidential business and patient health information, in connection with our clinical trials, 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 service providers may be affected by or subject to existing, amended, or new 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, thus creating potentially complex compliance issues for us and our service providers, strategic partners, and future customers. The cost of compliance with these laws, regulations, and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state, or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties, and damage to our reputation, any of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the United States, numerous federal and state laws and regulations, including health information privacy laws, data breach notification laws, and consumer protection laws, that govern the collection, use, storage, transfer, disclosure, protection, and other processing of health-related and other personal information could apply to our operations or the operations of our collaborators and third-party providers. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Consequently, depending on the facts and circumstances, we could be subject to significant 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, certain state laws govern the privacy and security of health-related and other personal information, many of which may differ from each other and from HIPAA, thus, complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. By way of example, the California Consumer Privacy Act, as amended by the California Privacy Rights Act (collectively, the CCPA), requires covered businesses that process the personal information of California residents to, among other things: (i) provide certain disclosures to California residents regarding the business's collection, use, and disclosure of their personal information; (ii) receive and respond to requests from California residents to access, delete, and correct their personal information, or to opt out of certain disclosures of their personal information; and (iii) enter into specific contractual provisions with service providers that process California resident personal information on the business's behalf. Additional compliance investment and potential business process changes may be required. Similar laws have been passed in other states and are continuing to be proposed at the state and federal level, reflecting a trend toward more stringent privacy

legislation in the United States. In the event that we are subject to or affected by HIPAA, the CCPA, or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In addition to the state comprehensive data privacy laws, recent years have brought substantial changes to the federal and state treatment of non-HIPAA consumer health information. The Federal Trade Commission (FTC) and many state Attorneys General continue to enforce federal and state consumer protection laws against companies for online collection, use, dissemination, and security practices that appear to be unfair or deceptive. The FTC brought three enforcement actions in 2023 against a range of companies that handle electronic health information relating to collection and disclosure of non-HIPAA covered consumer health information under Section 5 of the FTC Act, two of which included allegations made under the FTC's Health Breach Notification Rule (HBNR). The FTC's focus on health information continued in 2024 with changes to the HBNR that clarified its scope and emphasized applicability to non-HIPAA health care providers as well as three additional enforcement actions against companies for their use of health information for advertising purposes. At the state level, Washington and Nevada have adopted significant new legislation addressing businesses treatment of consumer health information, and Connecticut added more stringent protections for health information to its existing comprehensive state privacy law. In both Washington's law provides a separate private right of action for violations.

There are also privacy laws in other countries that may impact our operations, now or in the future. For example, in Europe, the General Data Protection Regulation (GDPR) went into effect in May 2018, and imposes stringent requirements regarding the collection, use, disclosure, storage, transfer, or other processing of personal data of individuals within the European Economic Area (EEA). Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to ϵ 20 million or 4% of the annual global revenue of the noncompliant company, whichever is greater. The GDPR also confers a private right of action in some circumstances 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 to fines, a breach of the GDPR may result in regulatory investigations, reputational damage, orders to cease or change our data processing activities, enforcement notices, assessment notices (for a compulsory audit), and/or civil claims (including class actions).

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 EEA and the United States remains uncertain. Case law from the Court of Justice of the European Union (CJEU) states that reliance on the standard contractual clauses—a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis. On July 10, 2023, the European Commission adopted its Adequacy Decision in relation to the new EU-US Data Privacy Framework (DPF), rendering the DPF effective as a GDPR transfer mechanism to U.S. entities self-certified under the DPF. We expect the existing legal complexity and uncertainty regarding international personal data transfers to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result, we may have to make certain operational changes and we will have to implement revised standard contractual clauses and other relevant documentation for existing data transfers within required time frames.

Further, following the withdrawal of the United Kingdom from the European Union and the end of the transition period, from January 1, 2021, companies could also be subject to the United Kingdom General Data Protection Regulation and Data Protection Act 2018 (collectively, the UK GDPR). The UK GDPR mirrors the fines under the GDPR and has the ability to fine up to the greater of \notin 20 million/£17 million or 4% of global turnover. On October 12, 2023, the UK Extension to the DPF came into effect (as approved by the UK Government), as a data transfer mechanism from the UK to U.S. entities self-certified under the DPF. As we expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

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, store, use, transfer, disclose, and otherwise process data, update our data privacy and security policies and procedures, or in some cases, impact our ability to operate in certain jurisdictions. Failure or perceived failure by us or our collaborators and our service providers 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, and/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 such 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, could result in adverse publicity, and adversely affect our business, financial condition, results of operations, and prospects.

Our information technology systems, or those of any of our service providers, may fail or suffer security incidents and other disruptions, which could result in a material disruption of our ecDTx development programs, compromise sensitive information related to our business, or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.

In the ordinary course of business, we collect, store, and transmit confidential information including but not limited to intellectual property, clinical trial data, proprietary and confidential business information, and personal information of our employees and contractors (collectively, Confidential Information). Our information technology systems and those of our third-party service providers, strategic partners, and other contractors or consultants are vulnerable to attack, damage, and interruption from computer viruses and malware (e.g. ransomware), malicious code, misconfigurations, "bugs" or other vulnerabilities, natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, and sophisticated nation-state and nation-state-supported actors. In addition, attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication, and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security incidents that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. There can also be no assurance that our and our third-party service providers', strategic partners', contractors', or consultants' cybersecurity risk management program and processes, including policies, controls, or procedures, will be fully implemented, complied with or effective in protecting our systems. networks, and Confidential Information.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. If any such event, whether actual or perceived, were to occur, it could impact our reputation and/or operations, cause us to incur significant costs, including legal expenses, harm customer confidence, hurt our expansion into new markets, cause us to incur remediation costs, or cause us to lose existing customers. For example, the loss of clinical trial data from clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. We also rely on a third party to manufacture our ecDTx, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any actual or perceived disruption or security incident affects our systems (or those of our third-party collaborators, service providers, contractors or consultants) or were to result in a loss of or accidental, unlawful, or unauthorized access to, use of, release of, or other processing of Confidential Information, we could incur liability, the further development and commercialization of our ecDTx could be delayed, and we could be subject to significant fines, penalties or liabilities for any noncompliance to certain privacy and security laws.

We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our Confidential Information. If our third-party vendors fail to protect their information technology systems and our Confidential Information, we may be vulnerable to disruptions in service and unauthorized access to our Confidential Information and we could incur liability and reputational damage. If the information technology systems of our third-party vendors and other contractors and consultants become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring. Some of the federal, state, and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular categories of personally identifiable information, which could result from incidents experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Any adverse impact to the availability, integrity, or confidentiality of our or third-party systems or Confidential Information can result in legal claims or proceedings (such as class actions), regulatory investigations and enforcement actions, fines, and penalties. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. Although we currently hold cybersecurity insurance, the costs related to significant security breaches or disruptions could be material and cause us to incur significant expenses.

Our business is subject to risks arising from pandemic and epidemic diseases.

The COVID-19 worldwide pandemic presented substantial public health and economic challenges and affected our employees, patients, physicians and other healthcare providers, communities, and business operations, as well as the U.S. and global economies and financial markets. Any future pandemic or epidemic disease outbreaks could disrupt the supply chain and the manufacture or shipment of drug substances and finished drug products for our ecDTx for use in our clinical trials and research and preclinical studies and, delay,
limit or prevent our employees and CROs from continuing research and development activities, impede our clinical trial initiation and recruitment and the ability of patients to continue in clinical trials, alter the results of the clinical trial based on participants contracting the disease or otherwise increasing the number of observed adverse events, impede testing, monitoring, data collection and analysis and other related activities, any of which could delay our preclinical studies and clinical trials and increase our development costs, and have a material adverse effect on our business, financial condition, and results of operations. Any future pandemic or epidemic disease outbreak could also potentially further affect the business of the FDA, EMA, or other regulatory authorities, which could result in delays in meetings related to our planned clinical trials, as well have an adverse impact on global economic conditions, which could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed.

Our business could be affected by litigation, government investigations, and enforcement actions.

We currently operate in a number of jurisdictions in a highly regulated industry, and we could be subject to litigation, government investigation, and enforcement actions on a variety of matters in the United States or foreign jurisdictions, including, without limitation, intellectual property, regulatory, product liability, environmental, whistleblower, false claims, privacy, anti-kickback, anti-bribery, securities, commercial, employment, and other claims and legal proceedings that may arise from conducting our business. Any determination that our operations or activities are not in compliance with existing laws or regulations could result in the imposition of fines, civil and criminal penalties, equitable remedies, including disgorgement, injunctive relief, and/or other sanctions against us, and remediation of any such findings could have an adverse effect on our business operations.

Legal proceedings, government investigations, and enforcement actions can be expensive and time-consuming. An adverse outcome resulting from any such proceedings, investigations or enforcement actions could result in significant damages awards, fines, penalties, exclusion from the federal healthcare programs, healthcare debarment, injunctive relief, product recalls, reputational damage, and modifications of our business practices, which could have a material adverse effect on our business and results of operations. Even if such a proceeding, investigation, or enforcement action is ultimately decided in our favor, the investigation and defense thereof could require substantial financial and management resources.

Our employees and independent contractors, including principal investigators, CROs, consultants, and vendors, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees and independent contractors, including principal investigators, CROs, consultants, and vendors may engage in misconduct 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: (i) the laws and regulations of the FDA and other similar regulatory requirements, including those laws that require the reporting of true, complete, and accurate information to such authorities, (ii) manufacturing standards, including cGMP requirements, (iii) federal and state data privacy, security, fraud, and abuse and other healthcare laws and regulations in the United States and abroad (iv) laws that require the true, complete, and accurate reporting of financial information or data, or (v) laws that prohibit insider trading. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. 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 be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government 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 and financial results, including, without limitation, the imposition of significant civil, criminal, and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may engage in strategic transactions that could impact our liquidity, increase our expenses, and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases, and out-licensing or in-licensing of intellectual property, products, or technologies. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations, and investments. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity, and

results of operations. Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of our management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky, and costly endeavor for which we may never realize the full benefits. Furthermore, we may experience losses related to investments in other companies, including as a result of failure to realize expected benefits or the materialization of unexpected liabilities or risks, which could have a material negative effect on our results of operations and financial condition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition, and prospects.

Our ability to use net operating loss carryforwards and other tax attributes may be limited.

We have incurred substantial losses during our history, do not expect to become profitable in the near future, and may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any (subject to limitations), until such unused losses expire (if at all). As of December 31, 2024, we had net operating loss (NOL) carryforwards of approximately \$91.9 million for federal income tax purposes and \$183.3 million for state income tax purposes, which may be available to offset our future taxable income, if any. Our federal NOL carryforwards will not expire but may generally be used to offset only 80% of taxable income, which may require us to pay federal income taxes in future years despite having additional federal NOL carryforwards to utilize. Our state NOL carryforwards begin to expire in various amounts in 2038. Our NOL carryforwards and other tax attributes are subject to review and possible adjustment by the Internal Revenue Service (IRS) and state tax authorities.

In addition, under Section 382 of the U.S. Internal Revenue Code of 1986, as amended (the Code), our federal NOL carryforwards may be or become subject to an annual limitation in the event we have had or have in the future an "ownership change." For these purposes, an "ownership change" generally occurs if one or more stockholders or groups of stockholders who own at least 5% of a company's stock increase their ownership by more than 50 percentage points over their lowest ownership percentage within a rolling three-year period. Similar rules may apply under state tax laws. We have not determined the amount of the cumulative change in our ownership resulting from our IPO or other transactions, or any resulting limitations on our ability to utilize our NOL carryforwards and other tax attributes. However, we believe that our ability to utilize our NOL carryforwards and other tax attributes to offset future taxable income or tax liabilities may be limited as a result of ownership changes, including potential changes in connection with our IPO. If we earn taxable income, such limitations could result in increased future income tax liability to us, and our future cash flows could be adversely affected. We have recorded a full valuation allowance related to our NOL carryforwards and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

Inflation could adversely affect our business and results of operation.

While inflation in the United States has been relatively low in recent years, the economy in the United States encountered a material level of inflation since 2021. Although inflation eased somewhat in 2024, it has raised our costs for commodities, labor, materials, and services and other costs required to grow and operate our business, and failure to secure these on reasonable terms may adversely impact our financial condition. Additionally, increases in inflation, along with public health concerns, geopolitical developments, and global supply chain disruptions, have caused, and may in the future cause, global economic uncertainty, and uncertainty about the interest rate environment, which may make it more difficult, costly, or dilutive for us to secure additional financing. A failure to adequately respond to these risks could have a material adverse impact on our financial condition and results of operations.

Risks Related to Our Intellectual Property

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

We rely upon a combination of patent, trade secret, and trademark protection for our ecDTx, our ecDNA diagnostic, and proprietary technologies to prevent third parties from exploiting our achievements, thus eroding our competitive position in our market. These legal measures afford only limited protection, and competitors or others may gain access to or use our intellectual property and proprietary information. Our success depends in large part on our ability to obtain, maintain, expand, enforce, and defend the scope of our intellectual property protection in the United States and other countries with respect to our ecDTx, our ecDNA diagnostic, and other proprietary technologies we may develop. We generally seek to protect our proprietary position, in part, by filing patent applications in the United States and abroad relating to our ecDTx and diagnostics, manufacturing processes, and methods of use. We may also seek to protect our proprietary position by acquiring or in-licensing relevant issued patents or pending patent applications from third parties. If

we are unable to obtain, maintain, expand, enforce, and defend the scope of our intellectual property protection, our business, financial condition, results of operations, and prospects could be materially harmed.

Changes in either the patent laws or their interpretation in the United States and other jurisdictions may diminish our ability to protect our intellectual property, obtain, maintain, expand, enforce, and defend our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our protection. We cannot predict whether the patent applications we currently or may in the future pursue or may in-license will issue as patents in any particular jurisdiction, whether the claims of any issued patents will provide sufficient protection against competitors or other third parties, or if these patents are challenged by our competitors, whether the patents will be found to be invalid, unenforceable, or not infringed.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, defend, or license all necessary or desirable patent applications or patents at a reasonable cost or in a timely manner or in all jurisdictions. Additionally, recent reforms and changes at government agencies of the United States and those of non-U.S. jurisdictions could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications, and the maintenance, enforcement, or defense of our issued patents. For example, the ability of the USPTO and other applicable patent authorities to properly administer their functions is highly dependent on the levels of funding available to the agency and their ability to retain key personnel and fill key leadership appointments, among various factors. Termination of employees or delays in replacing or hiring for key positions could significantly impact the ability of the USPTO and other applicable patent authorities to fulfill their functions and could greatly impact our ability to timely and adequately prosecute or maintain our patent applications, and our ability to timely and adequately maintain, enforce, or defend our issued patents. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, third-party collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Consequently, we may not be able to prevent any third party from using any of our technology that is in the public domain to compete with our ecDTx or technologies. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable in light of the prior art. Furthermore, 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 in some cases not at all. Therefore, we cannot be certain that we were the first to invent the inventions claimed in any of our owned patents or pending patent applications, or that we or any future licensors were the first to file for patent protection of such inventions. If a third party can establish that we were not the first to make or the first to file for patent protection of such inventions, our patents and patent applications may not issue as patents and even if issued, may be challenged and invalidated or rendered unenforceable.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our current and future patent applications may not result in patents being issued.

Any issued patents may not afford sufficient protection of our ecDTx or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive technologies or products. Further, even if these patents are granted, they may be difficult to enforce. Obtaining and maintaining our 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 if we fail to comply with these requirements. In the event we experience noncompliance events that cannot be corrected and we lose our patent rights, competitors could enter the market, which would have a material adverse effect on our business. Further, any issued patents that we own or may license in the future covering our ecDTx could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the United States or other countries, including the U.S. Patent and Trademark Office (USPTO). Also, patent terms, including any extensions or adjustments that may or may not be available to us, may be inadequate to protect our competitive position on our ecDTx for an adequate amount of time, and we may be subject to claims challenging the inventorship, validity, or enforceability of our patents and/or other intellectual property. Changes in United States patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our ecDTx. Further, if we encounter delays in our development and testing of our ecDTx, clinical trials, or regulatory review and approval of our ecDTx, the period of time during which we could market our ecDTx under patent protection may be reduced (i.e., patents protecting the ecDTx might expire before or shortly after such ecDTx are commercialized). Thus, our patents may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or afford us any meaningful competitive advantage.

Moreover, the claim coverage in a patent application can be significantly reduced before the corresponding patent is granted. Even if patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents issuing

from our owned and any future in-licensed patent applications may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether our ecDTx and other proprietary technology will be protectable or remain protected by valid and enforceable patents. Even if a patent is granted, our competitors or other third parties may be able to circumvent the patent by developing similar or alternative technologies or products in a non-infringing manner, which could materially adversely affect our business, financial condition, results of operations, and prospects. Furthermore, our competitors or other third parties may avail themselves of safe harbors under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments) to conduct research and clinical trials.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patent rights may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third-party post-issuance submission of prior art to the USPTO challenging the validity of one or more claims of our patents or patents we may license in the future. Third-party submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on our pending patent application or patent application we may license in the future. A third party may also claim that our patent rights are invalid or unenforceable in a litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In addition, we may become involved in opposition, derivation, revocation, reexamination, reissue, post-grant, proceedings, inter partes review, interference proceedings, or other similar proceedings in the United States and/or foreign jurisdictions challenging our patent rights. An adverse determination in any such submission, proceeding, or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, and may allow third parties, including generic drug companies, to commercialize our ecDTx and other proprietary technologies we may develop and compete directly with us.

