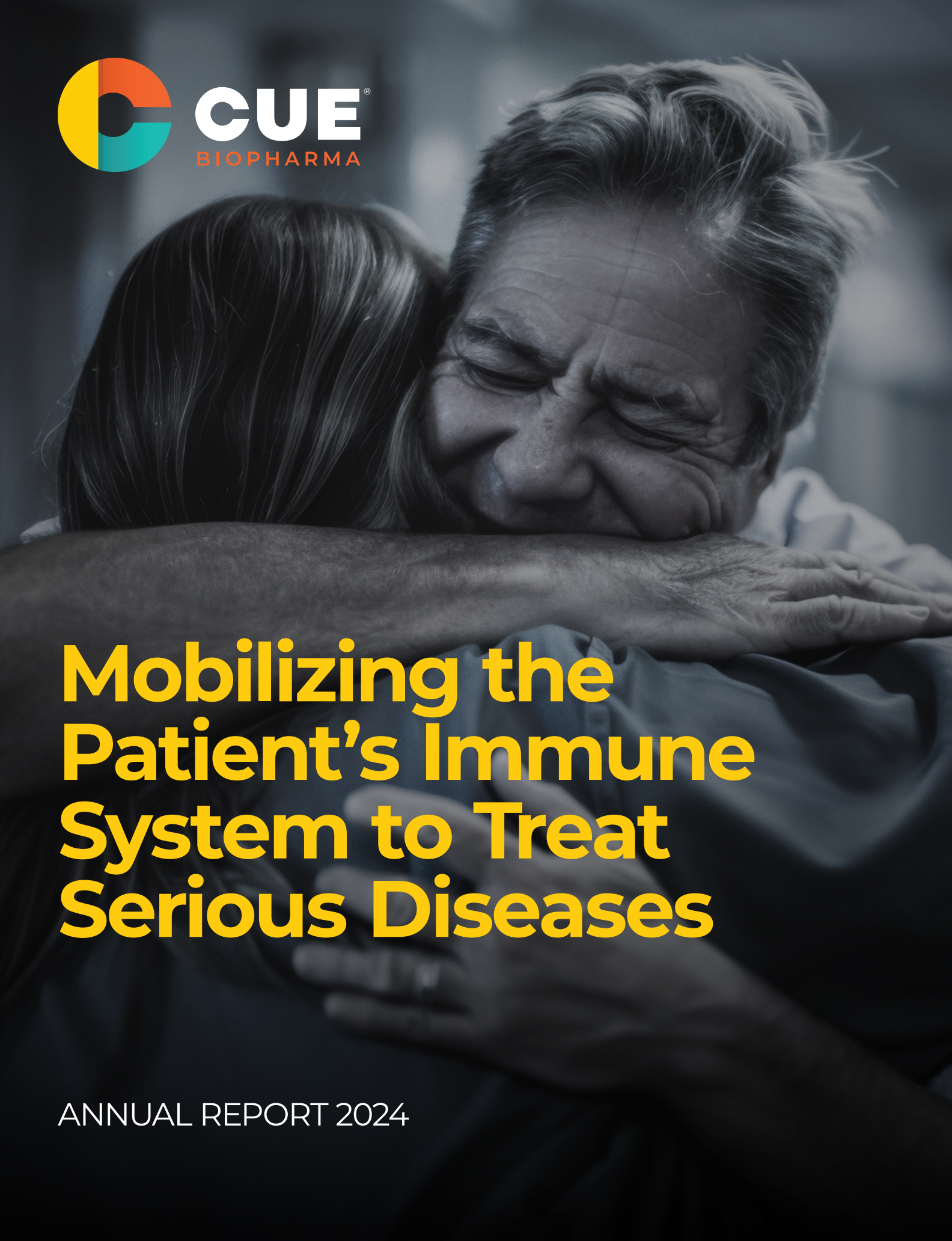


CUE BIOPHARMA

Mobilizing the Patient's Immune System to Treat Serious Diseases

ANNUAL REPORT 2024

About Cue Biopharma

Cue Biopharma, a clinical-stage biopharmaceutical company, is developing a novel class of therapeutic biologics to selectively engage and modulate disease-specific T cells for the treatment of cancer and autoimmune disease.

The company's proprietary platform, Immuno-STAT™ (*Selective Targeting and Alteration of T cells*) and biologics are designed to harness the curative potential of the body's intrinsic immune system through the selective modulation of disease-specific T cells without the adverse effects of broad systemic immune modulation.

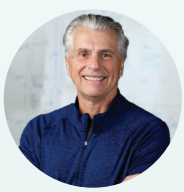
Headquartered in Boston, Massachusetts the company is led by an experienced management team with deep expertise in immunology and protein engineering as well as the design and clinical development of protein biologics.

Management Team

Daniel Passeri, M.Sc., J.D.
Chief Executive Officer

Lucinda Warren
Chief Business Officer

Matteo Levisetti, M.D.
Chief Medical Officer



Daniel Baker, M.D.
Interim Chief Development Officer

Kerri-Ann Millar, CPA
Chief Financial Officer

Colin Sandercock, M.S.E., J.D.
Senior Vice President & General Counsel

Board of Directors

Frank Morich, M.D., Ph.D.
Chairman of the Board

Fred Driscoll
Former Chief Financial Officer at Flexion Therapeutics

Pasha Sarraf, M.D., Ph.D.
Chairman of Praesidia Biotherapeutics

Daniel Passeri, M.Sc., J.D.
Chief Executive Officer

Patrick Verheyen
Former, Global Head, Janssen Business Development at Johnson and Johnson

Peter Kiener, D.Phil.
Former Chief Scientific Officer at Sucampo

Pamela D. Garzone, Ph.D.
Chief Development Officer, Anixa Biosciences

APRIL 2025

Dear Cue Biopharma Shareholders,

To address the ongoing challenges confronting the biotechnology sector, we have prioritized our resources and focused our efforts on our autoimmune programs while enabling the clinical survival data from our ongoing CUE-101 and CUE-102 Phase 1 oncology trials to mature. We believe this maturing survival data will position us to pursue strategic partnerships to continue clinical development of the CUE-100 series and differentiate its targeted approach over competing programs within the oncology sector. Through this approach, it is our aim to position Cue Biopharma with an optimized, balanced business model that provides strategic flexibility for partnering specific programs while retaining control over prioritized, potentially disruptive drug product candidates that we believe represent breakthrough market potential.

Our strategy is exemplified by the CUE-501 program, designed to target and deplete B cells to rebalance the immune system in patients with autoimmune disease caused by autoreactive, pathogenic B cells. We have entered into a strategic research and development collaboration and license agreement with Boehringer Ingelheim (BI), which we believe underscores the promise and importance of our approach. Through this partnership we have successfully gained access to capital resources and support for the CUE-501 program. By collaborating with BI as our strategic partner for the development of CUE-501, the first asset in our novel CUE-500 series, we have enabled the potential derisking and validation of not only CUE-501, but also the CUE-500 series, which is designed to target various pathogenic cell types.

As part of our core strategy, we also successfully regained worldwide development and commercialization rights for CUE-401 from Ono Pharmaceuticals, enabling us to control and further develop what we believe to be a high impact, disruptive and differentiated asset, with the

Shareholder Letter (Cont'd)

We believe regaining worldwide rights and control for CUE-401 and the recent partnership with BI place us in a position of strength to further advance CUE-401 toward the clinic, while exploring additional portfolio optimization to further our core objectives.

potential to establish a new standard of care for treating autoimmune disease. To date, we have made significant progress in the preclinical development of CUE-401, which has led to the identification of a lead candidate and initiation of Investigational New Drug (IND) enabling studies. Preclinical data continues to support the premise that CUE-401 selectively expands and induces stable and durable T regulatory cells (Tregs) —both natural Tregs (nTregs) and induced (iTregs)— that are functionally suppressive of the autoimmune disease-causing cells in preclinical models of disease. Additional preclinical studies across multiple animal species have provided a body of mechanistic and tolerability data further providing insights toward the potential translation to human clinical studies. We believe regaining worldwide rights and control for CUE-401 and the recent partnership with BI place us in a position of strength to further advance CUE-401 toward the clinic, while exploring additional portfolio optimization to further our core objectives.

During 2024, we also strengthened our corporate and clinical development capabilities with the addition of key high-profile appointments: industry veteran Lucinda Warren as chief business officer, Daniel Baker, M.D., as interim chief development officer and Pasha Sarraf, M.D., Ph.D. as a member of our Board of Directors. Their collective areas of expertise in business development, portfolio optimization and clinical drug development in autoimmune and inflammatory disease have proven instrumental in driving recent strategic initiatives.

We would like to extend our sincere thanks and appreciation to our committed shareholders, passionate employees, board of directors, scientific advisory board, clinical investigators and our collaboration partners for their continued support, guidance and trust. Most importantly, we extend our profound appreciation and respect to the patients who have participated in our clinical trials, and their families, enabling us to gain insights and knowledge essential for continued progress forward in our mission to establish more effective standards of care in the fight against cancer, autoimmune disease and other debilitating diseases.

Sincerely,

Daniel Passeri, M.Sc., J.D.
Chief Executive Officer

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

☐ **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: 001-38327

Cue Biopharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**47-3324577**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
40 Guest Street Boston, MA	**02135**
(Address of principal executive offices)	**(Zip Code)**

(617) 949-2680
(Registrant's telephone number, including area code)

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

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

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

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

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

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

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

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

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

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

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

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 Act): Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, as of the last business day of the registrant's most recently completed second fiscal quarter, was approximately $59.9 million (based on the closing price of the registrant's common stock on June 28, 2024 of $1.24 per share).