Moreover, some of our patent rights may in the future be co-owned with third parties. In the United States, each co-owner has the freedom to license and exploit the technology. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patent rights, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of such patent rights in order to enforce such patent rights against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, maintaining, enforcing, and defending patents on our ecDTx in all countries throughout the world is expensive, and the laws of foreign countries may not protect our intellectual property rights to the same extent as the laws of the United States. Prosecution of foreign patent applications is often a longer process and patents may grant at a later date, and with a shorter term, than in the United States. The requirements for patentability differ in certain jurisdictions and countries. Additionally, the patent laws of some countries do not afford intellectual property protection to the same extent as the laws of the United States. For example, other countries may impose substantial restrictions on the scope of claims, limiting patent protection to specifically disclosed embodiments. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our intellectual property in and into the United States or other jurisdictions. Competitors may use our intellectual property in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or patents we may license in the future or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, some jurisdictions, such as Europe, Japan, and China, may have a higher standard for patentability than in the United States, including, for example, the requirement of claims having literal support in the original patent filing and the limitation on using supporting data that is not in the original patent filing. Under those heightened patentability requirements, we may not be able to obtain sufficient patent protection in certain jurisdictions even though the same or similar patent protection can be secured in the United States and other jurisdictions.

Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents and any patents we may license in the future at risk of being invalidated or interpreted narrowly, could put our patent applications and any patent applications we may license in the future at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop.

Many countries have compulsory licensing laws under which a patent owner may be compelled to 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 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. In addition, geopolitical actions in the United States and in foreign countries (such as the geopolitical conflicts in and around Ukraine and Israel) could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any future licensors and the maintenance, enforcement, or defense of our issued patents, which could impair our competitive intellectual property position. For example, government actions may prevent filing, prosecution, and maintenance of issued patents in various jurisdictions experiencing geopolitical conflict. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in such jurisdictions. In addition, jurisdictions outside of the U.S. could also permit our patents to be exploited without consent or compensation. In such circumstances we would not be able to prevent third parties from practicing our inventions or form selling or impaired, and our business, and our business in and into such jurisdictions. Accordingly, our competitive position may be impaired, and our business, and our business of operations and prospects may be adversely affected.

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

The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. In some circumstances, we may be dependent on any future licensors to take the necessary action to comply with these requirements with respect to any licensed intellectual property. For example, periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our patents and applications. In certain circumstances, we may rely on licensing partners to pay these fees due to the U.S. and non-U.S. patent agencies. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

The USPTO and various non-U.S. government agencies require compliance with certain foreign filing requirements during the patent application process. For example, in some countries, including the United States, China, India, and some European countries, a foreign filing license is required before certain patent applications are filed. The foreign filing license requirements vary by country and depend on various factors, including where the inventive activity occurred, citizenship status of the inventors, the residency of the inventors and the invention owner, the place of business for the invention owner, and the nature of the subject matter to be disclosed (e.g., items related to national security or national defense). In some cases, a foreign filing license may be obtained retroactively in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment of a pending patent application or can be grounds for revoking or invalidating an issued patent, resulting in the loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the relevant markets with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. We would also be dependent on any future licensors to take the necessary actions to comply with these requirements with respect to any intellectual property we may license in the future.

Public health pandemics (such as the COVID-19 pandemic), geopolitical instability (war and terrorism), natural disasters, or similar events may impair our and our licensors' ability to comply with these procedural, document submission, fee payment, and other requirements imposed by government patent agencies, which may materially and adversely affect our ability to obtain or maintain patent protection for our products and ecDTx.

Changes in patent laws or their interpretations could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the United States or in other countries could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act (the America Invents Act) enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first to invent the claimed invention.

A third party that files a patent application in the USPTO after March 2013, but before us or our licensors could therefore be awarded a patent covering an invention of ours or our licensors even if we or our licensors had made the invention before it was made by such third party. This requires us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors are the first to either (i) file any patent application related to our ecDTx and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our patents or patent applications.

The America Invents Act also included a number of significant changes that affect the way patent applications are prosecuted and also affect patent litigation. These include allowing third party protests and submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO-administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims or any patent claims we may license in the future that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. We cannot predict how decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patent rights. For example, the U.S. Supreme Court held in *Amgen v. Sanofi (2023)* that a functionally claimed genus was invalid for failing to comply with the enablement requirement of the Patent Act. As such, our patent rights with functional claims may be vulnerable to third party challenges seeking to invalidate these claims for lacking enablement or adequate support in the specification. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have or may obtain or license in the future.

In 2012, the European Union Patent Package (EU Patent Package) regulations were passed with the goal of providing a single pan-European Unitary Patent and a new European Unified Patent Court (UPC) for litigation involving European patents. The EU Patent Package was implemented on June 1, 2023. As a result, all European patents, including those issued prior to ratification of the EU Patent Package, now by default automatically fall under the jurisdiction of the UPC, unless otherwise opted out. It is uncertain how the UPC will impact granted European patents in the biotechnology and pharmaceutical industries. Our European patent applications, if issued, could be challenged in the UPC. During the first seven years of the UPC's existence, the UPC legislation allows a patent owner to opt its European patents out of the jurisdiction of the UPC. Moreover, if we do not meet all of the formalities and requirements for opt-out under the UPC, our future European patents could remain under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patent, and allow for the possibility of a competitor to obtain pan-European injunction. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and ecDTx dues to increased competition and, resultantly, on our business, financial condition, results of operations, and prospects. The UPC and Unitary Patent are significant changes in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation in the UPC.

Issued patents covering our ecDTx could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

Our patent rights may be subject to priority, validity, inventorship, ownership, and enforceability disputes. Legal proceedings relating to intellectual property claims, with or without merit, are unpredictable and generally expensive and time-consuming and likely to divert significant resources from our core business, including distracting our management and scientific personnel from their normal responsibilities and generally harm our business. If we or any future licensors are unsuccessful in any of these proceedings, such patents and patent applications may be narrowed, invalidated, or held unenforceable. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If we initiate legal proceedings against a third party to enforce a patent covering our ecDTx, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement, lack of sufficient written description, failure to claim patenteligible subject matter, or obviousness-type double patenting. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading or inconsistent statement, during prosecution. Third parties may raise claims challenging the validity or enforceability of a patent before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patent rights or any patent rights we may obtain or license in the future in such a way that they no longer cover our ecDTx or prevent third parties from competing with our ecDTx. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection for our ecDTx. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

Patent terms may be inadequate to protect the competitive position of our ecDTx for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, 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, but the life of a patent, and the protection it affords, is limited. Even if patents covering our ecDTx are obtained, once the patent has expired, we may be vulnerable to competition from competitive products, including generics. Given the amount of time required for the development, testing, and regulatory review of new ecDTx, patents protecting such ecDTx might expire before or shortly after such ecDTx are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. If we do not have sufficient patent life to protect our products, our business, financial condition, results of operations, and prospects will be adversely affected.

If we do not obtain patent term extension and equivalent extensions outside of the United States for our ecDTx, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA regulatory approval of any of our ecDTx, one or more of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension 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. Similar patent term restoration provisions to compensate for commercialization delay caused by regulatory review are also available in certain foreign jurisdictions, such as in Europe under Supplemental Protection Certificate. However, we may not be granted an extension for various reasons, including 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 failing to satisfy other applicable requirements. Additionally, administrative changes at the USPTO or other applicable patent authorities, such as reduced hiring and/or funding, may result in delays in issuance of a patent or in accrual of patent term extension, thereby reducing the amount of patent term extension that could otherwise be received. Administrative changes (e.g., at the FDA or USPTO) may also lead to delays in review and analysis of requests for patent term extension, which could result in a patent term extension not being timely granted (e.g., before the expiration of the patent). Moreover, the applicable time period or the scope of patent protection afforded could be less than we project or request. In addition, to the extent we wish to pursue patent term extension based on a patent that we may license from a third party in the future, we may need the cooperation of that third party. If we are unable to obtain patent term extension, or the foreign equivalent, or if the term of any such extension is less than we project or request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed).

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, consultants, collaborators, or other third parties have an interest in our patent rights, trade secrets, or other intellectual property as an inventor, co-inventor, or owner of trade secrets. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our ecDTx and other proprietary technologies we may develop. Litigation may be necessary to defend against these and other claims challenging inventorship or our patent rights, trade secrets, or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or the right to use intellectual property that is important to our ecDTx and other proprietary technologies we may develop. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our 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 are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for our ecDTx and proprietary technologies, we may rely on trade secret protection and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, third-party collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Trade secrets and know-how can be difficult to protect. We cannot guarantee that we have entered into applicable agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. 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. We cannot guarantee that any potential trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to trade secrets. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. 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 from using that technology or information to compete with us. Furthermore, others may independently discover similar trade secrets and proprietary information. If any of our trade secrets were to be disclosed or misappropriated or if any such information were to be independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

We may be subject to claims that third parties have an ownership interest in our trade secrets. For example, we may have disputes arise from conflicting obligations of our employees, consultants, or others who are involved in developing our ecDTx. Litigation may be necessary to defend against these and other claims challenging ownership of our trade secrets. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable trade secret rights, such as exclusive ownership of, or right to use, trade secrets that are important to our ecDTx and other proprietary technologies we may develop. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management and other employees. Any of the foregoing could have a material adverse effect on our business, and prospects.

We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Some of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope, or expiration of a third-party patent, which might adversely affect our ability to develop and market our products and ecDTx.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims, or the expiration of relevant patents, are or will be complete or thorough, nor can we be certain that we have identified or will identify each and every third-party patent and pending patent application in the United States and abroad that is relevant to or necessary for the commercialization of our current and future ecDTx in any jurisdiction. Patent applications in the United States and elsewhere are not published until approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our ecDTx could have been filed by others without our knowledge. The scope of a patent claim is determined by the interpretation of the law, the words of a patent claim, the written disclosure in a patent, and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending patent application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products or ecDTx are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, and we may incorrectly conclude that a third-party patent is invalid and unenforceable or not infringed. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our ecDTx. If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. Also, because the claims of published patent applications can change between publication and patent grant, there may be published patent applications that may ultimately issue with claims that we infringe. As the number of competitors in the market grows and the number of patents issued in this area increases, the possibility of patent infringement claims escalates. Moreover, in recent years, individuals and groups that are non-practicing entities, commonly referred to as "patent trolls," have purchased patents and other intellectual property assets for the purpose of making claims of infringement in order to extract settlements. From time to time, we may receive threatening letters, notices or "invitations to license," or may be the subject of claims that our products and business operations infringe or violate the intellectual property rights of others. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our ecDTx that are held to be infringing. We might, if possible, also be forced to redesign ecDTx or services so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Third-party claims of intellectual property infringement, misappropriation, or other violations against us or our collaborators could be expensive and time consuming and may prevent or delay the development and commercialization of our ecDTx.

Our commercial success depends in part on our ability to avoid infringing, misappropriating, and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions.

Numerous U.S. and foreign-issued patents and pending patent applications owned by third parties exist in the fields in which we plan to commercialize our therapeutic and diagnostic programs and in which we are developing other proprietary technologies. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our ecDTx and diagnostic programs and commercializing activities may give rise to claims of infringement of the patent rights of others. We cannot assure that our ecDTx and diagnostic programs and other proprietary technologies we develop will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued for which a third party, such as a competitor in the fields in which we are developing our ecDTx and diagnostic programs, might assert as infringed by us. It is also possible that patents owned by third parties of which we are aware, but which we do not believe we infringe or that we believe we have valid defenses to any claims of patent infringement, could be found to be infringed by us. It is not unusual that corresponding patents issued in different countries have different scopes of coverage, such that in one country a third-party patent does not pose a material risk, but in another country, the corresponding third-party patent may pose a material risk to our ecDTx. As such, we monitor third-party patents in the relevant pharmaceutical markets. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that we may infringe. For example, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover ecDTx or the use of our ecDTx. We are aware of certain patent applications in the United States and elsewhere that contain claims that, if issued in their present form, may cover one of our ecDTx. While we believe we would have valid defenses

to claims of patent infringement, we cannot be certain that we would prevail in any dispute, and we cannot be certain how an adverse determination would affect our business.

In the event that any third-party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable, and infringed by us. Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing the infringing products or technologies. In addition, we may be required to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties, and/or redesign our infringing products or technologies, which may be impossible or require substantial time and monetary expenditure. Such licenses may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms or at all, we may be unable to commercialize the infringing products or technologies or such license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain

Even if resolved in our favor, the foregoing proceedings could be very expensive, particularly for a company of our size, and timeconsuming. Such proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such proceedings adequately. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Such proceedings may also absorb significant time of our technical and management personnel and distract them from their normal responsibilities. Uncertainties resulting from such proceedings could impair our ability to compete in the marketplace. 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. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, or results of operations.

We may in the future pursue invalidity proceedings with respect to third-party patents. The outcome following legal assertions of invalidity is unpredictable. Additionally, we may be subject to claims of patent infringement during those proceedings, and delays caused by the federal agencies may increase the time period that we are subject to such claims. For example, administrative changes, including reduced staff and budgets experienced by the Patent and Trial Appeal Board, could further delay our ability to timely challenge any such patents. Even if resolved in our favor, these legal proceedings may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. 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 proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such proceedings adequately. Some of these third parties may be able to sustain the costs of such proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent proceedings could compromise our ability to compete in the marketplace. If we do not prevail in the patent proceedings the third parties may assert a claim of patent infringement directed at our ecDTx.

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

Third parties, such as a competitor, may infringe our patent rights. In an infringement proceeding, a court may decide that a patent we own or a patent we may license in the future is invalid or unenforceable or may refuse to stop the other party from using the invention at issue. In addition, our patent rights may become involved in inventorship, ownership, priority, enforceability, or validity disputes. To counter or defend against such claims can be expensive and time-consuming. An adverse result in any litigation proceeding could put our patent rights at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation and proceedings, there is a risk that some of our confidential information could be compromised by disclosure during such litigation and proceedings.

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. 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. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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, diluted, circumvented, or declared generic or determined to be infringing, misappropriating, or violating other marks. 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 the markets of interest. 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 the event that our trademarks are successfully challenged or determined to be infringing, misappropriating, or violating other marks, we could be forced to rebrand our products, which could result in loss of brand recognition, and could require us to devote resources to advertising and marketing new brands. 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 may propose to use with our ecDTx 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, misappropriate, or otherwise violate 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 obtain, protect, or enforce 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, dilution, 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 obtain, 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.

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 ecDTx or utilize similar technology but that are not covered by the claims of the patents that we own or may license in the future;
- we or our licensors or collaborators might not have been the first to make the inventions covered by our current or future patent applications;
- we or our licensors or collaborators might not have been the first to file patent applications covering our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending and future patent applications that we own or may license will not lead to issued patents;
- any issued patent that we own or license in the future may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- others may have access to the same intellectual property rights licensed to us in the future on a non-exclusive basis;

- our competitors or other third parties might conduct research and development activities in countries where we or our licensors do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- we may fail to identify potential patentable subject matter and/or may fail to file on it;
- the patents or other intellectual property rights of others may harm our business; and
- we may choose not to file for patent protection in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property or disclose information resulting in a loss of protection for such trade secret.

Should any of the foregoing occur, it could adversely affect our business, financial condition, results of operations, and prospects.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

The growth of our business may depend in part on our ability to acquire, in-license, or use third-party intellectual property and proprietary rights. For example, our ecDTx may require specific formulations to work effectively and efficiently, we may develop ecDTx containing our compounds and pre-existing pharmaceutical compounds, or we may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our ecDTx, any of which could require us to obtain rights to use intellectual property held by third parties. In addition, with respect to any patent or other intellectual property rights we may co-own with third parties, we may require licenses to such co-owners' interest to such patents. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. In addition, we may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. Were that to happen, we may need to cease use of the compositions or methods covered by those third-party intellectual property rights and may need to seek to develop alternative approaches that do not infringe, misappropriate, or otherwise violate those intellectual property rights, which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, which means that our competitors may also receive access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Additionally, we may collaborate with academic institutions to accelerate our research and development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Even if we hold such an option, we may be unable to negotiate a license from the institution within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. Even if we are able to obtain a license, it may be non-exclusive, and our competitors may also receive access to the same technologies licensed to us.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies that may be more established or have greater resources than we do may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our ecDTx. More established companies may have a competitive advantage over us due to their size, cash resources, or greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. There can be no assurance that we will be able to successfully complete these types of negotiations and ultimately acquire the rights to the intellectual property surrounding the additional ecDTx that we may seek to develop or market. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of certain programs and our business financial condition, results of operations, and prospects could suffer.

Risks Related to Ownership of Our Common Stock

An active, liquid, and orderly market for our common stock may not be sustained, or we may in the future fail to satisfy the continued listing requirements of Nasdaq.

Prior to our IPO, there was no public market for our common stock. Our common stock began trading on The Nasdaq Global Select Market (Nasdaq) in late March 2024, and we can provide no assurance that an active trading market for our common stock will be sustained. If an active market for our common stock is not sustained, it may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. An inactive market may also impair our ability to raise capital by selling

shares and may impair our ability to acquire other businesses or technologies using our shares as consideration, which, in turn, could materially adversely affect our business.