As of March 27, 2025, the registrant had 61,819,101 shares of Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days after the end of the fiscal year ended December 31, 2024. Portions of such proxy statement are incorporated by reference into Part III of this Form 10-K.

CUE BIOPHARMA, INC.
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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS 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, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements, which are based on certain assumptions and describe our future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such as "believe," "expect," "may," "will," "should," "would," "could," "seek," "intend," "plan," "goal," "project," "estimate," "anticipate," "strategy," "future," "likely" or other comparable terms. All statements, other than statements of historical fact, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the initiation, timing, progress and results of our ongoing and planned preclinical studies and any future clinical trials and our research and development programs;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing;
- our expectations regarding our ability to fund our projected operating requirements with our existing cash resources and the period in which we expect that such cash resources will enable us to fund such operating requirements;
- our plans to develop our drug product candidates, including our intention to prioritize our autoimmune programs, including CUE-401 and CUE-501;
- our plans to pursue third party support through partnerships and collaborations to further develop the CUE-100 series programs, including CUE-101 and CUE-102, as well as CUE-501;
- the timing of and our ability to submit applications for, and to obtain and maintain regulatory approvals for, our drug product candidates;
- the potential advantages of our drug product candidates;
- the rate and degree of market acceptance and clinical utility of our drug product candidates, if approved;
- our estimates regarding the potential market opportunity for our drug product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional products, drug product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to continue as a going concern; and
- our ability to maintain and establish collaborations or obtain additional funding.

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include the factors discussed below under the heading "Risk Factor Summary," and the risk factors detailed further in Item 1A., "Risk Factors" of Part I of this Annual Report on Form 10-K.

This report includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this report

involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our drug product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Any forward-looking statement made by us in this Annual Report on Form 10-K is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

RISK FACTOR SUMMARY

Investment in our securities involves risk. You should carefully consider the following summary of what we believe to be the principal risks facing our business, in addition to the risks described more fully in Item 1A, "Risk Factors" of Part I of this Annual Report on Form 10-K and other information included in this report. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations.

If any of the following risks occurs, our business, financial condition and results of operations and future growth prospects could be materially and adversely affected, and the actual outcomes of matters as to which forward-looking statements are made in this report could be materially different from those anticipated in such forward-looking statements.

- Our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern.
- We are a clinical-stage biopharmaceutical company, have no history of generating commercial revenue, have a history of operating losses and may never achieve or maintain profitability.
- We currently do not have, and may never develop, any FDA-approved or commercialized products.
- We are substantially dependent on the success of our drug product candidates, only two of which are currently being tested in clinical trials, and significant additional research and development and clinical testing will be required before we can potentially seek regulatory approval for or commercialize any of our drug product candidates.
- We have limited experience in conducting clinical trials and no history of commercializing biologic products, which may make it difficult to evaluate the prospects for our future viability.
- Success in preclinical studies or early clinical trials may not be indicative of results obtained in later trials.
- We plan to continue to seek collaborations or strategic alliances. However, we may not be able to establish such relationships, and relationships we have established may not provide the expected benefits.
- We may not be successful in our efforts to identify additional drug product candidates. Due to our limited resources and access to capital, we must prioritize the development of certain drug product candidates; these decisions may prove to be wrong and may adversely affect our business.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results than our drug product candidates.
- We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to successfully complete development of, obtain

regulatory approval for, or commercialize our drug product candidates and our business could be substantially harmed.

- We rely completely on third parties to manufacture our preclinical and clinical drug supplies for our drug product candidates.
- If we or our licensor(s) are unable to protect our or its intellectual property, then our financial condition, results of operations and the value of our technology and potential products could be adversely affected.
- Even if we, or any collaborators we may have, obtain marketing approvals for any of our drug product candidates, the terms of approvals and ongoing regulation of our products could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.
- We will need substantial additional financing to support our growth and ongoing operations. Additional capital may be difficult to obtain, restrict our operations, require us to relinquish rights to our technologies or drug product candidates, encumber our assets and result in ongoing debt service cost, or result in additional dilution to our stockholders.
- We have a loan agreement that requires us to meet certain operating covenants and place restrictions on our operating and financial flexibility.