If we fail to satisfy the continued listing requirements of Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement, or prevent future non-compliance with the listing requirements of Nasdaq.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price is likely to be volatile. The stock market in general and the market for stock of biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their shares of our common stock at or above the price they paid to purchase them. The market price for our common stock may be influenced by those factors discussed in this "Risk Factors" section and many others, including:

- results of our clinical trials and preclinical studies, and the results of trials of our competitors or those of other companies in our market sector;
- our ability to enroll patients in our future clinical trials;
- our ability to obtain and maintain regulatory approval of our ecDTx or additional indications thereof, or limitations to specific label indications or patient populations for their use, or changes or delays in the regulatory review process;
- regulatory or legal developments in the United States and foreign countries;
- changes in the structure of healthcare payment systems;
- the success or failure of our efforts to develop, acquire, or license additional ecDTx;
- innovations, clinical trial results, product approvals and other developments regarding our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, or capital commitments;
- manufacturing, supply, or distribution delays or shortages;
- any changes to our relationship with any manufacturers, suppliers, collaborators, or other strategic partners;
- achievement of expected product sales and profitability;
- variations in our financial results or development timelines or those of companies that are perceived to be similar to us, including variations from expectations of securities analysts or investors;
- market conditions in the biopharmaceutical sector and issuance of securities analysts' reports or recommendations;
- trading volume of our common stock;
- an inability to obtain additional funding;
- sales of our stock by us, our insiders, or our stockholders;
- general economic, industry, geopolitical, and market conditions, such as military conflict or war, inflation and financial institution instability, or pandemic or epidemic disease outbreaks, many of which are beyond our control;
- additions or departures of senior management, directors, or key personnel;
- intellectual property, product liability, or other litigation against us or our inability to enforce our intellectual property;
- changes in our capital structure, such as future issuances of securities and the incurrence of additional debt; and
- changes in accounting standards, policies, guidelines, interpretations, or principles.

In addition, in the past, stockholders have initiated class action lawsuits against biopharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs, divert our management's attention and resources and damage our reputation, which could have a material adverse effect on our business, financial condition and results of operations and prospects.

Our executive officers, directors, and principal stockholders, if they choose to act together, have the ability to significantly influence all matters submitted to stockholders for approval.

As of December 31, 2024, our executive officers, directors and greater than 5% stockholders, in the aggregate, owned approximately 51.4% of our outstanding common stock. As a result, such persons, acting together, have the ability to significantly influence all matters submitted to our stockholders for approval, including the election and removal of directors and approval of any significant transaction. This concentration of ownership may have the effect of delaying, deferring, or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

We do not currently intend to pay dividends on our common stock, so any returns on your investment will be limited to the value of our common stock.

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, any future debt agreements may preclude us from paying dividends. Any return to stockholders will therefore be limited to the appreciation of their stock. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.

As of December 31, 2024, 4,578,055 shares of our outstanding common stock, or 20.5%, were held by our directors, executive officers, and other affiliates. Such shares may be sold under Rule 144 under the Securities Act, subject to volume limitations. Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

The holders of 4,193,340 shares of our outstanding common stock, or approximately 18.8% of our total outstanding common stock as of December 31, 2024, may have registration rights that entitle such holders to require us to register their shares for resale under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders, or the registration of such shares, could also significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

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

We are an emerging growth company, as defined in the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of our IPO, or December 31, 2029. However, if certain events occur prior to the end of such five-year period, including if we become a "large accelerated filer", as defined under the Exchange Act, our annual gross revenue exceeds \$1.235 billion, or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to December 31, 2029. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002 (Sarbanes-Oxley);

- 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, unless the SEC determines the new rules are necessary for protecting the public;
- 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.

We have taken advantage of reduced reporting burdens in this report. In particular, in this report, we have provided only two years of audited financial statements and have not included all of the executive compensation-related information that would be required if we were not an emerging growth company. Investors may find our common stock less attractive because we 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 price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected to avail ourselves of this exemption and, therefore, we may not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. We intend to rely on other exemptions provided by the JOBS Act, including without limitation, not being required to comply with the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley.

We are also a smaller reporting company as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than \$100.0 million during the most recently completed fiscal year, and our voting and non-voting common stock held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquiror or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- that the total number of directors on our board of directors is established by our board of directors, which may delay the ability of stockholders to change the composition of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to fill any vacancy on our board of directors however occurring, which prevents stockholders from being able to fill vacancies on our board of directors, subject to any special rights of the holders of any series of preferred stock;
- no director may be removed from office except for cause and, in addition to any other vote required by law, upon the approval of at least 66-2/3% of the voting power of all of our then outstanding shares of our voting stock entitled to vote at an election of directors, subject to any special rights of the holders of any then outstanding series of preferred stock;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to amend or repeal our amended and restated bylaws without obtaining stockholder approval;
- the required approval of at least 66-2/3% of the then outstanding shares entitled to vote to adopt, amend, or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;

- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- an exclusive forum provision providing that the Court of Chancery of the State of Delaware will be the exclusive forum for certain actions and proceedings;
- that a special meeting of stockholders may be called only by or at the direction of our board of directors, the chair of our board of directors, our chief executive officer, or our president, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law, under which a corporation may not engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders and that the federal district courts are the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act, 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 the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided, that, this provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other 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 federal district courts of the United States are the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. These choice of forum provisions 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 other employees and result in increased costs for investors to bring a claim. By agreeing to this provision, however, stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. If a court were to find the choice of forum provisions in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

General Risk Factors

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.

As a public company, we incur significant legal, accounting, and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly, and current reports with respect to our business and financial condition. In addition, Sarbanes-Oxley, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and certain corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted additional rules and regulations in these areas, such as mandatory "say on pay" voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies substantially increase our legal and financial compliance costs and make some activities more time consuming and costly. The increased costs decrease our net income or increase our net loss, and may require us to reduce expenditures in other areas of our business. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, and we incur substantial costs to maintain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees, or as executive officers. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition, and results of operations.

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. We could face criminal liability and other serious consequences for violations, which could 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, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls and anti-corruption and anti-money laundering laws and regulations, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, 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, CROs, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting, or receiving, 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 if and when we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We 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, CROs, contractors, and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities, and any training or compliance programs or other initiatives we undertake to prevent such activities may not be effective.

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.

Furthermore, U.S. export control laws and economic sanctions prohibit the provision of certain products and services to countries, governments, and persons targeted by U.S. sanctions. U.S. sanctions that have been or may be imposed as a result of military conflicts in other countries may impact our ability to continue activities at future clinical trial sites within regions covered by such sanctions. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges. These export and import controls and economic sanctions could also adversely affect our supply chain.

We and any of our third-party manufacturers or suppliers may use potent chemical agents and hazardous materials, and any claims relating to improper handling, storage, or disposal of these materials could be time-consuming or costly.

We and any of our third-party manufacturers or suppliers and current or potential future collaborators may use biological materials, potent chemical agents, and hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety of the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state, and local laws and regulations govern the use, generation, manufacture, storage, handling, and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, neither we or our third-party manufacturers and suppliers can eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. In the event of contamination or injury at our or our manufacturers' or suppliers' sites, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended. Although we maintain workers' compensation insurance for certain costs and expenses, we may incur due to injuries to our employees resulting from work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with the storage or disposal of biologic, hazardous, or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development, or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations, and prospects.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations and the operations of our suppliers, CROs, CMOs, and clinical sites could be subject to earthquakes, power shortages, telecommunications or infrastructure failures, cybersecurity incidents, physical security breaches, water shortages, floods, hurricanes, typhoons, blizzards and other extreme weather conditions, fires, public health pandemics or epidemics (including, for example, the COVID-19 pandemic), and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers or suppliers to produce our ecDTx and its components and on CROs and clinical sites to conduct our clinical trials, and do not have a redundant source of supply for all components of our ecDTx. Our ability to obtain clinical or, if approved, commercial, supplies of our ecDTx could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption, and our ability to commence, conduct or complete our clinical trials in a timely manner could be similarly adversely affected by any of the foregoing. In addition, our corporate headquarters is located in San Diego, California near major earthquake faults and fire zones, and the ultimate impact on us of being located near major earthquake faults and fire zones and being consolidated in a certain geographical area is unknown. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Unstable market and economic conditions and adverse developments with respect to financial institutions and associated liquidity risk may have serious adverse consequences on our business, financial condition, and stock price.

From time to time, the global credit and financial markets have experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability including changes related to the U.S. and foreign governments in tariffs and trade policies affecting trade between the United States and other countries. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military conflict, including geopolitical conflict in and around Ukraine and Israel, terrorism, or other geopolitical events. Sanctions imposed by the United States and other countries in response to such conflicts, including the one in Ukraine, may also adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability. In addition, in 2023 the closures of financial institutions and their placement into receivership with the FDIC created bank-specific and broader financial institution liquidity risk and concerns. Future adverse developments with respect to specific financial institutions or the broader financial services industry may lead to market-wide liquidity shortages, impair the ability of companies to access near-term working capital needs, and create additional market and economic uncertainty. There can be no assurance that future credit and financial market instability and a deterioration in confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, liquidity shortages, volatile business environment, changes in tariffs and trade policies or continued unpredictable and unstable market conditions. If the equity and credit markets deteriorate, or if adverse developments are experienced by financial institutions, it may cause short-term liquidity risk and also make any necessary debt or equity financing more difficult, more costly, more onerous with respect to financial and operating covenants and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, financial institutions, manufacturers, and other partners may be adversely affected by the foregoing risks, which could directly affect our ability to attain our operating goals on schedule and on budget.

Changes in tax law may materially adversely affect our financial condition, results of operations and cash flows, or adversely impact the value of an investment in our common stock.

New income, sales, use or other tax laws, statutes, rules, regulations, or ordinances could be enacted at any time, or interpreted, changed, modified, or applied adversely to us, any of which could adversely affect our business operations and financial performance.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us, our business, our market, or our competitors. If one or more of the analysts who covers us downgrades our stock, or if we fail to meet the expectations of one or more of these analysts, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting, and the trading price of our common stock may decline.

Pursuant to Section 404 of Sarbanes-Oxley, our management will be required to report upon the effectiveness of our internal control over financial reporting beginning with the annual report for our fiscal year ending December 31, 2025. When we lose our status as an "emerging growth company" and do not qualify as a non-accelerated filer, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for our management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. If we or, if required, our auditors are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins its Section 404 reviews, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to legal proceedings or sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, even if ultimately decided in our favor, it could result in substantial costs and a diversion of our management's attention and resources, which could harm our business.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Risk Management Strategy

We have developed our cybersecurity risk management program, including a cybersecurity incident response plan, based on the National Institute of Standards and Technology Cybersecurity Framework's (NIST CSF) principles: Identify, Protect, Detect, Respond, and Recover. This does not, however, imply that we meet any particular technical standards, specifications, or requirements, only that we use the NIST CSF as a guide to help us identify, assess, and manage cybersecurity risks relevant to our business.

Our cybersecurity risk management program, which is integrated into our overall enterprise risk management program, and shares common methodologies, reporting channels and governance processes that apply across the enterprise risk management program to other legal, compliance, strategic, operational, and financial risk areas, is intended to address current vulnerabilities and anticipate future cybersecurity threats and risks to our cyber ecosystem. Our cybersecurity risk management program includes: (a) assessments designed to help identify material cybersecurity risks to our critical systems, information, products, services, and our broader enterprise IT environment; (b) a security team principally responsible for managing our cybersecurity risk assessment processes, our security controls, and our response to cybersecurity incidents; (c) the use of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security controls; (d) cybersecurity awareness training of our employees, including our senior management, and incident response personnel; (e) a cybersecurity incident response process that includes procedures for responding to cybersecurity incidents; and (f) a risk evaluation of the service providers, suppliers, and vendors of critical systems during contracting.

As of the filing date of this report, we have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected or are reasonably likely to materially affect us, including our operations, business strategy, results of operations, or financial condition. There can be no assurance, however, that our cybersecurity risk management program and processes, including our policies, controls, or procedures, will be fully implemented, complied with or effective in protecting our systems and information. For more information, see the section titled "Risk Factors—Risks Related to Our Business Operations and Industry— Our information technology systems, or those of any of our service providers, may fail or suffer security incidents and other disruptions, which could result in a material disruption of our ecDTx development programs, compromise sensitive information related to our business, or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business."

Governance

Our board of directors considers cybersecurity risk as part of its risk oversight function and has delegated to our audit committee oversight of cybersecurity and other information technology risks. Our audit committee oversees our management team's implementation of our cybersecurity risk management program, receives periodic reports from our management team on our cybersecurity risks, and receives reports from our management team, as necessary, regarding material cybersecurity incidents, as well as any incidents with lesser impact potential.

Our audit committee reports to our board of directors regarding its activities, including those related to cybersecurity. Our board of directors also receives briefings from our management team on our cyber risk management program.

Our management team is responsible for assessing and managing our material risks from cybersecurity threats, and has primary responsibility for our overall cybersecurity risk management program and supervises both our internal cybersecurity personnel and our retained external cybersecurity consultants. Our management team oversees efforts to prevent, detect, mitigate, and remediate cybersecurity risks and incidents through various means, which may include briefings from internal security personnel; threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us; and alerts and reports produced by security tools deployed in the IT environment.

Item 2. Properties.

Our corporate headquarters are currently located in San Diego, California, where we lease approximately 80,168 square feet of laboratory and office space pursuant to a lease that expires in October 2034. We believe our existing facilities are adequate to meet our current business requirements for the near term, and that additional space will be available on commercially reasonable terms, if required.

Item 3. Legal Proceedings.

There currently is no material pending legal proceeding to which we are a party or to which any of our property is subject. From time to time, we may become involved in legal proceedings or subject to claims incident to the ordinary course of business. Regardless of outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources, negative publicity, reputational harm, and other factors and there can be no assurances that favorable outcomes will be obtained.

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 began trading under the symbol "BOLD" on the Nasdaq Global Select Market on March 28, 2024.

Holders of Our Common Stock

As of March 21, 2025, there were approximately 70 holders of record of our common stock. This number was derived from our shareholder records and does not include beneficial owners of our common stock whose shares are held in the name of various dealers, clearing agencies, banks, brokers, and other fiduciaries.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We intend to retain all available funds and future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

Unregistered Sales of Equity Securities

During 2024, we granted stock options under our 2018 Equity Incentive Plan, as amended (Predecessor Plan), to purchase up to an aggregate of 840,292 shares of our common stock at an exercise price of \$8.19 per share to certain of our employees and directors in connection with services provided to us by such persons, of which 116,243 of these shares had been cancelled as of December 31 2024. During 2024, 15,104 shares of our common stock were issued upon the exercise of options granted under our Predecessor Plan at a weighted-average exercise price of \$3.90 per share. The foregoing weighted-average exercise price gives effect to a repricing in June 2023 of then-outstanding stock options to purchase up to an aggregate of 1,019,029 shares of our common stock, following which all such options as of such date were modified to have an exercise price of \$4.10 per share. The foregoing exercise prices do not give effect to a repricing in August 2024 of then-outstanding stock options to purchase shares of our common stock held by eligible employees, following which all such options were modified to have an exercise price of \$3.56 per share, subject to satisfaction by such employees of specified service requirements. See Note 11 to our financial statements included elsewhere in this Annual Report on Form 10-K for information about these option repricings.

The foregoing securities were issued pursuant to written compensatory plans or arrangements with our employees and directors, in reliance on the exemption from the registration requirements of the Securities Act provided by Rule 701 promulgated under the Securities Act or the exemption set forth in Section 4(a)(2) under the Securities Act and Regulation D promulgated thereunder relative to transactions by an issuer not involving any public offering. All recipients either received adequate information about us or had access, through employment or other relationships, to such information. All of the foregoing securities are deemed to be restricted securities for purposes of the Securities Act. All certificates representing the issued shares of capital stock described in this Item 15 included appropriate legends setting forth that the securities had not been registered and the applicable restrictions on transfer.

On March 28, 2024, we filed a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding options and all shares of our common stock otherwise issuable pursuant to our equity compensation plans.

Use of Proceeds from our IPO

On March 27, 2024, our registration statement on Form S-1 (File No. 333-277696), as amended, was declared effective by the SEC for our IPO. At the closing of the IPO on April 2, 2024, we sold 6,250,000 shares of common stock at a public offering price of \$16.00 per share and received gross proceeds of \$100.0 million, which resulted in net proceeds to us of approximately \$87.7 million, after deducting underwriting discounts and commissions and other offering expenses.

Pending the uses described below, the net proceeds from our IPO have been held in cash, cash equivalents, and short-term investments. There has been no material change in our planned use of net proceeds from our IPO from that described in the prospectus for our IPO, except that, due to our strategic decision not to advance the clinical development of BBI-825, funds that would have been directed toward the advancement of BBI-825 and are not used to wind down that program, are now expected to be directed to fund the

continued development of BBI-355 and research and development of our other ecDTx development programs, including our Kinesin program, and to be used for working capital and other general corporate purposes, including our ecDNA diagnostic and Spyglass platform. We may also use a portion of the net proceeds and our existing cash, cash equivalents, and short-term investments to inlicense, acquire, or invest in complementary businesses, technologies, products, or assets. However, we have no current commitments or obligations to do so. We cannot predict with certainty all of the particular uses for the net proceeds from our IPO. Our expected use of the net proceeds from our IPO represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress and costs of our development activities, the status of and results from clinical trials and preclinical studies, as well as any collaborations that we may enter into with third parties for our ecDTx, and the amount of cash used in our operations and any unforeseen cash needs, as well as other factors described in Part I, Item 1A, "Risk Factors" of this report. Our management has broad discretion in the application of the net proceeds from our IPO, and investors will be relying on their judgment regarding the application of the net proceeds.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. [Reserved]

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 financial statements and notes thereto included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties, including those described in the section titled "Special Note Regarding Forward Looking Statements." As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results and the timing of events could differ materially from the results and timing described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage oncology company dedicated to unlocking a new paradigm in cancer therapeutics that addresses the significant unmet need in patients with oncogene amplified tumors by interrogating extrachromosomal DNA (ecDNA), a root cause of oncogene amplification observed in 14 to 17% of cancer patients. Using our proprietary Spyglass platform, we identify targets essential for ecDNA functionality in oncogene amplified cancer cells, then design and develop small molecule drugs called ecDNA-directed therapeutic candidates (ecDTx) to inhibit those targets, with the aim to prevent cancer cells from using amplified oncogenes, which is the approach of traditional targeted therapies. Instead of directly targeting the proteins produced by amplified oncogenes, which is the approach of traditional targeted therapies, our ecDTx are intended to be synthetic lethal in tumor cells reliant on amplification biology. In the context of drug development, synthetic lethality is a therapeutic approach wherein using a drug to inhibit one target is lethal to cancer cells harboring a specific genetic alteration to a second target, but not lethal to healthy cells that lack the genetic alteration to the second target. Accordingly, our ecDTx are designed to preferentially kill amplification-dependent cancer cells, but not healthy cells. They are engineered to disrupt the underlying cellular machinery that enables functional amplification.