PART I

Item 1. Business

Executive Summary

We are a clinical-stage biopharmaceutical company developing precision immunotherapies to treat cancer and autoimmune diseases. Unlike conventional approaches that broadly activate the immune system, our Immuno-STAT™ platform is designed to selectively modulate disease-relevant T cells, enhancing efficacy while minimizing off-target effects. Our lead programs include drug product candidates designed to:

- CUE-400 series (Autoimmune Diseases): Enhance regulatory T cells (Tregs) with a novel and unique mechanism to not only proliferate but also generate Tregs, and restore immune balance (e.g., CUE-401 for autoimmune condition).
- CUE-500 series (Targeted Cell Depletion): Redirect antiviral T cells to target eliminate pathogenic cells (e.g., CUE-501 for autoimmune B cell depletion).
- CUE-100 series (Oncology): Selectively activate tumor-specific T cells (e.g., CUE-101 for HPV+ cancers, CUE-102 for WT-1 expressing cancers).

We aim to leverage our differentiated platform to establish new standards of care, forge strategic partnerships, and accelerate clinical development.

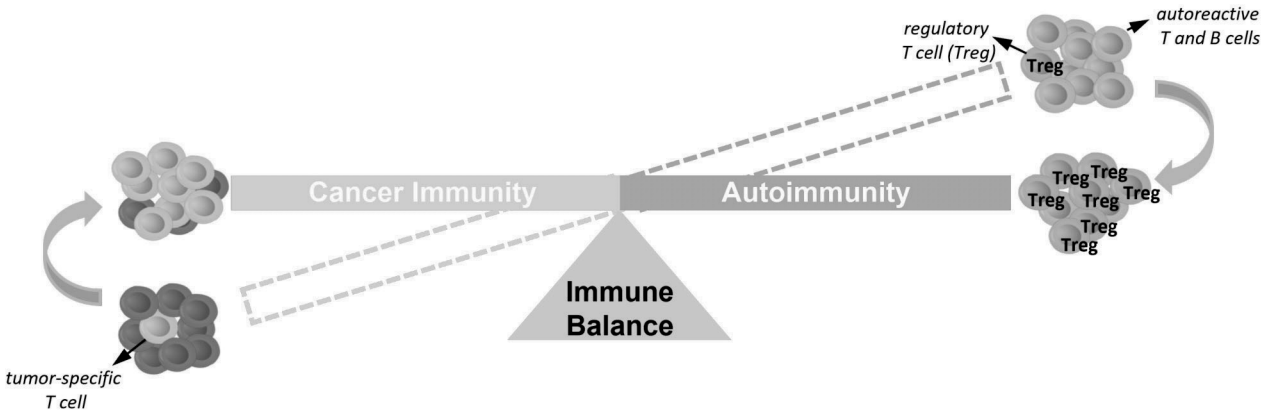
Overview

We are developing a novel class of injectable therapeutics engineered to selectively engage and modulate targeted, disease-relevant T cells. Through our approach, we aim to establish a new standard of care for diseases that cause human suffering and mortality, with an initial focus on cancer and autoimmune disease, by selectively modulating the immune system to restore function and re-establish immune balance. We believe our proprietary Immuno-STAT™ (Selective Targeting and Alteration of T Cells) platform, as described below, will enable us to therapeutically enhance a patient's own immune system to potentially restore health.

Cancer and autoimmune disease cause immeasurable pain and suffering, shortening the life expectancy of those afflicted and impacting large populations worldwide. There are approximately 20 million new cancer diagnoses worldwide each year with approximately 2 million new cases annually in the United States, or U.S., alone. Of these new cases, approximately 50% will progress to recurrent metastatic disease, ultimately resulting in death. In addition, approximately 4% of the world's population is diagnosed with an autoimmune disease each year, resulting in approximately 24 million cases annually in the U.S.

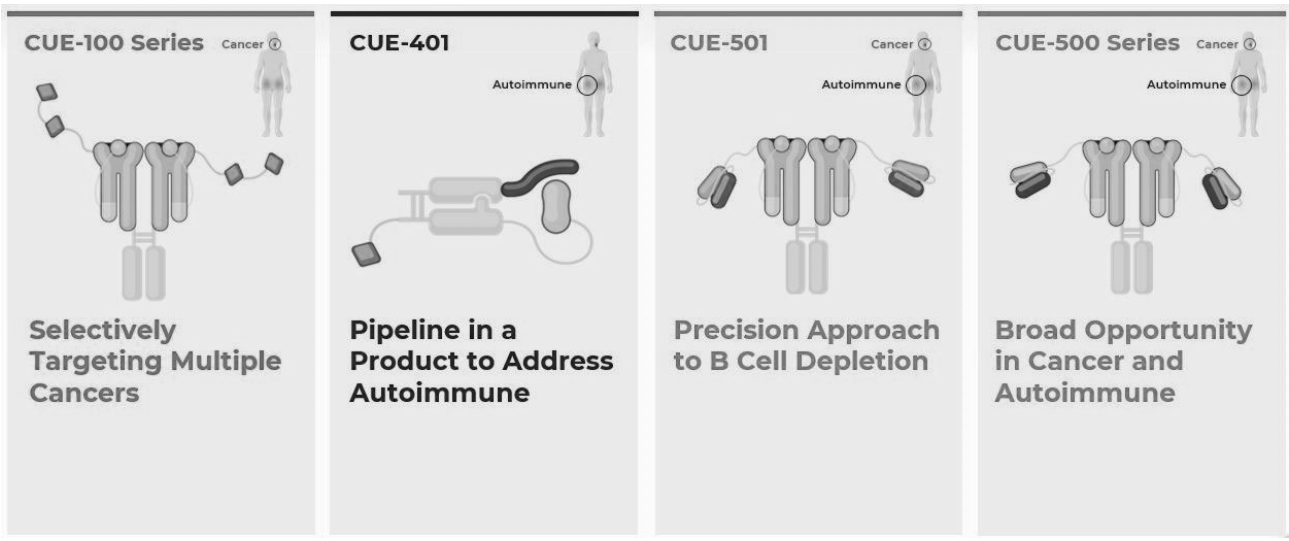
A key factor in susceptibility to cancer is inadequate immunity against malignant cancer cells and inversely, autoimmune disease is caused by excessive immune activation against self-tissue. T cells are central to enhancing tumor-immunity as well as maintaining tolerance against self-tissue antigens and are regulated with a highly selective "command and control" instruction process through interactions with antigen-presenting cells, or APCs. We have designed and engineered our Immuno-STAT platform to mimic nature's "command and control" system to restore immune balance.

Immuno-STAT Platform for Restoration of Immune Balance



The immune system's specificity of T cell engagement is achieved through the T cell receptor, or TCR, binding to a highly specific, targeted peptide segment, referred to as an "epitope". The epitope is presented by a specialized protein scaffold, referred to as HLA molecules, present on the surface of APCs. TCR engagement along with "command" secondary signals, such as interleukin 2, or IL-2, transforming growth factor beta, or TGF-β, PD-1, determines the activation state and effector function of T cells. For example, IL-2 signals result in potent activation of CD8+ T cells into killer T cells in cancer, while other signals may differentiate T cells into regulatory T cells, or Tregs, to suppress autoimmunity. These "cues", or signals, when engaged at the same time, as is the case with our Immuno-STATs, are able to "dial-in" selective activation of targeted tumor-specific T cells to attack cancer while avoiding potentially harmful broad immune activation of T cells. Conversely, in autoimmunity, our autoimmune drug product candidates are designed to deploy signals to generate Tregs to selectively inhibit, or dampen, autoreactive T cells while avoiding broad immune suppression that can increase susceptibility to other diseases. It is through the specificity of the TCR and the simultaneous delivery of "co-stimulatory" signals that we aim to "command and control" disease-relevant T cells with necessary precision for the treatment of cancer and autoimmune disease. We have generated supportive clinical data with our CUE-100 series, namely CUE-101 in HPV+ head and neck cancer and CUE-102 in Wilms' tumor 1 protein, or WT1, expressing cancers, as well as preclinical data supporting the advancement of our CUE-400 and CUE-500 series for autoimmune disease. We believe our Immuno-STAT platform has the potential to develop drug product candidates with the potential of becoming new standards of care in the treatment of cancer and autoimmune disease. The graphic below summarizes the pipeline of assets that we have in development for restoration of immune balance.

Immuno-STAT Platform Pipeline of Assets for Restoration of Immune Balance



The Immuno-STAT framework is engineered to be highly flexible and modular, potentially enabling us to deploy the same or similar core functional elements to restore immune balance across diverse therapeutic approaches. In the case of oncology, Immuno-STATs are designed to selectively engage and activate tumor-specific T cells while avoiding systemic immune activation. In contrast, for autoimmune diseases, CUE-401 has been designed to induce and proliferate Tregs to selectively down regulate autoreactive T cells, referred to as Teff cells, while avoiding broad immuno-suppression.

In oncology, we have observed in our Phase 1 clinical trials that our CUE-100 series selectively delivered a cancer protein-specific TCR that activated a signal along with an IL-2 variant cytokine to preferentially activate and proliferate tumor-specific T cells while sparing all other irrelevant T cells.

In autoimmune, we have developed novel approaches to restoring immune balance and health. CUE-401 is a novel bispecific composed of a masked, attenuated TGF-β with an IL-2 attenuated variant that together has demonstrated preclinically the ability to potently stimulate the generation and proliferation of Tregs. The masking of TGF-β enables the drug to have a biased, or "conditional" binding to immune cells having both the IL-2 receptor, as well as the TGF-β receptors, enabling concurrent, conditional signaling. In autoimmune disease, Tregs are the master regulators of maintaining immune homeostasis, or "balance" and health. Teff cells are reactive against "self" proteins and foster inflammation and induce chronic tissue damage. Tregs are important to maintaining "immune balance" in that they possess the ability to dampen and control the Teff cells. CUE-401 has been specifically engineered and designed to foster Treg control by proliferating existing natural regulatory T cells, or nTregs, that develop in the thymus as well as inducing new Tregs, or iTregs, and reducing the number of inflammatory Teff cells, thereby restoring the essential Treg/Teff balance. As such, we believe that CUE-401 represents a novel approach to selectively induce and expand Tregs with the potential to provide superior therapeutic effects for the treatment for chronic autoimmune diseases.