Our lead ecDTx, BBI-355, is a novel, oral, selective inhibitor of checkpoint kinase 1 (CHK1), which manages replication stress associated with gene amplification in cancer cells. BBI-355 demonstrated CHK1 inhibition and tumor regressions in oncogene amplified preclinical cancer models, including those enabled by ecDNA, and is currently being studied in a first-in-human, Phase 1/2 clinical trial in patients with oncogene amplified cancers. We refer to this trial as POTENTIATE (Precision Oncology Trial Evaluating Novel Therapeutic Interrupting Amplifications Tied to ecDNA). We expect to have preliminary clinical proof of concept safety and antitumor activity data of BBI-355 in the second half of 2025.

Our next program is directed at a previously undrugged kinesin target that we identified as essential for proper ecDNA segregation and inheritance during cell division. We are advancing our Kinesin program through drug discovery and expect to select a development candidate by mid-2025 and submit an investigational new drug application (IND) in the first half of 2026.

In December 2024, we announced that we determined not to advance an ecDTx known as BBI-825, an oral, selective small molecule inhibitor of RNR, that we had been evaluating in a first-in-human, open-label, non-randomized, 3-part, Phase 1/2 clinical trial (which we refer to as STARMAP) in patients with solid tumors, including those with *BRAF^{V600E}* or *KRAS^{G12C}* mutated colorectal cancer that developed resistance oncogene amplifications, into the Part 2 portion of that trial. We initiated the trial in February 2024. Following an assessment of preliminary PK data from the Part 1 portion of the trial, we made the strategic decision not to continue dose escalation of Part 1 or to proceed into the Part 2 portion of STARMAP. With that strategic decision, we are prioritizing resource allocation to BBI-355 and our Kinesin program.

To assist in identifying patients that may benefit from our ecDTx, we have developed an ecDNA diagnostic, which we internally call ECHO (ecDNA Harboring Oncogenes), to detect ecDNA in patient tumor samples. This test analyzes the genomic data obtained from routine next-generation sequencing (NGS) of patient tumor samples. ECHO is currently being used as a clinical trial assay to determine ecDNA status of patients enrolled in the BBI-355 POTENTIATE trial.

Our pipeline consists of programs directed against targets critical for functional gene amplifications in cancer. We continue to identify new targets, both novel and previously clinically validated, through our proprietary Spyglass platform. To our knowledge, Spyglass is the only platform in the biopharma industry using ecDNA biology to identify specific druggable targets in oncogene amplified cancers. All of our ecDTx have been discovered internally, and we retain global rights for all of our programs.

Since we commenced operations in 2018, we have devoted substantially all of our efforts and resources to organizing and staffing our company, business planning, raising capital, building our proprietary Spyglass platform, discovering our ecDTx, developing our ecDNA diagnostic, establishing our intellectual property portfolio, conducting research, preclinical studies, and clinical trials, establishing arrangements with third parties for the manufacture of our ecDTx and related raw materials, and providing general and administrative support for these operations. During this time, we have incurred significant operating losses and, as of December 31, 2024, we had an accumulated deficit of \$201.5 million. We expect to continue to incur losses for the foreseeable future, and anticipate these losses will increase substantially as we continue our development of, seek regulatory approval for, and potentially commercialize

any of our ecDTx, seek to discover and develop additional ecDTx, develop our ecDNA diagnostic, conduct our ongoing and planned clinical trials and preclinical studies, continue our research and development activities, utilize third parties to manufacture our ecDTx and related raw materials, hire additional personnel, seek to expand and protect our intellectual property, as well as incur additional costs associated with being a public company. If we obtain regulatory approval for any of our ecDTx, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials, preclinical studies, and our other research and development activities and capital expenditures.

Through December 31, 2024, we have raised a total of \$353.7 million to fund our operations primarily from the gross proceeds from the sale and issuance of our convertible preferred and common stock. In April 2024, we completed our initial public offering, or IPO, pursuant to which we sold and issued 6,250,000 shares of our common stock, which generated gross proceeds of \$100.0 million. As of December 31, 2024, we had cash, cash equivalents, and short-term investments of \$152.1 million. Based upon our current operating plans, we believe that our existing cash, cash equivalents, and short-term investments will be sufficient to fund our operations into 2027.

We do not have any products approved for sale and have not generated any revenue to date. We do not expect to generate any revenue from product sales until we successfully complete development and obtain regulatory approval for one or more of our ecDTx, which we expect will take several years and may never occur. We will need substantial additional funding to support our continuing operations and pursue our long-term business plan, including to complete the development and commercialization of our ecDTx, if approved. Accordingly, until such time as we can generate significant revenue from sales of our ecDTx, if ever, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, including potential collaborations, licenses, and other similar arrangements. However, we may be unable to raise additional funds or enter such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, limit, reduce, or terminate our research and development programs or other operations, or grant rights to develop and market ecDTx that we would otherwise prefer to develop and market ourselves.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our ecDTx for preclinical and clinical testing, as well as for commercial manufacture if any of our ecDTx obtain marketing approval. We are working with our current manufacturers to ensure that we will be able to scale up our manufacturing capabilities to support our clinical plans. In addition, we rely on third parties to package, label, store, and distribute our ecDTx, and we intend to rely on third parties for our commercial products if marketing approval is obtained. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment, and personnel while also enabling us to focus our expertise and resources on the discovery and development of our ecDTx.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from the sale of products. We do not expect to generate any such revenue unless and until such time that our ecDTx have advanced through clinical development and regulatory approval, if ever. If we fail to complete preclinical and clinical development of ecDTx or obtain regulatory approval for them, our ability to generate future revenues, and our results of operations and financial position would be adversely affected.

Operating Expenses

Our operating expenses consist of research and development expenses and general and administrative expenses.

Research and Development

Our research and development (R&D) expenses have related primarily to building our Spyglass platform, our ecDTx discovery efforts, our preclinical and clinical development activities, and the development of an ecDNA diagnostic test. R&D expenses are recognized as incurred, and payments made prior to the receipt of goods or services to be used in R&D are capitalized until the goods or services are received. We use internal resources primarily to conduct our research and discovery activities, as well as for managing our preclinical development, process development, manufacturing, and clinical development activities. We track direct costs on a development program specific basis. Indirect costs are not included in program costs, as these costs are general in nature and benefit all our discovery efforts and development programs.

Our direct, or development program specific, R&D costs consist of:

- costs incurred under agreements with our contract research organizations (CROs), investigative sites, and consultants to conduct our clinical trials and preclinical studies, as well as third party costs related to the development of an ecDNA diagnostic test,
- expenses related to manufacturing our ecDTx for clinical trials and preclinical studies, including fees paid to third-party manufacturers; and

Our indirect R&D costs, include:

- personnel-related costs, including salaries, bonuses, benefits, travel, and stock-based compensation expenses for employees engaged in research and development functions,
- the costs of outside services from third parties, including consultants,
- the costs of lab and pharmacology supplies,
- facilities-related costs, including rent and maintenance costs, and other costs including insurance, depreciation, supplies, and miscellaneous expenses, and
- other costs, including costs related to travel, repairs and maintenance, service contracts, computer supplies, software, and publications and subscription services.

Although R&D activities are central to our business model, the successful development of our ecDTx is highly uncertain. There are numerous factors associated with the successful development of any ecDTx, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. In addition, future regulatory factors beyond our control may impact our clinical development programs. Product candidates in later stages of development generally have higher development costs than those in earlier stages of development. As a result, we expect that our R&D expenses will increase substantially for the foreseeable future as we continue to conduct our ongoing R&D activities, advance preclinical research programs toward clinical development, conduct clinical trials, hire additional personnel, and maintain, expand, protect, and enforce our intellectual property portfolio.

Our future R&D expenses may vary significantly based on a wide variety of factors such as:

- the number, scope, rate of progress, expense, and results of our discovery and preclinical activities and clinical trials;
- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the cost of developing an ecDNA diagnostic test;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- the potential additional safety monitoring requested by regulatory agencies;

- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing our ecDTx;
- the phase of development of our ecDTx;
- a decision not to advance the clinical development of an ecDTx;
- the extent of changes in government regulation and regulatory guidance;
- the efficacy and safety profile of our ecDTx;
- the timing, receipt, and terms of any approvals from applicable regulatory authorities; and
- the extent to which we establish collaboration, license, or other arrangements.

A change in the outcome of any of these variables with respect to development of any of our ecDTx could significantly change the costs and timing associated with the development of that ecDTx. While we made a strategic decision in late 2024 not to advance the clinical development of BBI-825, we expect to incur significant R&D expenses in 2025 in connection with winding down that program.

The process of conducting the necessary preclinical and clinical research to obtain regulatory approval is costly and timeconsuming. The actual probability of success for our current ecDTx or any future ecDTx may be affected by a variety of factors. We may never succeed in achieving regulatory approval for any of our ecDTx. Preclinical and clinical development timelines, the probability of success, and total development costs can differ materially from expectations. We anticipate that we will make determinations as to which ecDTx to pursue and how much funding to direct to each ecDTx on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments, and our ongoing assessments as to each ecDTx's commercial potential. We will need to raise substantial additional capital in the future. In addition, we cannot forecast which ecDTx may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

General and Administrative

General and administrative (G&A) expenses consist primarily of personnel-related costs, including salaries, bonuses, benefits, travel, and stock-based compensation expenses for employees in executive, accounting and finance, business development, legal, and other administrative functions. Other significant costs include allocated facility-related costs, legal fees relating to intellectual property and corporate matters, professional fees for accounting and consulting services, insurance costs, and business development expenses.

We expect that our G&A expenses will increase substantially in the future due to increased facility and stock-based compensation costs, as well as increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with securities exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Other Income (Expense), Net

Other income (expense), net consists primarily of interest income earned on our cash, cash equivalents, and investments.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for each of the periods indicated (in thousands):

		Year Ended December 31,					
	-	2024		2023	Change		
Operating expenses:							
Research and development		\$	55,267	\$	42,637	\$	12,630
General and administrative			18,000		12,159		5,841
Total operating expenses			73,267		54,796		18,471
Loss from operations	-		(73,267)		(54,796)		(18,471)
Other income, net:							
Interest income			7,892		5,282		2,610
Other income, net			12		80		(68)
Total other income, net	-		7,904		5,362		2,542
Net loss		\$	(65,363)	\$	(49,434)	\$	(15,929)

Research and Development Expenses

The following table summarizes our R&D expenses for each of the periods indicated (in thousands):

	 Year Ended December 31,				
	2024 2023		Change		
Direct program costs:					
BBI-355	\$ 10,024	\$	7,252	\$	2,772
BBI-825	11,644		5,912		5,732
Other development programs	5,178		4,456		722
Total direct program costs	26,846		17,620		9,226
Indirect program costs:					
Personnel-related (including stock compensation)	16,820		13,688		3,132
Outside services and consulting	4,079		4,326		(247)
Lab and pharmacology supplies	1,899		2,897		(998)
Facilities-related (including depreciation)	3,818		2,776		1,042
Other indirect program costs	1,805		1,330		475
Total indirect program costs	28,421		25,017		3,404
Total R&D expenses	\$ 55,267	\$	42,637	\$	12,630

R&D expenses were \$55.3 million and \$42.6 million for the years ended December 31, 2024 and 2023, respectively. The increase in R&D expenses was primarily due to (i) a \$9.2 million increase in direct program costs primarily related to our ongoing Phase 1/2 POTENTIATE clinical trial of BBI-355 and the Phase 1/2 STARMAP clinical trial of BBI-825, the latter of which was initiated in the first quarter 2024, (ii) a \$1.5 million increase in employee compensation costs due to the expansion of our clinical operations team, annual and other salary increases, and severance costs related to a reduction in our R&D workforce in the third quarter of 2024, (iii) \$1.6 million of additional stock-based compensation primarily due to option awards granted in 2024, the initiation of our employee stock purchase plan in April 2024, as well as the incremental expense from the option repricing (see Note 11 to our financial statements included elsewhere in this Annual Report on Form 10-K for information about the option repricing in 2024), and (iv) a \$1.0 million increase in facilities-related costs primarily due to relocation of our corporate headquarters in the fourth quarter of 2024, partially offset by decreases in laboratory supplies expenses, third-party services, and other miscellaneous R&D costs.

General and Administrative Expenses

G&A expenses were \$18.0 million and \$12.2 million for the years ended December 31, 2024 and 2023, respectively. The increase in G&A expenses was due to (i) a \$1.2 million increase in personnel-related costs resulting from an increase in personnel, annual and

other salary increases, and severance costs related to the departure of an executive officer, (ii) \$2.6 million of additional stock-based compensation primarily due to option awards granted in 2024, the initiation of our employee stock purchase plan in April 2024, and the incremental expense from the option repricing noted above, (iii) a \$0.8 million increase in costs primarily associated with operating as a public-traded company after our IPO in March 2024, (iv) a \$0.6 million increase in facilities-related costs primarily due to relocation of our corporate headquarters in the fourth quarter of 2024, and (iii) a \$0.6 million increase in other G&A costs.

Other Income, Net

Other income, net was \$7.9 million and \$5.4 million for the years ended December 31, 2024 and 2023, respectively. The increase resulted from the additional interest income generated by our available-for-sale investment securities portfolio due to the net proceeds from the sale of our common stock in our IPO in April 2024.

Liquidity and Capital Resources

Sources of Liquidity

Through December 31, 2024, we have raised a total of \$353.7 million to fund our operations primarily from the gross proceeds from the sale and issuance of our convertible preferred stock and the sale and issuance of 6,250,000 shares of our common stock in our IPO in April 2024 for gross proceeds of \$100.0 million.

Future Funding Requirements

As of December 31, 2024, we had cash, cash equivalents, and short-term investments of \$152.1 million. Based upon our current operating plans, we believe that our existing cash, cash equivalents, and short-term investments will be sufficient to fund our operations into 2027. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. We have based this estimate on assumptions that may prove to be wrong, and we could deplete our capital resources sooner than we expect. Additionally, the process of conducting preclinical studies, manufacturing ecDTx, developing our ecDNA diagnostic, and testing ecDTx in clinical trials is costly, and the timing of progress and expenses in these studies and trials is uncertain.

We have incurred significant operating losses since our inception and, as of December 31, 2024, we had an accumulated deficit of \$201.5 million. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as we continue our development of, seek regulatory approval for, and potentially commercialize any of our ecDTx, seek to discover and develop additional ecDTx, develop our ecDNA diagnostic, conduct our ongoing and planned clinical trials and preclinical studies, continue our research and development activities, utilize third parties to manufacture our ecDTx and related raw materials, hire additional personnel, seek to expand and protect our intellectual property, as well as incur additional costs associated with being a public company. If we obtain regulatory approval for any of our ecDTx, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials, preclinical studies, and our other research and development activities and capital expenditures.

Our future capital requirements are difficult to predict and depend on many factors, including but not limited to:

- the initiation, type, number, scope, progress, expansions, results, costs, and timing of clinical trials and preclinical studies of our ecDTx that we are pursuing or may choose to pursue in the future, including the costs of any third-party products used as combination agents in our combination clinical trials;
- the costs and timing of manufacturing for our ecDTx, including commercial manufacture at sufficient scale, if any ecDTx is approved;
- the costs and timing of developing ecDNA diagnostics, if required, and the outcome of their regulatory review;
- the costs, timing, and outcome of regulatory meetings and reviews of our ecDTx;
- changes in regulatory policies or approval pathways;
- disruptions at the FDA that hinder its ability to perform routine activities or function in the normal course;
- the costs of obtaining, maintaining, enforcing, and protecting our patents and other intellectual property and proprietary rights;

- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal control over financial reporting;
- the costs associated with hiring additional personnel and consultants as our clinical and preclinical activities increase and as we operate as a public company;
- the costs and timing of establishing or securing sales and marketing capabilities if any ecDTx is approved;
- our ability to achieve sufficient market acceptance, coverage, and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- patients' willingness to pay out-of-pocket for any approved products in the absence of coverage and/or adequate reimbursement from third-party payors;
- the terms and timing of establishing and maintaining collaborations, licenses, and other similar arrangements;
- costs associated with any products or technologies that we may in-license or acquire; and
- the effects of competing technological and market developments as well as disruptions to and volatility in the credit and financial markets.

We have no committed sources of capital. Until we can generate sufficient product revenue to finance our cash requirements, if ever, we expect to finance our future cash needs primarily through equity offerings, debt financings, or other capital sources, including potential collaborations, licenses, and other similar arrangements. However, we may be unable to raise additional funds or enter such other arrangements when needed on favorable terms or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt 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 additional funds through other collaborations or licensing arrangements with third parties, we may have to relinquish valuable rights to our future revenue streams, ecDTx, research programs, intellectual property or proprietary technology, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce, or terminate our R&D programs or other operations, or grant rights to develop and market ecDTx to third parties that we would otherwise prefer to develop and market ourselves, or on less favorable terms than we would otherwise choose.