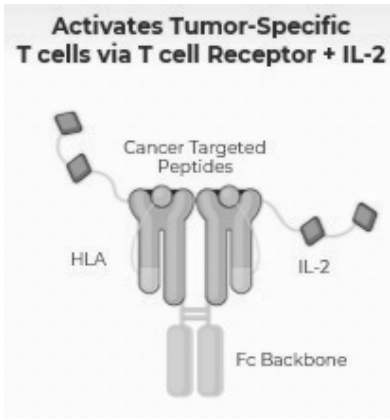
In addition to CUE-401, we have also developed the CUE-500 series to enable T cell-mediated depletion of pathogenic cell types. We believe these biologics have the potential to achieve immune balance in autoimmune patients and are significantly differentiated from other competing approaches such as antibody drug conjugates, or ADCs, pan-T cell engagers. IL-2 muteins, TNFR2 agonists, or CAR-T therapies. The CUE-500 series represents a novel approach to selectively target disease-causing cells and redirect existing anti-viral memory T cells to targeted disease-causing cells and deplete these cells. From this series, CUE-501 is being specifically developed to target and deplete autoimmune disease-causing B cells, an effective therapeutic objective which has been validated by others through the ablation of B cells with CAR-T and bispecific T cell engager therapies with pan-T cell activation. Targeted B cell depletion is widely recognized in the industry as a clinically validated and important approach for the treatment of B cell mediated autoimmune and inflammatory diseases, such as Lupus. We believe the preclinical data generated to date for the CUE-401 and the CUE-500 series demonstrates clear evidence of the intended mechanistic effect of these novel approaches for the potential treatment of autoimmune disease, and each represent potential breakthrough therapeutic opportunities for significant patient populations.

Immuno-STAT Platform for Oncology: CUE-100 Series-Combining TCR and IL-2 to Selectively Target Cancer

Historically, we have primarily focused our resources on the development of our CUE-100 series for oncology, namely the CUE-101 and CUE-102 drug product candidates, which are representative of our approach to selectively activate targeted CD8+ T cells against cancer. Although we are prioritizing CUE-401 and CUE-501, we are currently continuing to treat and monitor patients in a Phase 1b open-label expansion study investigating CUE-101 in the treatment of HPV+ recurrent metastatic, or R/M, head and neck squamous cell carcinoma, or HNSCC, in second line, or 2L, and beyond patients as a monotherapy. We are also conducting a Phase 1b clinical trial investigating CUE-101 in the treatment of HNSCC, as a first line, or 1L, therapy in combination with standard of care KEYTRUDA. We are also currently continuing to monitor patients in a Phase 1b clinical trial of CUE-102 as a monotherapy in late line R/M WT1+ colorectal, gastric, ovarian, and pancreatic cancer.

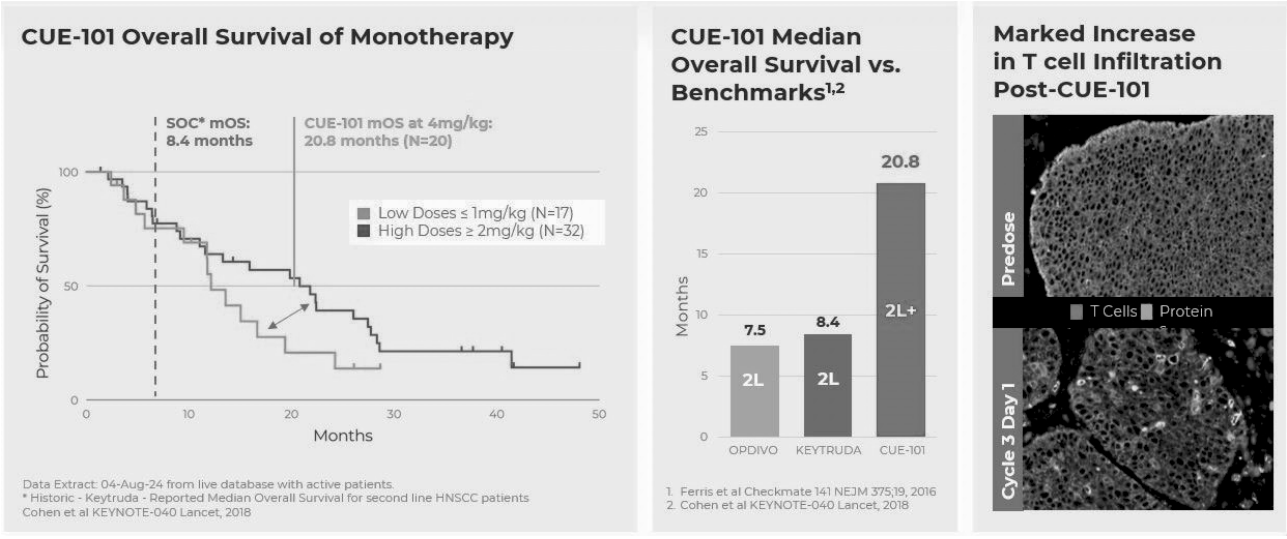
The figure below depicts our CUE-100 series Immuno-STAT platform for selectively expanding tumor-specific T cells by building upon nature's "cues" for selective T cell engagement and activation.

CUE-100 Series Potential Best-in-Class IL-2 Based T Cell Engager



The data from the CUE-101 and CUE-102 clinical trials has demonstrated clinical evidence of targeted activation and expansion of T cells with the specific TCR for the selected cancer-epitope, e.g., HPV E7 epitope for HPV+ R/M HNSCC, in the case of CUE-101, and WT1 epitope for cancers expressing WT1, such as ovarian, gastric, colorectal and pancreatic cancer, in the case of CUE-102. Activation and expansion of the targeted T cell populations have been demonstrated in patients from both the Phase 1b clinical trial for CUE-101 and the Phase 1b clinical trial for CUE-102, and a notable increase in median overall survival, or mOS, has been observed in the maturing clinical data with CUE-101. We have also observed an increased survival trend with the emerging CUE-102 Phase 1b clinical data.

CUE-100 Series Maturing Clinical Trial Data Shows Notable Increase in Survival

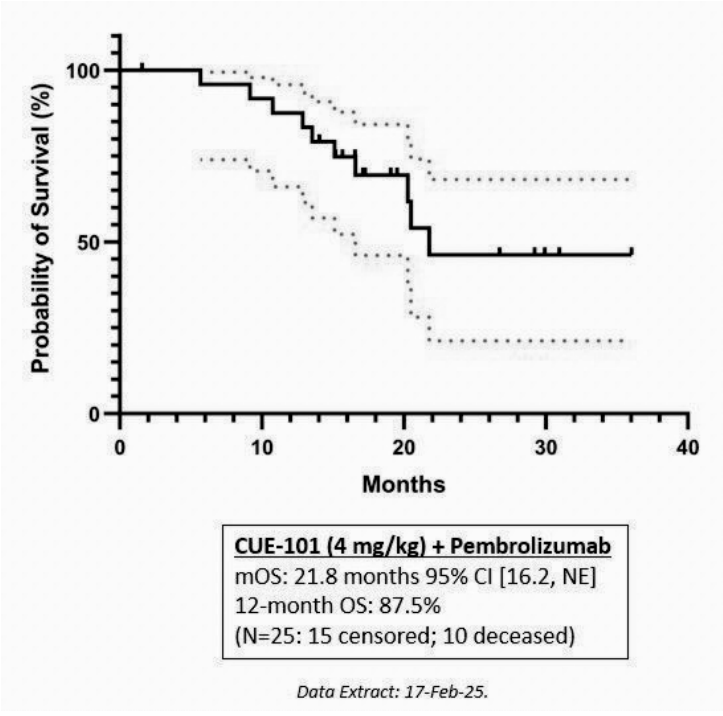


In our Phase 1 clinical trial for CUE-101 as a monotherapy, we have observed prolonged survival in patients with advanced R/M HNSCC. Notably, and as shown in the above figure, the median overall survival, or mOS, of 2L+ patients treated at monotherapy doses greater than 1mg/kg is 20.8 months, which compares favorably to the historical third-party mOS data of 8.4 months with KEYTRUDA and 7.5 months with OPDIVO in the 2L setting. As shown in the left graph above,

patients treated with higher dose levels (> 2 mg/kg) of CUE-101 exhibited greater mOS compared to patients from the same clinical trial that were treated with lower dose levels (< 1 mg/kg) of CUE-101. We believe this survival data is due to the repeated stimulation and expansion of tumor-specific T cells given the mechanism of action of CUE-101 especially in the tumor microenvironment. Having demonstrated in clinical trials the selective activation and expansion of tumor-specific T cells by the Immuno-STAT platform in patients fighting cancer, we are now seeking strategic partnerships to continue clinical development and move these drug product candidates towards a potential registration path.