Cash Flows

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

	Year Ended December 31,				
		2024		2023	 Change
Net cash used in operating activities	\$	(60,841)	\$	(46,855)	\$ (13,986)
Net cash used in investing activities		(26,101)		(38,260)	12,159
Net cash provided by financing activities		89,823		97,897	 (8,074)
Net increase in cash, cash equivalents, and restricted cash	\$	2,881	\$	12,782	\$ (9,901)

Operating Activities

Net cash used in operating activities was \$60.8 million and \$46.9 million for the years ended December 31, 2024 and 2023, respectively. The net cash used in operating activities during the year ended December 31, 2024 was primarily due to our reported net loss of \$65.4 million, net of noncash charges (including stock-based compensation expense, depreciation, and right-of-use (ROU) asset amortization) totaling \$6.2 million and a \$1.7 million increase of our net operating assets. The net cash used in operating activities during the year ended December 31, 2023 was primarily due to our reported net loss of \$49.4 million and a \$0.8 million increase in our net operating assets, adjusted for noncash charges (including stock-based compensation expense, depreciation, and ROU amortization) totaling \$3.4 million. The increase in cash used in operations during the year ended December 31, 2024 in comparison to the year ended

December 31, 2023 was primarily attributable to higher personnel-related costs and an increase in third-party spending associated with our discovery, development, and clinical activities.

Investing Activities

Investing activities consist primarily of the cash flows of purchases and maturities of investment securities and the cash outflow associated with purchases of property and equipment. Such activities resulted in a net outflow of funds of approximately \$26.1 million and \$38.3 million during the years ended December 31, 2024 and 2023, respectively, primarily from the net purchases of our available-for-sale securities portfolio.

Financing Activities

Our financing activities consist of the proceeds from sales of our common and convertible preferred stock and, to a lesser extent, the exercise of common stock options by our employees and consultants. Net cash provided by financing activities was \$89.8 million during the year ended December 31, 2024, primarily due to the net proceeds from our IPO. Net cash provided by financing activities was \$97.9 million during the year ended December 31, 2023, primarily due to the net proceeds generated from the sale and issuance of our Series C convertible preferred stock in the second quarter of 2023.

Contractual Obligations and Other Commitments

We lease office and lab space under a non-cancellable lease agreement that expires in October 2034. As of December 31, 2024, total future aggregate operating lease commitments was \$72.5 million, which is exclusive of variable lease payments for common area maintenance and property taxes. Of this amount, approximately \$2.6 million will be due in 2025 and approximately \$7.0 million will be due in 2026, with the remainder due in periods from 2027 through 2034. See Note 7 to our financial statements included elsewhere in this Annual Report on Form 10-K for further information.

We enter into contracts in the normal course of our business for clinical trial and preclinical research services, contract manufacturing services, professional services and other services and products for research and operating purposes. These contracts generally provide for termination after a notice period, and, therefore, are cancelable contracts and not separately presented.

Off-Balance Sheet Arrangements

Since our inception, we have not had, and we do not currently have, any off-balance sheet arrangements as defined under rules and regulations of the SEC.

Critical Accounting Policies and Significant Estimates and Judgments

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles (GAAP). The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued R&D expenses and stock-based compensation expense. 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. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are critical to understanding and evaluating our historical and future performance as these policies relate to areas that involve a significant level of estimation uncertainty and have had or are reasonably likely to have a material impact on our financial condition or results of operations.

Accrued R&D Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued R&D expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel 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. We make estimates of our accrued R&D expenses as of each balance sheet date based on facts and circumstances known to us at that time. The significant estimates in our accrued R&D

expenses include the costs incurred for services performed by our vendors in connection with services for which we have not yet been invoiced.

We base our expenses related to R&D activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct R&D 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 R&D 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 expense accordingly. Advance payments for goods and services that will be used in future R&D 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 actually 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. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-Based Compensation Expense

Stock-based compensation expense represents the grant date fair value of equity awards recognized over the requisite service period of the awards (usually the vesting period of the award) on a straight-line basis. We estimate the grant date fair value of stock-based awards, which for the years ended December 31, 2024 and 2023, consisted of stock option awards and, subsequent to completion of our IPO, rights to purchase shares under our 2024 Employee Stock Purchase Plan (ESPP), using the Black-Scholes option pricing model and recognize forfeitures as they occur. The Black-Scholes option pricing model requires the use of subjective assumptions, including the risk-free interest rate, the expected stock price volatility, the expected term of the award, the expected dividend yield, and, prior to the completion of our IPO, the estimated fair value of our common stock. Changes in these assumptions can materially affect the grant date fair value of our stock-based awards, and ultimately, how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant judgment to develop. See Note 2 under "Stock-Based Compensation" and Note 11 to our financial statements included elsewhere in this Annual Report on Form 10-K for information concerning the subjectivity and judgment involved in developing these assumptions and certain of the specific inputs we used in applying the Black-Scholes option pricing model to determine the estimated fair value of stock options granted and rights to purchase ESPP shares in the years ended December 31, 2024 and 2023.

Prior to our IPO, since there was no public market for our common stock, we were required to estimate the fair value of the common stock underlying our equity awards when performing fair value calculations. The fair value of the common stock underlying our equity awards was determined on each grant date by our board of directors, taking into account input from management and independent third-party valuation analyses. All options to purchase shares of our common stock are intended to be granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant. In the absence of a public trading market for our common stock, on each grant date we developed an estimate of the fair value of our common stock in order to determine an exercise price for the option grants. Our determinations of the fair value of our common stock were made using methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants Accounting and Valuation Guide: Valuation of Privately Held Company Equity Securities Issued as Compensation (the Practice Aid).

Following our IPO, the fair value of our common stock is based on the closing price per share on the Nasdaq Global Select Market on the date of grant. We will continue to use judgment in evaluating the interest rates, expected stock price volatility, expected terms of the stock-based awards, and expected dividend yield utilized for our stock-based compensation expense calculations on a prospective basis.

Emerging Growth Company and Smaller Reporting Company Status

As an emerging growth company under the Jumpstart Our Business Startups Act of 2012 (the JOBS Act), we can take advantage of an extended transition period for complying with new or revised accounting standards. This period allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates. We

also intend to rely on other exemptions provided by the JOBS Act, including without limitation, not being required to comply with the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley for so long as we are exempt from doing so.

We will remain an emerging growth company until the earliest of (i) December 31, 2029, which is the last day of the fiscal year following the fifth anniversary of the consummation of our IPO; (ii) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.235 billion; (iii) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded \$700.0 million as of the last business day of the second fiscal quarter of such year; or (iv) the date on which we have issued more than \$1.0 billion in nonconvertible debt securities during the prior three-year period.

We are also a smaller reporting company as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than \$250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than \$100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than \$700.0 million measured on the last business day of our second fiscal quarter.

Recently Adopted and Issued Accounting Pronouncements

See Note 2 to our financial statements included elsewhere in this Annual Report on Form 10-K for recently adopted accounting pronouncements not yet adopted.

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

Interest Rate Risk

As of December 31, 2024, our cash, cash equivalents, and short-term investments consisted of cash held in readily available checking and money market accounts, as well as short-term debt securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of United States interest rates. However, because of the short-term nature of the instruments in our portfolio, we believe that our exposure to interest rate risk is not significant, and a hypothetical sudden 10% change in market interest rates would not be expected to have a material impact on our financial condition or results of operations during the periods presented.

Foreign Currency

We contract with vendors in foreign countries, including countries in Europe and the Asia Pacific. We are therefore subject to fluctuations in foreign currency rates in connection with these agreements, however we believe our exposure to foreign currency exchange rate risk is not significant and we do not hedge our foreign currency exchange rate risk.

Net realized and unrealized gains and losses from foreign currency transactions are reported in other income (expense), net, in the statements of operations and comprehensive loss. The impact of foreign currency costs on our operations have been negligible for all periods presented.

Inflation Risk

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented.

Item 8. Financial Statements and Supplementary Data.

Our financial statements required to be filed pursuant to this Item 8, together with the report of our independent registered public accounting firm, appear 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 that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on that evaluation, our principal executive officer and principal financial officer have concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report and Attestation Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies. In addition, following such transition period, our future Annual Reports on Form 10-K will not include an attestation report of our independent registered public accounting firm for so long as we qualify as an "emerging growth company" or a non-accelerated filer.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting during the three months ended December 31, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Rule 10b5-1 Trading Arrangements

From time to time, our officers (as defined in Rule 16a-1(f) of the Exchange Act) and directors may enter into Rule 10b5-1 or non-Rule 10b5-1 trading arrangements (as each such term is defined in Item 408 of Regulation S-K). During the three months ended December 31, 2024, our officers or directors adopted, modified, or terminated such trading arrangements as set forth below.

			-			
	<u>Action</u>	<u>Date</u>	<u>Rule</u> 10b5-1*	<u>Non-</u> <u>Rule</u> 10b5-1**	<u>Total Shares</u> <u>Subject to Plan</u>	Expiration Date
David Hinkle, Senior Vice President, Finance, Controller and Treasurer	Adopt	December 27, 2024	Х		12,000 ⁽¹⁾	December 31, 2025 ⁽²⁾
Jami Rubin, former Chief Financial Officer ⁽³⁾	Terminate	October 18, 2024	Х		9,000 ⁽⁴⁾	Not applicable

* Intended to satisfy the affirmative defense of Rule 10b5-1(c)

^{**} Not intended to satisfy the affirmative defense of Rule 10b5-1(c)

- (1) In addition, 100% of shares purchased in 2025 after the date of this report pursuant to Mr. Hinkle's participation in our ESPP are also subject to this trading plan.
- (2) This trading plan may expire earlier if all transactions under the trading plan are completed before the scheduled expiration date.
- (3) Ms. Rubin's employment terminated effective October 11, 2024.
- (4) No sales occurred pursuant to this trading plan prior to its termination.

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

None.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance.

The information required by this Item 10 will be included in our definitive proxy statement for our 2025 Annual Meeting of Stockholders, which we expect to be filed with the SEC within 120 days of the end of our fiscal year ended December 31, 2024 (Definitive Proxy Statement), under the headings "Election of Directors," "Corporate Governance," "Executive Officers," and "Section 16(a) Beneficial Ownership Reporting Compliance," 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 under the heading "Executive Compensation and Other Information," 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 under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance Under Equity Compensation Plans," 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 under the headings "Certain Relationships and Related Person Transactions," "Board Independence" and "Committees of the Board of Directors" and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this Item 14 will be included in our Definitive Proxy Statement under the heading "Independent Registered Public Accountants' Fees," and is incorporated herein by reference.

Our independent public accounting firm is KPMG LLP, San Diego, CA, PCAOB Auditor ID: 185.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

- (1) For a list of the financial statements included herein, see Index to the Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.
- (2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the financial statements or the notes thereto.
- (3) Exhibits:

Exhibit Index

Exhibit			Incorporated by Reference			
Number	Description	Form	Date	Number	Herewith	
3.1	Amended and Restated Certificate of Incorporation	8-K	4/2/2024	3.1		
3.2	Amended and Restated Bylaws	8-K	4/2/2024	3.2		
4.1	Specimen stock certificate evidencing the shares of common stock	S-1/A	3/21/2024	4.1		
4.2	Amended and Restated Investor Rights Agreement, dated April 5, 2023, by and among the Registrant and certain of its stockholders	S-1	3/6/2024	4.2		
4.3	Description of the Registrant's securities				Х	
10.1#	Boundless Bio, Inc. 2018 Equity Incentive Plan, as amended, and form of stock option agreement and form of restricted stock agreement thereunder	S-1	3/6/2024	10.1		
10.2#	Boundless Bio, Inc. 2024 Incentive Award Plan and form of stock option agreement and form of restricted stock unit agreement thereunder	S-1/A	3/21/2024	10.2		
10.3#	Boundless Bio, Inc. 2024 Employee Stock Purchase Plan	S-1/A	3/21/2024	10.3		
10.4#	Non-Employee Director Compensation Program (as amended and restated effective June 20, 2024)	10-Q	8/12/2024	10.1		
10.5#	Amended and Restated Employment Offer Letter Agreement, dated March 5, 2024, between Zachary D. Hornby and the Registrant	S-1	3/6/2024	10.6		
10.6#	Amended and Restated Employment Offer Letter Agreement, dated March 5, 2024, between Christian Hassig, Ph.D. and the Registrant	S-1	3/6/2024	10.12		
10.7#	Amended and Restated Employment Offer Letter Agreement, dated March 5, 2024, between Jessica Oien and the Registrant	S-1	3/6/2024	10.16		
10.8#	Amended and Restated Employment Offer Letter Agreement, dated April 2, 2024, between David Hinkle and the Registrant				Х	
10.9#	Employment Offer Letter Agreement, dated January 27, 2025, between Robert Doebele, M.D. Ph.D. and the Registrant				Х	
10.10#	Severance Agreement and Release of All Claims, dated October 13, 2024, between Jamilu Rubin and the registrant	10-Q	11/14/2024	10.1		
10.11#	Severance and Change in Control Severance Plan	S-1	3/6/2024	10.17		
10.12#	Corporate Bonus Plan	S-1	3/6/2024	10.18		
10.13#	Form of Indemnification Agreement for Directors and Officers	S-1/A	3/21/2024	10.19		
19.1	Boundless Bio, Inc. Insider Trading Compliance Policy and Procedures				Х	
23.1	Consent of KPMG LLP, independent registered public accounting firm				Х	
24.1	Power of attorney (included on signature page)				Х	
31.1	<u>Certification of Principal Executive Officer Pursuant to Rules 13a-14(a)</u> and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				Х	
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31.2	<u>Certification of Principal Financial Officer Pursuant to Rules 13a-14(a)</u> and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				Х	
32.1*	<u>Certifications of Principal Executive Officer and Principal Financial</u> <u>Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to</u> <u>Section 906 of the Sarbanes-Oxley Act of 2002.</u>				Х	
97.1#	Policy for Recovery of Erroneously Awarded Compensation	S-1	3/6/2024	10.20		
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.				Х	
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents				Х	
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)				Х	

Indicates management contract or compensatory plan.
* These certifications are deemed not filed for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

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.

	Boundless Bio, Inc.
Date: March 27, 2025	By: /s/ Zachary D. Hornby Zachary D. Hornby President and Chief Executive Officer (Principal Executive Officer)
Date: March 27, 2025	By: <u>/s/ David Hinkle</u> David Hinkle Senior Vice President, Finance, Controller and Treasurer (Principal Financial and Accounting Officer)

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POWER OF ATTORNEY AND SIGNATURES

Each person whose individual signature appears below hereby authorizes and appoints Zachary D. Hornby and David Hinkle, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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 and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Zachary D. Hornby	President and Chief Executive Officer	March 27, 2025
Zachary D. Hornby	(Principal Executive Officer)	
/s/ David Hinkle	_ Senior Vice President, Finance, Controller and Treasurer	March 27, 2025
David Hinkle	(Principal Financial and Accounting Officer)	
/s/ Jonathan E. Lim	_ Chairman	March 27, 2025
Jonathan E. Lim, M.D.		
/s/ Christine Brennan	Director	March 27, 2025
Christine Brennan, Ph.D.	-	,
<i>,</i>		
/s/ Kristina Burow	Director	March 27, 2025
Kristina Burow		
/s/ James Christensen	Director	March 27, 2025
James Christensen, Ph.D.		1141011 27, 2020
/s/ Jennifer Lew	Director	March 27, 2025
Jennifer Lew	-	
/s/ Nancy Whiting	Director	March 27, 2025
Nancy Whiting, Pharm.D		

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Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors Boundless Bio, Inc.:

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Boundless Bio, Inc. (the Company) as of December 31, 2024 and 2023, the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity/ (deficit), and cash flows for the years then ended, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for the years then ended, 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 these 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/ KPMG LLP

We have served as the Company's auditor since 2020.

San Diego, California March 27, 2025

Boundless Bio, Inc. Balance Sheets

(in thousands, except par value data)

		Decem	ber 31,	
		2024		2023
Assets				
Current assets				
Cash and cash equivalents	\$	26,587	\$	23,706
Short-term investments		125,527		97,046
Prepaid expenses and other current assets		2,276		3,452
Total current assets		154,390		124,204
Property and equipment, net		4,321		2,573
Right-of-use asset, net		47,039		2,002
Restricted cash		560		560
Other assets		99		555
Total assets	\$	206,409	\$	129,894
Liabilities, convertible preferred stock, and stockholders' equity/ (deficit)				
Current liabilities				
Accounts payable and accrued liabilities	\$	5,354	\$	4,266
Accrued compensation		2,781		2,898
Lease liabilities, current portion				2,195
Total current liabilities		8,135		9,359
Lease liabilities, non-current		47,632		
Total liabilities		55,767		9,359
Commitments and contingencies (Note 8)				
Convertible preferred stock, \$0.0001 par value; no shares authorized, issued, or outstanding as of December 31, 2024; 287,447 shares authorized, issued, and outstanding as of December 31, 2023 liquidation preference of \$252.1 million as of December 31, 2023		_		247,617
Stockholders' equity/ (deficit):				
Preferred stock, \$0.0001 par value; 70,000 shares authorized and no shares issued and outstanding as of December 31, 2024; no shares authorized and no shares issued and outstanding as of December 31, 2023		_		_
Common stock, \$0.0001 par value; 700,000 shares authorized,				
22,500 shares issued and outstanding as of December 21, 2024; 402,600 shares authorized, 1,248 shares				
issued and outstanding as of December 31, 2023		2		
Additional naid-in-capital		351 991		8 987
Accumulated other comprehensive income		121		40
Accumulated deficit		(201 472)		(136 109)
Total stockholders' equity/ (deficit)		150 642		$(127\ 082)$
Total liabilities convertible preferred stock and stockholders' equity/ (deficit)	\$	206 409	\$	129,894
Four nuonities, convertible preferred stock, and stockholders' equity/ (deficit)	Ψ	200,407	Ψ	127,074

Boundless Bio, Inc. Statements of Operations and Comprehensive Loss (in thousands, except per share data)

		Year H Decemi	Ended ber 31,		
		2024		2023	
Operating expenses:					
Research and development	\$	55,267	\$	42,637	
General and administrative		18,000		12,159	
Total operating expenses		73,267		54,796	
Loss from operations		(73,267)		(54,796)	
Other income, net:					
Interest income		7,892		5,282	
Other income, net		12		80	
Total other income, net		7,904		5,362	
Net loss	\$	(65,363)	\$	(49,434)	
Comprehensive loss:					
Net loss	\$	(65,363)	\$	(49,434)	
Unrealized gain on short-term investments		81		438	
Comprehensive loss	<u>\$</u>	(65,282)	\$	(48,996)	
Net loss per share, basic and diluted	\$	(3.85)	\$	(40.65)	
Shares used in calculation		16,984		1,216	

Boundless Bio, Inc. Statements of Convertible Preferred Stock and Stockholders' Equity/ (Deficit) *(in thousands)*

	-2	- Ctool				Additional	Accumul	ated		Post of	Total stockholder	's'
1	Shares	Amount	Shares	n Stock Amount		paiu-in capital	comprene income/ ()	lisive loss)	defici	it	equity/ (deficit)	
Balance at December 31, 2022	144,590	\$ 147,946	1,167	 \$	S	5,377	s	(398)	s S	86,675)	\$ (81,	(969)
Issuance of Series C convertible preferred stock, net of issuance costs of \$329	142,857	99,671										
Vesting of early exercised stock options	1	1	31	1		92				I		92
Exercise of stock options		I	49			182				I		182
Stock-based compensation						3,336					'n	3,336
Unrealized gain on short-term investments								438				438
Net loss		Ι	Ι						•	49,434)	(49,	,434)
Balance at December 31, 2023	287,447	\$ 247,617	1,247	\$	s	8,987	S	40	\$ (1	36,109)	\$ (127,	7,082)
Issuance of common stock in initial public offering, net of \$12,305 in discounts and offering costs			6.250	\$	\$	87.694	60	,	S	,	87.	7.695
Conversion of convertible preferred stock into common stock upon initial public offering	(287,447)	(247,617)	14,741	1		247,616				I	247,	7,617
Vesting of early exercised stock options			1			9				I		9
Exercise of stock options	Ι	Ι	16			62				I		62
Issuance of common stock under the Employee Stock Purchase Plan	I		45	I		110						110
Stock-based compensation						7,516					7,	7,516
Unrealized gain on short-term investments	I	I		I				81		I		81
Net loss										65,363)	(65,	(363)
Balance at December 31, 2024		 	22,300	\$ 2	Ś	351,991	S	121	\$ (2)	01,472)	\$ 150,),642

Boundless Bio, Inc. Statements of Cash Flows (in thousands)

	Year I Decem	Ended ber 31.	
	 2024		2023
Cash flows from operating activities			
Net loss	\$ (65,363)	\$	(49,434)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	7,516		3,336
Depreciation and amortization	1,086		957
Accretion of investments, net	(5,055)		(3,300)
Non-cash lease expense	2,551		2,360
Other	102		25
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(302)		85
Accounts payable and accrued liabilities	775		1,663
Operating lease liabilities	 (2,151)		(2,547)
Net cash used in operating activities	 (60,841)		(46,855)
Cash flows from investing activities			
Purchases of investments	(208,465)		(160,123)
Maturities of investments	184,900		122,496
Purchases of property and equipment	 (2,536)		(633)
Net cash used in investing activities	 (26,101)		(38,260)
Cash flows from financing activities			
Proceeds from the issuance of common stock from initial public offering, net			
of discounts	93,000		
Payments of common stock offering costs	(3,349)		(1,956)
Proceeds from issuance of Series C preferred stock, net of issuance costs			99,671
Proceeds from the exercise of stock options	62		182
Proceeds from issuance of common stock under the Employee Stock Purchase Plan	 110		
Net cash provided by financing activities	 89,823		97,897
Net increase in cash and cash equivalents	2,881		12,782
Cash, cash equivalents, and restricted cash at beginning of year	 24,266		11,484
Cash, cash equivalents, and restricted cash at end of year	\$ 27,147	\$	24,266
Components of cash, cash equivalents, and restricted cash			
Cash and cash equivalents	\$ 26,587	\$	23,706
Restricted cash	 560		560
Cash, cash equivalents, and restricted cash at end of year	\$ 27,147	\$	24,266
Non-cash investing and financing activities	 		
Change in unpaid common stock issuance costs	\$ (197)	\$	197
Addition to right-of-use assets obtained in exchange for lease obligation	\$ 47,588	\$	282
Decrease to right-of-use assets due to remeasurement of lease obligation	\$ 	\$	(723)
Vesting of early exercised stock options	\$ 6	\$	92
Unpaid property and equipment purchases	\$ 400	\$	

Boundless Bio, Inc.

Notes to Financial Statements

1. Organization and Basis of Presentation

Description of Business

Boundless Bio, Inc. (the Company) is a clinical-stage precision oncology company dedicated to unlocking a new paradigm in cancer therapeutics to address the significant unmet need in patients with oncogene amplified tumors by targeting extrachromosomal DNA (ecDNA). The Company is focused on designing and developing small molecule drugs called ecDNA directed therapeutic candidates (ecDTx). The Company was incorporated in the state of Delaware on April 10, 2018 and is headquartered in San Diego, California.

Initial Public Offering

On April 2, 2024, the Company completed its initial public offering (IPO), pursuant to which it sold 6,250,000 shares of its common stock at a public offering price of \$16.00 per share, resulting in net proceeds of approximately \$87.7 million, after deducting underwriting discounts, commissions, and other offering expenses. Immediately prior to the closing of the IPO, the Company's outstanding convertible preferred stock automatically converted into 14,740,840 shares of common stock. Following the closing of the IPO, no shares of convertible preferred stock were authorized or outstanding.

In connection with the closing of its IPO, on April 2, 2024, the Company's certificate of incorporation was amended and restated to authorize 700,000,000 shares of common stock, par value \$0.0001 per share, and 70,000,000 shares of undesignated preferred stock, par value of \$0.0001 per share.

Reverse Stock Split

On March 19, 2024, the Company effected a one-for-19.5 reverse stock split of its issued and outstanding shares of common stock. Accordingly, all share and per share amounts for all periods presented in the accompanying financial statements and these notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the conversion ratios for each series of the Company's convertible preferred stock. The par value and the number of authorized shares of the convertible preferred stock and common stock were not adjusted in connection with the reverse stock split.

Liquidity

Since the Company commenced operations in 2018, it has devoted substantially all of its efforts and resources to organizing and staffing the Company, business planning, raising capital, building its proprietary Spyglass platform, discovering its ecDTx, developing its ecDNA diagnostic, establishing its intellectual property portfolio, conducting research, preclinical studies, and clinical trials, establishing arrangements with third parties for the manufacture of its ecDTx and related raw materials, and providing other general and administrative support for these operations. The Company does not have any products for sale and has not generated any revenue to date. The Company has funded its operations primarily from the sale and issuance of shares of its convertible preferred stock and common stock.

As of December 31, 2024, the Company had cash, cash equivalents, and short-term investments of \$152.1 million. The Company believes that its existing cash, cash equivalents, and short-term investments will be sufficient to fund its operations for at least twelve months from the issuance date of the accompanying financial statements.

Since inception, the Company has incurred significant operating losses and negative cash flows from its operations and expects that it will continue to do so into the foreseeable future as it continues its development of, seeks regulatory approval for, and potentially commercializes any of its ecDTx and seeks to discover and develop additional ecDTx, utilizes third parties to manufacture its ecDTx and related raw materials, seeks to develop its ecDNA diagnostic, hires additional personnel, and expands and protects its intellectual property. If the Company obtains regulatory approval for any of its ecDTx, it expects to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution. The Company does not expect to generate any revenue from product sales until it successfully completes development of and obtains regulatory approval for one or more of its ecDTx, which the Company expects will take several years and may never occur. As of December 31, 2024, the Company had an accumulated deficit of \$201.5 million, and, during the year ended December 31, 2024, the Company incurred a net loss of \$\$65.4 million and had negative cash flows from operations of \$60.8 million. As the Company continues to pursue its business plan, it will need to acquire a substantial amount of additional funding until such time as it is able to generate significant revenues to fund its research and development activities and operations. Accordingly, the Company expects to finance its cash requirements through equity offerings, debt financings, or other capital

sources, including potential collaborations, licenses, and other similar arrangements. There can be no assurance that the Company will be successful in acquiring additional funding or that any additional funding would be sufficient to continue operations in future years.

Basis of Presentation

The accompanying financial statements have been prepared in accordance with United States generally accepted accounting principles (US GAAP). Any reference in these notes to applicable guidance is meant to refer to US GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Updates (ASU) promulgated by the Financial Accounting Standards Board (FASB).

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with US GAAP requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities, revenue and expenses, and the disclosure of contingent assets and liabilities in the Company's financial statements and accompanying notes. Although these estimates are based on the Company's knowledge of current events and actions it may undertake in the future, actual results may materially differ from these estimates and assumptions.

On an ongoing basis, management evaluates its estimates, primarily related to stock-based compensation, the fair value of its investments, accrued research and development costs and, prior to the closing of its IPO, its common stock. These estimates are based on historical data and experience, as well as various other factors that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. The Company's estimates relating to stock-based compensation expense require the selection of appropriate valuation methodologies and models, and significant judgment in evaluating ranges of assumptions and financial inputs.

Cash, Cash Equivalents, and Restricted Cash

The Company considers all highly liquid investments with an original maturity of three months or less when purchased to be cash equivalents. Cash and cash equivalents include cash in readily available checking and money market accounts.

The balance reflected in these financial statements as restricted cash represents a deposit account pledged as collateral to secure a standby letter of credit required as a security deposit under the Company's headquarters facility lease. The Company has classified the restricted cash as a noncurrent asset on its balance sheets as of December 31, 2024 and 2023.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to the concentration of credit risk, consist primarily of cash, cash equivalents, and investments. The Company maintains deposits in federally insured financial institutions which exceeded federally insured limits by \$1.4 million as of December 31, 2024. Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company's investment policy includes guidelines for the quality of the related institutions and financial instruments and defines allowable investments that the Company may invest in, which the Company believes minimizes its exposure to concentration of credit risk.

Short-Term Investments

Short-term investments consist of money market funds, U.S. government obligations, corporate debt securities, government agency securities, asset-backed securities, and commercial paper. The Company obtains pricing information from its investment manager and generally determines the fair value of investment securities using standard observable inputs, including reported trades, broker/dealer quotes, and bid and/or offers. The Company classifies its investment securities as available-for-sale, as the sale of such securities may be required prior to maturity. Management determines the appropriate classification of its investments in debt securities at the time of purchase. Investments with original maturities beyond three months at the date of purchase and which mature at, or less than 12 months from, the balance sheet date are classified as short-term investments. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported as accumulated other comprehensive income (loss) until realized. The amortized cost of available-for-sale debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such

amortization and accretion are included in interest income. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

At each balance sheet date, the Company reviews its available-for-sale debt securities that are in an unrealized loss position to determine whether the unrealized loss or any potential credit losses should be recognized in the statements of operations. For available-for-sale debt securities in an unrealized loss position, the Company first assesses whether it intends to sell, or it is more likely than not that it will be required to sell, the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security's amortized cost basis is written down to fair value through net income (loss). For available-for-sale securities that do not meet the aforementioned criteria, the Company evaluates whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, the Company considers the severity of the impairment, any changes in interest rates, changes to the underlying credit ratings and forecasted recovery, among other factors. The credit-related portion of unrealized losses, and any subsequent improvements, are recorded in other income, net through an allowance account. There have been no impairment or credit losses recognized during any of the periods presented.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under US GAAP. Fair value is defined as an 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 such, fair value is a market-based measurement determined based on assumptions that market participants would use in pricing an asset or liability. Financial assets and liabilities carried at fair value are classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

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

Level 2—Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability.

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.

Cash, cash equivalents, and short-term investments are carried at fair value, determined according to the fair value hierarchy described above. The carrying values of the Company's prepaid expenses, accounts payable, and accrued expenses approximate their fair value due to the short-term nature of these assets and liabilities. None of the Company's non-financial assets or liabilities are recorded at fair value on a non-recurring basis.

Deferred Offering Costs and Common Stock Issuance Costs

The Company capitalizes certain legal, professional, accounting, and other third-party fees that are directly associated with inprocess equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of proceeds generated as a result of the offering. As of December 31, 2024 and 2023, there were \$0 and \$2.2 million of deferred offering costs, respectively. At the closing of the IPO, the amounts recorded in deferred offering costs were reclassified to additional paid-in capital within stockholders' equity.

Property and Equipment, Net

Property and equipment, including leasehold improvements, are stated at cost less accumulated depreciation and amortization. Depreciation and amortization are recorded using the straight-line method over the estimated useful lives of the related assets, which range from three to seven years. Leasehold improvements are amortized on a straight-line basis over the shorter of the estimated useful lives of the assets or the remaining lease term. Repairs and maintenance charges that do not increase the useful life of the assets are charged to operating expenses as incurred.

Impairment of Long-Lived Assets

An impairment loss is recorded if and when events and circumstances indicate that any of the Company's long-lived assets might be impaired and the undiscounted cash flows estimated to be generated by those assets are less than the carrying amount of those assets. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses in any of the periods presented in these financial statements.

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease and whether such a lease should be classified as a financing lease or operating lease based on the unique facts and circumstances present, the existence of an identified asset(s), if any, and the Company's control over the use of the identified asset(s), if applicable. In 2024 and 2023, the Company leased real estate facilities under non-cancelable operating leases with various expiration dates through fiscal year 2034. As of December 31, 2024, the Company had only one such operating lease, which expires in 2034. As of December 31, 2024 and 2023, the Company had no financing leases.

Operating leases with a term greater than one year are recognized as right-of-use (ROU) assets and lease liabilities in the accompanying balance sheets. Operating lease ROU assets represent the Company's right to use an underlying asset for the lease term, and lease liabilities represent the Company's obligation to make lease payments arising from the lease. The Company considers the lease term to be the non-cancelable period that it has the right to use the underlying asset, together with any periods where it is reasonably certain it will exercise an option to extend (or not terminate) the lease. The Company does not assume renewals or early terminations unless it is reasonably certain to exercise these options.

Operating lease liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term discounted based on (i) the interest rate implicit in the lease if that rate is readily determinable, or if not, (ii) the Company's incremental borrowing rate (which is the estimated interest rate the Company would be required to pay for a collateralized borrowing equal to the total lease payments over a similar term as the lease term and in a similar economic environment). Because the Company's operating leases do not provide an implicit rate, the Company estimates its incremental borrowing rate based on the information available at the lease commencement date for borrowings with a similar term. The Company's operating lease ROU assets are measured based on the corresponding operating lease liability adjusted for (i) payments made to the lessor at or before the commencement date, (ii) initial direct costs incurred and (iii) tenant incentives under the lease.

Operating lease costs are recognized on a straight-line basis over the lease term. The Company elected not to allocate consideration between lease and non-lease components. Variable lease payments are recognized in the period in which the obligations for those payments are incurred. In addition, the Company elected not to recognize lease assets or lease liabilities for leases with a term of 12 months or less for all asset classes.

Segment Reporting

Operating segments are identified as components of an enterprise about which discrete financial information is available for evaluation by the chief operating decision-maker (CODM) in making decisions regarding resource allocation and assessing performance. The Company operates and manages its business as one reporting and one operating segment, which is the business of designing and developing ecDTx, for which no revenue has been recorded. All of the Company's long-lived assets are located in the United States. The Company's CODM is its Chief Executive Officer. For purposes of assessing the Company's financial performance and making resource allocation decisions, the CODM reviews total expenses, as well as expenses by nature and functional department.

Convertible Preferred Stock

The Company's convertible preferred stock is classified as temporary equity in the accompanying balance sheet as of December 31, 2023 and excluded from stockholders' equity/ (deficit) as the potential redemption of such stock was outside the Company's control and would have required the redemption of the then-outstanding convertible preferred stock. The convertible preferred stock was not redeemable except for in the event of a liquidation, dissolution, or winding up of the Company. Costs incurred in connection with the issuance of convertible preferred stock were recorded as a reduction of gross proceeds from issuance. The Company did not accrete the carrying values of the convertible preferred stock to the redemption values since the occurrence of these events was not considered probable as of December 31, 2023. Immediately prior to the closing of the IPO on April 2, 2024, the Company's outstanding convertible preferred stock automatically converted into 14,740,840 shares of common stock. Following the closing of the IPO, no shares of convertible preferred stock were authorized or outstanding.

Research and Development Expenses

Research and development (R&D) expenses are costs incurred by the Company in connection with its discovery and research efforts and the preclinical and clinical development of ecDTx. The Company's R&D expenses include direct program costs, consisting of expenses incurred under arrangements with third parties, such as contract research organizations, contract manufacturers, consultants and its scientific advisors; and indirect costs, consisting of personnel-related expenses, including salaries, bonuses, benefits, travel, and

stock-based compensation expenses, for those individuals involved in R&D efforts, the costs of lab and pharmacology supplies and acquiring, developing, and manufacturing preclinical and clinical study materials, and facilities and depreciation, which include direct and allocated expenses for rent of facilities and depreciation of equipment. R&D costs are expensed as incurred.

The Company records accruals for estimated R&D costs, comprising payments for work performed by third party contractors, labs, and others. Some of these contractors bill monthly based on actual services performed, while others bill periodically based upon achieving certain contractual milestones. For the latter, the Company accrues the expenses as goods or services are used or rendered. Non-refundable advance payments for goods or services that will be used or rendered for future R&D activities are deferred and capitalized as prepaid expenses until the related goods are delivered or services are performed.

General and Administrative Expenses

General and administrative (G&A) expenses consist primarily of personnel-related expenses, including salaries, bonuses, benefits, travel, and stock-based compensation expenses, for employees in executive, accounting and finance, business development, human resources, legal, and other administrative functions. Other significant G&A expenses include allocated facility-related costs, legal fees relating to corporate and intellectual property matters, professional fees for accounting and tax services, consulting fees, and insurance costs. G&A costs are expensed as incurred.

Costs related to filing and pursuing patent applications are recorded as G&A expense and are expensed as incurred since the recoverability of such expenditures is uncertain.

Stock-Based Compensation

The Company measures employee and nonemployee stock-based awards based on the estimated fair value of the awards on the date of grant and records compensation expense on a straight-line basis over the requisite service period of the award. All stock-based compensation costs are recorded in the statements of operations and comprehensive loss based upon the underlying employees' or nonemployees' roles within the Company. Forfeitures are accounted for as they occur.

The fair value of stock option grants and shares purchasable under the Company's 2024 Employee Stock Purchase Plan (ESPP) is estimated on the date of grant using the Black-Scholes options-pricing model, which requires inputs based on certain subjective assumptions, including the:

- Fair value of common stock. Subsequent to the closing of the IPO, the fair value of the Company's common stock is the closing price per share on the Nasdaq Global Select Market on the date of grant of the award. However, prior to the closing of the IPO, the Company utilized methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately Held Company Equity Securities Issued as Compensation* (The Practice Aid) to estimate the fair value of its common stock. The fair value of the common stock was determined based upon a variety of factors, including the Company's stage of development and material risks related to the business; the progress of the Company's R&D programs; business conditions and projections; financial position and historical and forecasted performance and operating results; the lack of an active public market for the Company's common stock and preferred stock; the prices of the Company's preferred stock sold to or exchanged between outside investors in arm's length transactions and the rights, preferences, and privileges of the preferred stock as compared to those of the Company's common stock, including liquidation preferences of the Company in light of prevailing market conditions; the hiring of key personnel and the experience of management; trends and developments in the Company's industry; and external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry.
- Risk-free interest rate. The risk-free interest rate is based on the U.S. Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to the expected term of the award being valued.
- Expected volatility. Given that there was no active trading market for the Company's common stock prior to the completion of the IPO and there is not yet sufficient trading history for the Company's common stock, the Company derived the expected volatility from the average historical volatilities of the common stock of a group of comparable publicly-traded companies in the biotechnology industry over a period approximately equal to the expected term of the award being valued. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

- Expected term. The expected term represents the period that the stock-based awards are expected to be outstanding. The expected term of stock options issued is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term) as the Company has concluded that its stock option exercise history does not provide a reasonable basis upon which to estimate expected term. For rights to purchase shares of common stock under the ESPP, the expected term represents the period from the first day of the offering period to the purchase date.
- Expected dividend yield. The Company has never paid dividends on its common stock and does not anticipate paying any dividends in the foreseeable future. Therefore, the Company used an expected dividend yield of zero.

The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of the Company's common stock on that same date.

The assumptions used in determining the estimated fair value of stock-based awards represent management's best estimates and involve inherent uncertainties and the application of significant judgment.

Income Taxes

The Company accounts for income taxes under 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 included in the Company's financial statements and related disclosures. Deferred tax assets and liabilities are determined on the basis of the differences between the Company's 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. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date. The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including projected future taxable income, future reversals of existing taxable temporary differences, tax-planning strategies, and results of recent operations. If management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes. Interest and penalties are included as a component of income tax expense.

The Company records uncertain tax positions on the basis of a two-step process whereby (i) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (ii) for those tax positions that meet the more-likely-than-not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement with the related tax authority. Any resulting unrecognized tax benefits are included within the related tax liability.

Comprehensive income (loss)

The Company reports all components of comprehensive income (loss), including net loss, in the financial statements in the period in which they are recognized. Comprehensive income (loss) is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources, including unrealized gains and losses on marketable securities. Other comprehensive income (loss) includes unrealized gains and losses on marketable securities, which was the only difference between net loss and comprehensive loss for the applicable periods.

Net Loss Per Share

Basic net loss per common share attributable to common stockholders is calculated by dividing the net loss by the weightedaverage number of shares of common stock outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share attributable to common stockholders is calculated by dividing the net loss by the weighted-average number of shares of common stock and potentially dilutive securities outstanding during the period. The Company's potentially dilutive securities, which include its options to purchase common stock, common stock subject to repurchase related to unvested restricted stock and options early exercised, and, for periods prior to April 2, 2024, convertible preferred stock, have been excluded from the calculation of diluted net loss per share as the effect would reduce the net loss per share. Therefore, the weighted-average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share is the same.

Emerging Growth Company Status

The Company is an emerging growth company (EGC) as defined in the Jumpstart Our Business Startups Act of 2012, as amended (the JOBS Act), and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not EGCs. The Company may take advantage of these exemptions until it is no longer an EGC under Section 107 of the JOBS Act and has elected to use the extended transition period for complying with new or revised accounting standards. As a result of this election, the Company's financial statements may not be comparable to companies that comply with public company FASB standards' effective dates.

Recently Adopted Accounting Pronouncements

In November 2023, the FASB issued Accounting Standard Update (ASU) 2023-07 – Segment Reporting (Topic 280) – Improvements to Reportable Segment Disclosures, which intends to improve financial reporting, primarily through enhanced disclosure requirements for significant segment expenses. ASU 2023-07 applies to all public entities that are required to report segment information, including those with only one reportable segment. The Company adopted the guidance in the fiscal year beginning January 1, 2024 and there was no impact on the Company's reportable segments identified. For further information, refer to the "Segment Reporting" section in this Note 2 and in Note 14 "Segment Information."

Recently Issued Accounting Pronouncements Pending Adoption

In December 2023, the FASB issued ASU No. 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures (ASU 2023-09) to improve the transparency of income tax disclosures by requiring consistent categories and greater disaggregation of information in the effective tax rate reconciliation and income taxes paid disaggregated by jurisdiction. ASU 2023-09 also includes certain other amendments to improve the effectiveness of income tax disclosures. This new standard will be effective for annual periods beginning after December 15, 2024. The new standard permits early adoption and can be applied prospectively or retrospectively. The Company does not expect the adoption of this guidance to have a material impact on its financial statements.

In November 2024, the FASB issued ASU No. 2024-03, Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses (ASU 2024-03). The new guidance requires more detailed information about specified types of expenses (including purchases of inventory, employee compensation, depreciation, amortization, and depletion) in commonly presented expense captions (such as R&D and G&A) presented on the face of the statement of operations on an annual and interim basis. This guidance will be effective for annual periods beginning after December 15, 2026, and interim periods beginning after December 15, 2027. The new standard permits early adoption and can be applied prospectively or retrospectively. The Company is evaluating the effect that this guidance will have on its financial statements and related disclosures.

3. Fair Value Measurements

The following tables summarize the Company's financial assets measured at fair value on a recurring basis and their respective input levels based on the fair value hierarchy described in Note 2 above (in thousands):

			Fair	Jsing			
As of December 31, 2024	Amount		Level 1		Level 2		Level 3
Assets							
Money market funds (1)	\$ 24,889	\$	24,889	\$		\$	
U.S. government obligations (2)	118,289				118,289		
Corporate debt securities (2)	7,238				7,238		
Total fair value of assets	\$ 150,416	\$	24,889	\$	125,527	\$	

(1) Included in cash and cash equivalents on the balance sheets.

(2) Included in short-term investments on the balance sheets.

		Fair Value Measurements Using					
As of December 31, 2023	Amount	Level 1		Level 2		Level 3	
Assets							
Money market funds (1)	\$ 21,737	\$ 21,737	\$		\$		
U.S. government obligations (2)	92,143			92,143			
Corporate debt securities (2)	4,903			4,903			
Total fair value of assets	\$ 118,783	\$ 21,737	\$	97,046	\$		

(1) Included in cash and cash equivalents on the balance sheets.

(2) Included in short-term investments on the balance sheets.

The Company's money market funds are classified as Level 1 because they are valued using quoted market prices in active markets for identical assets. The Company's investments consist of available-for-sale securities and are classified as Level 2 because their value is based on valuations using significant inputs derived from or corroborated by observable market data.

There were no transfers of assets between fair value levels for any period presented.

4. Investments

The following tables summarize investments accounted for as available-for-sale securities (in thousands):

			As of Decem	ber 31, 2	024		
	A	cquisition Cost	Unrealized Gain	Un	realized Loss	Est	timated Fair Value
Money market funds	\$	24,889	\$ 	\$		\$	24,889
U.S. government obligations		118,170	121		(2)		118,289
Corporate debt securities		7,236	2				7,238
Total cash equivalents and investments	\$	150,295	\$ 123	\$	(2)	\$	150,416
Classified as:			 				
Cash equivalents						\$	24,889
Short-term investments							125,527
Total cash equivalents and investments						\$	150,416

			As of Decem	ber 31	1, 2023		
A	cquisition		Unrealized		Unrealized	Es	stimated Fair
	Cost		Gain		LOSS		value
\$	21,737	\$	—	\$	—	\$	21,737
	92,106		58		(21)		92,143
	4,900		5		(2)		4,903
\$	118,743	\$	63	\$	(23)	\$	118,783
						\$	21,737
							97,046
						\$	118,783
	A \$ \$	Acquisition Cost \$ 21,737 92,106 4,900 \$ 118,743	Acquisition Cost \$ 21,737 \$ 92,106 4,900 \$ 118,743 \$	As of Decem Acquisition Cost Unrealized Gain \$ 21,737 \$ 92,106 58 4,900 5 \$ 118,743 \$ 63	As of December 31 Acquisition Cost Unrealized Gain \$ 21,737 \$ \$ 92,106 58 4,900 5 \$ 118,743 \$ 63 \$	As of December 31, 2023 Acquisition Unrealized Unrealized Cost Gain Loss \$ 21,737 \$ — \$ — 92,106 58 (21) 4,900 5 (2) \$ 118,743 \$ 63 \$ (23)	As of December 31, 2023 Acquisition Unrealized Unrealized Es $Cost$ $Gain$ $Loss$ Es $\$$ 21,737 $\$$ $ \$$ $92,106$ 58 (21) $4,900$ 5 (2) $\$$ 118,743 $\$$ 63 $\$$ (23) $\$$ $\$$ 5 5 $$$ $$$ $$$ $$$ $$$ $\$$ $$$ $$$ $$$ $$$ $$$ $$$ $\$$ $$$ $$$ $$$ $$$ $$$ $$$ $\$$ $$$ $$$ $$$ $$$ $$$ $$$ $\$$ $$$ $$$ $$$ $$$ $$$ $$$ $\$$ $\$$ $$$ $$$ $$$ $$$ $$$ $\$$ $\$$ $\$$ $$$ $$$ $$$ $$$

On December 31, 2024 and 2023, the remaining contractual maturities of all the Company's available-for-sale investments were less than twelve months. As of December 31, 2024 and 2023, the Company has not established an allowance for credit losses for any of its available-for-sale securities.

As of December 31, 2024, there was one available-for-sale security, with an estimated fair value of \$8.0 million in a gross unrealized loss position. As of December 31, 2023, there were 24 available-for-sale securities, with an estimated fair value of \$40.3 million in gross unrealized loss positions. Based on its review of these investments as of December 31, 2024 and 2023, the Company believed that the unrealized losses as of December 31, 2024 and 2023 reflected the impact of the rising interest rate environment and were not other-than-temporary in nature.

5. Property and Equipment

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

	 As of December 31,			
	2024		2023	
Lab equipment	\$ 4,338	\$	4,264	
Computers and software	895		833	
Leasehold improvements	981		46	
Furniture and fixtures	 1,816		157	
Total property and equipment	8,030		5,300	
Less accumulated depreciation and amortization	3,709		2,727	
Property and equipment, net	\$ 4,321	\$	2,573	

Depreciation and amortization expense related to property and equipment was \$1.1 million and \$1.0 million for the years ended December 31, 2024 and 2023, respectively.

6. Accounts Payable and Accrued Liabilities

Accounts payable and accrued liabilities consisted of the following (in thousands):

	 As of December 31,			
	 2024		2023	
Accounts payable	\$ 1,274	\$	2,222	
Accrued research and development costs	2,584		1,575	
Other accrued liabilities	1,496		469	
Total accounts payable and accrued liabilities	\$ 5,354	\$	4,266	

7. Lease Agreements

Operating leases

As of December 31, 2024, the Company has one facility lease for lab and office space under a non-cancellable operating lease that expires in 2034. Total lease costs were approximately \$4.0 million and \$2.6 million, including operating lease costs of \$3.6 million and \$2.6 million, and variable lease costs of \$0.4 million and \$0 during the years ended December 31, 2024 and 2023, respectively. The Company paid \$2.6 million and \$2.8 million in cash for operating leases that were included in the operating activities section of the statements of cash flows for the years ended December 31, 2024 and 2023, respectively. The remaining lease term and the discount rate of the Company's operating lease was 9.8 years and 8.3% at December 31, 2024. The remaining lease term and the discount rate of the Company's operating lease was 0.8 years and 8.0% at December 31, 2023. The remaining lease term does not include any renewal options at the election of the Company. The Company's lease agreement does not contain any material residual value guarantees or material restrictive covenants.

2022 Lease

In March 2021, the Company entered into a non-cancelable operating lease for a facility in San Diego, California, which was amended in November 2021 (as amended, the 2022 Lease). The term of the 2022 Lease ended in November 2024. The 2022 Lease provided for the rental of lab and office space, contained rent escalation provisions, and required the Company to pay a portion of the operating costs related to the underlying multi-tenant facility. Based on the terms of the lease, the Company recorded a ROU asset and an associated lease liability based on the present value of the lease payments using an estimated incremental borrowing rate of

approximately 8.0% as the 2022 Lease did not have a stated rate and the implicit rate was not readily determinable. The net ROU asset of \$0 and \$2.0 million and associated lease liability of \$0 and \$2.2 million are reflected in the Company's balance sheet as of December 31, 2024 and 2023, respectively.

As of December 31, 2024, there are no future minimum lease payments required under the 2022 Lease as the term of the lease ended in November 2024.

2024 Lease

In December 2021, the Company entered into a non-cancelable facility lease for approximately 80,168 square feet of lab and office space in San Diego, California (the 2024 Lease). The 2024 Lease commenced in November 2024 and has a 120-month term from the lease commencement date, with base rent payments under the lease commencing in July 2025, after an abatement period of 270 consecutive calendar days, and continuing through the conclusion of the term. The 2024 Lease includes base rent payments totaling \$72.5 million, as well as additional payment obligations for common area maintenance and property taxes. The Company has the right to extend the term of the 2024 Lease for an additional 60 months; however, this option has not been included in the lease term as it is not reasonably assured of exercise. Additionally, as a security deposit under the 2024 Lease, the Company is required to maintain a standby letter-of-credit in the amount of \$560,000, which must remain in place until November 2034 and is classified as restricted cash on the balance sheet. The Company has recorded an operating lease liability based on the present value of the lease payments using an estimated incremental borrowing rate of approximately 8.3% as the 2024 Lease does not have a stated rate and the implicit rate was not readily determinable, and an ROU asset based on the corresponding operating lease liability. The net ROU asset and associated lease liability are reflected in the Company's balance sheet as of December 31, 2024.

Future minimum lease payments under the 2024 Lease as of December 31, 2024, exclusive of future variable lease payments, are as follows (in thousands):

Year ending December 31, 2025 \$ 2,628 2026 7,056 2027 7,259 2028 7.469 2029 7,684 Thereafter 40,387 \$ Total minimum lease payments 72,483 Less: Amount representing interest (24, 851)Operating lease liabilities \$ 47,632

8. Commitments and Contingencies

Contracts

The Company enters into contracts in the normal course of business with various third parties for preclinical research studies, clinical trials, testing, manufacturing, and other services. These contracts generally provide for termination upon notice and are cancellable without significant penalty or payment and do not contain any minimum purchase commitments.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with officers and members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as officers or directors. The maximum potential future payments the Company could be required to make under these indemnification arrangements is, in many cases, unlimited. To date, the Company has not incurred any material costs because of these indemnifications. The Company has not accrued any liabilities related to

such indemnification arrangements in its financial statements as of December 31, 2024 or 2023 because it determined the likelihood of incurring a payment obligation pursuant to such arrangements was not probable.

Litigation

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, penalties, and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. There are no matters currently outstanding for which any liabilities have been accrued. The Company was not a defendant in any lawsuit for the years ended December 31, 2024 and 2023.

9. Convertible Preferred Stock

Series A, B, and C Convertible Preferred Stock

The Company issued its previously outstanding convertible preferred stock in a series of transactions as follows:

- In August 2018, 7,142,857 shares of Series A convertible preferred stock were issued for cash at a price of \$0.70 per share, resulting in aggregate net proceeds of \$4.9 million;
- In June 2019, an additional 26,046,438 shares of Series A convertible preferred stock were issued for cash at a price of \$0.70 per share, resulting in aggregate net proceeds of \$18.1 million;
- In July 2020, an additional 33,189,295 shares of Series A convertible preferred stock were issued for cash at a price of \$0.70 per share, resulting in aggregate net proceeds of \$23.2 million;
- In April 2021, 78,211,116 shares of Series B convertible preferred stock were issued for cash at a price of \$1.35 per share, resulting in aggregate net proceeds of \$105.3 million;
- In April and May 2023, 142,857,138 shares of Series C convertible preferred stock were issued for cash at a price of \$0.70 per share, resulting in aggregate net proceeds of \$99.7 million.

Common Stock Issued for Conversion of Convertible Preferred Stock

Immediately prior to the closing of the IPO on April 2, 2024, the Company's outstanding convertible preferred stock automatically converted into 14,740,840 shares of common stock, as adjusted for the reverse stock split. Following the closing of the IPO, no shares of convertible preferred stock were authorized or outstanding.

10. Common Stock

Common Stock Rights

The holder of each outstanding share of common stock is entitled to one vote on all matters submitted to a vote of the holders of common stock. Subject to the rights of the holders of any class of the Company's capital stock having any preference or priority over common stock, the holders of common stock are entitled to receive dividends that are declared by the Company's board of directors out of legally available funds. In the event of a liquidation, dissolution or winding-up, the holders of common stock are entitled to share ratably in the net assets remaining after payment of liabilities and the liquidation value of any class of the Company's capital stock having any preference or priority over the common stock then outstanding, if any. The common stock has no preemptive rights, conversion rights, redemption rights, preference rights, or exchange rights, or sinking fund provisions, and there are no dividends in arrears or default. All shares of common stock have equal distribution, liquidation and voting rights.

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance consisted of the following (in thousands):

	As of Dece	As of December 31,			
	2024	2023			
Conversion of outstanding convertible preferred stock		14,741			
Common stock options issued and outstanding	3,818	2,814			
Equity awards available for future issuance	2,648	861			
Shares available for purchase under the ESPP	187	_			
Total	6,653	18,416			

11. Stock-Based Compensation

Equity Incentive Plan

In March 2024, the Company's board of directors adopted, and the Company's stockholders approved, the 2024 Incentive Award Plan (the Plan), which became effective in connection with the IPO and has a term of ten years. The Plan provides for the grant of incentive stock options, nonqualified stock options, restricted stock, dividend equivalents, restricted stock units, stock appreciation rights, and other stock or cash-based awards to the Company's employees, consultants, and directors. Options granted under the Plan are exercisable at various dates as determined upon grant and will expire no more than 10 years from their date of grant. Stock options generally vest over terms of either 36 or 48 months. The exercise price of awards granted under the Plan shall not be less than 100% of the fair market value of the Company's common stock on the date of grant. In addition, the Plan includes an "evergreen" provision whereby the number of shares of common stock available for issuance under the Plan will be increased annually on the first day of each calendar year during the term of the Plan, beginning in 2025, by an amount equal to the lesser of (i) 5% of the shares of common stock outstanding on the final day of the immediately preceding calendar year or (ii) such number of shares as determined by the Company's board of directors or an authorized committee of the board of directors. As of December 31, 2024, a total of 2,832,714 shares of common stock were authorized for issuance under the Plan, the aggregate number of shares that may be issued under the Plan. On January 1, 2025, pursuant to the evergreen provision of the Plan, the aggregate number of shares that may be issued under the Plan was automatically increased by 1,115,002 shares to 3,947,716.

Prior to the adoption of the Plan, the Company had awarded common stock options under the 2018 Equity Incentive Plan (as amended, the Predecessor Plan). Under the provisions of the Plan, the shares subject to awards issued under the Predecessor Plan that were outstanding as of March 27, 2024, the effective date of the Plan, and that are subsequently cancelled or forfeited, will become available for issuance under, and will increase the number of shares that may be issued under, the Plan.

Repricing of Outstanding Options

In August 2024, the compensation committee of the Company's board of directors, as administrator of the Plan and the Predecessor Plan, approved an option repricing (2024 Repricing), which was effective on August 19, 2024 (the Repricing Effective Date). The repricing applied to options to purchase up to an aggregate of 3,484,346 shares of the Company's common stock with an exercise price per share in excess of the closing price per share of the Company's common stock on the Repricing Effective Date, held by eligible employees of the Company that were granted under the Plan or the Predecessor Plan and were outstanding as of the Repricing Effective Date (the Repriced Options). As of the Repricing Effective Date, the exercise price of each of the Repriced Options was reduced to \$3.56 per share, which was the closing price of the Company's common stock on the Repricing Effective Date; provided, however, that if prior to the Premium End Date (as defined below), a Repriced Option is exercised or an employee's employment or service with the Company terminates for any reason other than due to a Qualifying Termination (as defined below), the exercise price. The "Premium End Date" means the earliest of: (1) August 19, 2026, (2) the date immediately prior to the closing of a Change in Control (as defined in the Plan), or (3) the date of the employee's Qualifying Termination. A "Qualifying Termination" means (a) the involuntary termination of the employee's employment by the Company due to a reduction in force (and other than for Cause (as defined in the Plan)), subject to the employee's employment by the Company due to a reduction in force (and other than for Cause (as defined in the Plan)), subject to the employee's employment by the Company following the employee's Disability (as defined in the Plan). Except

for the reduction in the exercise prices of the Repriced Options as described above, the Repriced Options retain their existing terms, including their respective original vesting schedules.

The repricing resulted in a total incremental non-cash stock-based compensation expense of \$857,000, which was calculated using the Black-Scholes option-pricing model, of which \$157,000 is associated with vested Repriced Options and will be recognized on a straight-line basis through the Premium End Date. The remaining \$700,000 of the incremental non-cash stock-based compensation expense is associated with unvested Repriced Options and will be recognized as follows: (i) if the Premium End Date occurs later than the end of the remaining vesting period of the Repriced Option, the incremental cost will be amortized on a straight-line basis through the Premium End Date occurs earlier than the end of the remaining vesting period of the Repriced Option, the incremental cost will be amortized on a straight-line basis over the remaining vesting period. During the year ended December 31, 2024, the Company recognized incremental stock-based compensation expense totaling \$106,000 associated with the 2024 Repricing.

In June 2023, the Company's board of directors approved an option repricing to reprice certain underwater options to purchase the Company's shares of common stock held by its employees (including officers of the Company) and non-employee directors. Under this option repricing, options with an exercise price at or above \$9.75 per share, representing an aggregate of 1,019,029 shares of common stock, were amended to reduce such exercise price to \$4.10 per share. This repricing resulted in one-time stock-based compensation expense in the year ended December 31, 2023 of approximately \$263,000 related to vested options and incremental stock option expense of approximately \$377,000 related to unvested options which will be amortized on a straight-line basis over the remaining vesting period of those options.

Stock Options

Stock option activity under the Plan and the Predecessor Plan and certain other related information is as follows (in thousands except weighted-average exercise price and remaining term):

	Number	Weighted- Average Exercise Price	Weighted- Average Remaining Term (years)	Aggregate- Intrinsic Value
Balance as of December 31, 2023	2,814	\$ 4.10	7.8	\$ 562
Granted	4,980	\$ 7.70		
Exercised	(16)	\$ 3.86		
Forfeited and expired	(3,960)	\$ 6.46		
Balance as of December 31, 2024	3,818	\$ 6.37	7.2	\$
Vested and expected to vest at December 31, 2024	3,818	\$ 6.37	7.2	\$
Exercisable as of December 31, 2024	1,861	\$ 5.13	6.1	\$ _

Aggregate intrinsic value in the above table is the difference between the estimated fair value of the Company's common stock as of either December 31, 2024 or 2023, and the exercise price of stock options that had exercise prices below that value.

For the Repriced Options, the calculation of the weighted-average prices and intrinsic value information in the table above is based on the exercise price per share that applied immediately prior to the Repricing Effective Date pending satisfaction of the requisite service requirement.

The options exercised during the years ended December 31, 2024 and 2023 had an insignificant intrinsic value at exercise.

Employee Stock Purchase Plan

In March 2024, the Company's board of directors adopted, and the Company's stockholders approved, the Company's 2024 Employee Stock Purchase Plan, which became effective in connection with the IPO. The ESPP permits participants to contribute up to a specified percentage of their eligible compensation during a series of offering periods of 24 months, each comprised of four six-month purchase periods, to purchase shares of the Company's common stock. The purchase price of the shares will be 85% of the fair market value of the Company's common stock on the first day of trading of the applicable offering period or on the applicable purchase date, whichever is lower. A total of 231,919 shares of common stock were initially reserved for issuance under the ESPP. In addition, the ESPP includes an "evergreen" provision whereby the number of shares of common stock available for issuance under the ESPP will be increased annually on the first day of each calendar year during the term of the ESPP, beginning in 2025, by an amount equal to the

lesser of (i) 1% of the shares of common stock outstanding on the final day of the immediately preceding calendar year or (ii) such number of shares as determined by the Company's board of directors or an authorized committee of the board of directors. On January 1, 2025, pursuant to the evergreen provision of the ESPP, the aggregate number of shares that may be issued under the ESPP was automatically increased by 223,000 shares to 454,919.

The Company recognized stock-based compensation expense related to the ESPP of \$0.5 million and \$0 for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, the unrecognized compensation cost related to the ESPP was \$0.9 million which is expected to be recognized as expense over approximately 1.5 years.

The Company issued and sold 44,532 and 0 shares under the ESPP during the years ended December 31, 2024 and 2023, respectively.

Stock-Based Compensation Expense

Stock-based compensation expense, including the expense related to the ESPP, as recorded in the accompanying statements of operations and comprehensive loss was as follows (in thousands was as follows (in thousands):

	 Year En December	ded · 31,	
	2024		2023
Research and development	\$ 3,050	\$	1,420
General and administrative	4,466		1,916
Total stock-based compensation	\$ 7,516	\$	3,336

As of December 31, 2024, unrecognized compensation cost related to outstanding stock options (all of which have time-based vesting) was \$15.3 million, which is expected to be recognized over a weighted-average period of 2.5 years.

As of December 31, 2024, unrecognized compensation cost related to the ESPP was \$0.9 million, which is expected to be recognized as expense over approximately 1.5 years.

Excluding any effect of the Repriced Options, the weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of the stock options granted during the periods indicated in the table were as follows:

	Year Ei December	Year Ended December 31,		
	2024	2023		
Expected option life (in years)	6.0	6.0		
Assumed volatility	90.8%	6 92.4%		
Assumed risk-free interest rate	3.9%	6 3.9%		
Expected dividend yield		_		

Excluding any effect due to the Repriced Options, the weighted-average grant date per share fair value of options granted during the years ended December 31, 2024 and 2023 were \$7.19 and \$3.23, respectively.

12. Income Taxes

The Company is subject to taxation in the United States and certain states therein, however, due to the net losses incurred in each of the years ended December 31, 2024 and 2023, the Company has not recorded a provision for income taxes for either year. A reconciliation of the federal statutory tax rate and the Company's effective tax rate is as follows:

	Year Ended D	ecember 31,
	2024	2023
Federal statutory income tax rate	21.0%	21.0%
State income taxes, net of federal benefit	6.3	6.6
Tax credits	6.7	7.0
Change in valuation allowance	(31.5)	(23.0)
Other permanent differences	—	
Stock compensation	(0.9)	(0.7)
Uncertain tax position	(1.6)	(11.0)
Other		0.1
Effective income tax rate	%	%

The Company has established a full valuation allowance against its net deferred tax assets due to the uncertainty surrounding the realization of such assets that preclude it from determining that is more likely than not that such assets will be realized. The Company periodically evaluates the recoverability of the deferred tax assets. When it is determined that it is more likely than not that deferred assets are realizable, the valuation allowance will be reduced. Management's assessment as of December 31, 2024 and 2023 considered the generation of pre-tax book losses, no ability to carryback its operating losses, the lack of feasible tax-planning strategies, the limited existing taxable temporary differences, and the subjective nature of forecasting future taxable income. During 2024 and 2023, total deferred tax assets increased by \$20.5 million and \$11.3 million, respectively. Due to its full valuation allowance position, the Company's valuation allowance increased by the same amount during those time periods.

Deferred Tax Assets and Liabilities

As of December 31, 2024 and 2023, the significant components of deferred income taxes are as follows (in thousands):

	As of December 31,			
	 2024		2023	
Deferred tax assets:				
Net operating loss carryforward	\$ 27,618	\$	18,327	
Research tax credits	8,313		5,052	
Lease liability	13,335		615	
Capitalized R&D	20,155		13,396	
Intangible assets	44		48	
Other, net	2,637		1,567	
Total deferred tax assets	72,102		39,005	
Less valuation allowance	(58,844)		(38,323)	
Net deferred tax assets	13,258		682	
Deferred tax liabilities:				
ROU asset	(13,169)		(561)	
Property and equipment	 (89)		(121)	
Total deferred tax liabilities	 (13,258)		(682)	
Net deferred tax assets	\$ 	\$		

As of December 31, 2024 and 2023, federal net operating loss (NOL) carryforwards totaled \$91.9 million and \$66.4 million, respectively, before consideration of limitations under Section 382 of the Internal Revenue Code of 1986, as amended (IRC). The Company also had state NOL carryforwards of \$183.3 million and \$127.0 million as of December 31, 2024 and 2023, respectively. Unused federal NOLs carry forward indefinitely, while unused state NOL carryforwards begin to expire in 2038. As of December 31, 2024 and 2023, federal research tax credit carryforwards totaled approximately \$7.7 million and \$4.5 million, respectively, and state research tax credit carryforwards totaled approximately \$4.9 million and \$3.4 million, respectively. Unused federal credits begin to expire in 2040, while the unused state credits carry forward indefinitely.

Pursuant to IRC Sections 382 and 383, the Company's ability to use its NOL and research tax credit carry forwards to offset future taxable income may be limited if the Company experiences a cumulative change in ownership of more than 50% within a three-year testing period. The Company has not completed an ownership change analysis pursuant to IRC Section 382. If ownership changes within the meaning of IRC Section 382 are identified as having occurred, the amount of NOL and research tax carryforwards available to offset

future taxable income and income tax liabilities in future years may be significantly reduced, restricted, or eliminated. The Company has also not performed a formal research and development credit study with respect to these credits. As such, the amount of such credits may be reduced in the future should the Company complete such a study. Moreover, deferred tax assets associated with such NOLs and research tax credits could be significantly reduced upon realization of an ownership change within the meaning of IRC Section 382.

The Inflation Reduction Act of 2022 (IRA), which incorporates a Corporate Alternative Minimum Tax (CAMT), requires companies to compute two separate calculations for federal income tax purposes and pay the greater of the new minimum tax or their regular tax liability.

The Tax Cuts and Jobs Act of 2017 requires taxpayers to capitalize and amortize R&D expenditures over five years for domestic research and 15 years for foreign research pursuant to Section 174 of the IRC.

There are no accruals for interest or tax penalties in the accompanying balance sheets, and the Company has not recognized any such interest or tax penalties in the accompanying statements of operations and comprehensive loss.

Although it is not currently under a tax examination, all of the Company's tax years remain open to audit in all of the tax jurisdictions in which it operates due to the Company's net operating losses carryforwards.

Uncertain Tax Benefits

Activity in the Company's gross unrecognized tax benefits was as follows (in thousands):

	 Year Ended December 31,			
	2024		2023	
Balance at beginning of period	\$ 8,048	\$	1,198	
Increase related to current year positions	1,164		982	
Increase related to prior year positions	 		5,868	
Balance at the end of the year	\$ 9,212	\$	8,048	

Company policy is to recognize a tax benefit from uncertain tax positions when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, based on the technical merits. Due to the existence of the full valuation allowance, future changes in unrecognized tax benefits will not impact the Company's effective tax rate. The Company does not foresee any material changes to its liability for uncertain tax benefits within the next twelve months.

13. Net Loss Per Common Share

The following table summarizes the calculation of basic and diluted net loss per common share attributable to common stockholders (in thousands, except per share data):

	 Year I Decem	Ended ber 31,	
	2024		2023
Net loss	\$ (65,363)	\$	(49,434)
Weighted-average shares of common stock used in			
computing net loss per share, basic and diluted	16,984		1,216
Net loss per share, basic and diluted	\$ (3.85)	\$	(40.65)

The Company excluded the following potential shares of its common stock, presented based on amounts outstanding at each period end, from the calculation of diluted net loss per share for the periods indicated because including them would have had an antidilutive effect (in thousands):

	As of Dece	mber 31,
	2024	2023
Conversion of outstanding convertible preferred stock		14,741
Options to purchase common stock	3,818	2,814
Options early exercised subject to future vesting		1
Total	3,818	17,556

14. Segment Information

The CODM reviews the budget versus actual expense by nature of expense. We have applied ASU 2023-07 retrospectively for the years ended December 31, 2024 and 2023. The following table sets forth our segment loss disclosure for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,			
		2024		2023
R&D – Compensation and benefits (1)	\$	13,758	\$	12,262
R&D – Clinical trial costs		11,507		4,075
R&D – Outsourced services & Consulting		19,022		17,482
R&D – Lab and pharmacology supplies		2,295		3,266
R&D - Other costs (2)		1,818		1,356
G&A – Compensation and benefits (1)		6,438		5,200
G&A – Professional service fees		2,866		2,494
G&A – Insurance		678		90
G&A - Other costs (3)		2,333		1,667
Facilities related		3,951		2,611
Stock-based compensation and depreciation		8,601		4,293
Total operating expense		73,267		54,796
Loss from operations		(73,267)		(54,796)
Interest and other income, net		7,904		5,362
Segment net loss	\$	(65,363)	\$	(49,434)

(1) Excludes stock-based compensation expense.

(2) Includes software expense, database subscriptions expense, lab service contract expense, travel expense, and other miscellaneous expenses.

(3) Includes travel expense, public & investor relations expense, software expense, employee training & development expense, and other miscellaneous expenses.