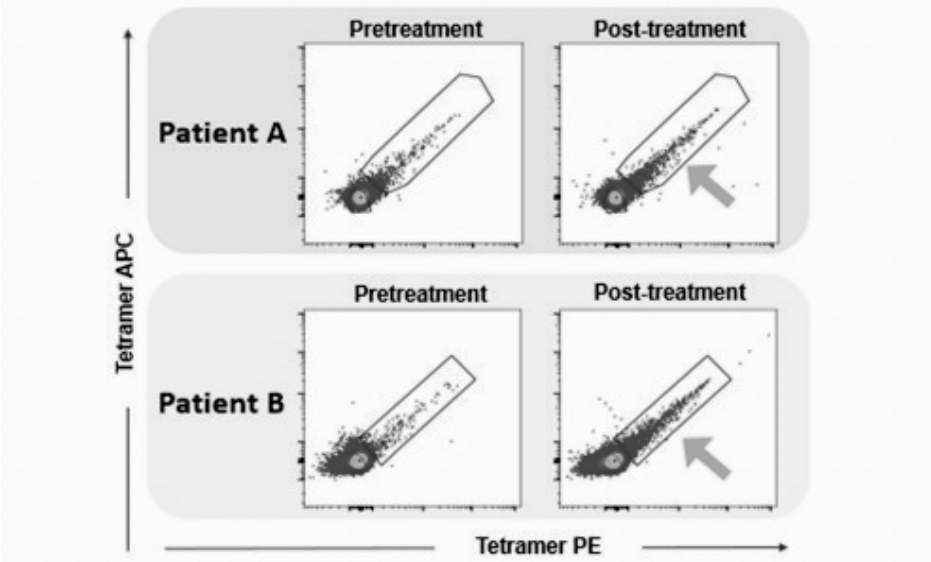
As shown in the figure below, the data from our CUE-101 Phase 1b clinical trial investigating CUE-101 in combination with standard of care pembrolizumab (Keytruda), continues to mature with a mOS of 21.8 months and a 12-month landmark survival of 87.5% as of February 17, 2025. We believe these results appear favorable compared with the historical pembrolizumab mOS of 12.3 months. Also of importance is the observation of a 46% objective response rate, or ORR, for the combination treatment of CUE-101 and pembrolizumab compared to a 19% ORR for pembrolizumab alone from historic data.

Median Overall Survival of CUE-101 (4mg/kg) and Pembrolizumab



In our Phase 1 clinical trial for CUE-102 as a monotherapy for treating WT-1 expressing tumors, including colorectal, gastric, pancreatic and ovarian, we have observed evidence of WT-1 specific T cell proliferation as shown in the figure below. Importantly, as the data continues to mature, we have observed what appears to be a trend of enhanced survival in colorectal cancer and pancreatic cancer patients, where the number of enrolled patients allows for a possible pattern to be observed. We have also observed reductions in tumor burden in patients with pancreatic, gastric, and ovarian cancer.

Selective Expansion of WT1-Specific T Cells Demonstrated in Patients Treated with CUE-102



Increased frequency of WT1-specific CD8+ T cells are observed following CUE-102 treatment. Representative plots are shown from preliminary analyses following direct flow staining of PBMCs from 2 patients

We continue to monitor and assess the maturing clinical data and believe it continues to strengthen and enhance the potential of establishing a third-party partnership to further develop this promising approach for addressing the pressing need for more effective and well tolerated cancer therapeutics.

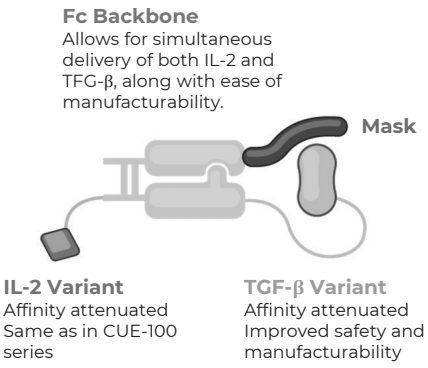
As previously announced, we are strategically prioritizing CUE-401 and the CUE-500 series, including CUE-501. We believe these programs represent near-term value creation opportunities for our shareholders and have the potential to be innovations providing transformative therapies, with large, underserved market opportunities.

Immuno-STAT Platform for Autoimmune Disease: CUE-400 Series-Combining a Masked TGF-b and IL-2 to Potentially Transform the Treatment of Autoimmune Diseases

Recently we have observed significant focus within the pharmaceutical industry to identify approaches that target and foster Tregs for more effective therapeutic intervention and management of autoimmune disease. It is well established that TGF-β exerts direct suppressive effects on multiple immune cells, including inhibition of the cytotoxic activity of CD8+ T cells, CD4+ T cells, and NK cells, and enhances the functionality of Tregs, which are a critical immunosuppressive population essential for maintaining immune balance. We prioritized our autoimmune disease assets due to the pressing need for more effective therapies in autoimmune disease, coupled with our observations from the preclinical data generated with our CUE-401 program, which is specifically designed to foster the immunosuppressive features of TGF-β with the complimentary/ synergistic properties of Il-2.

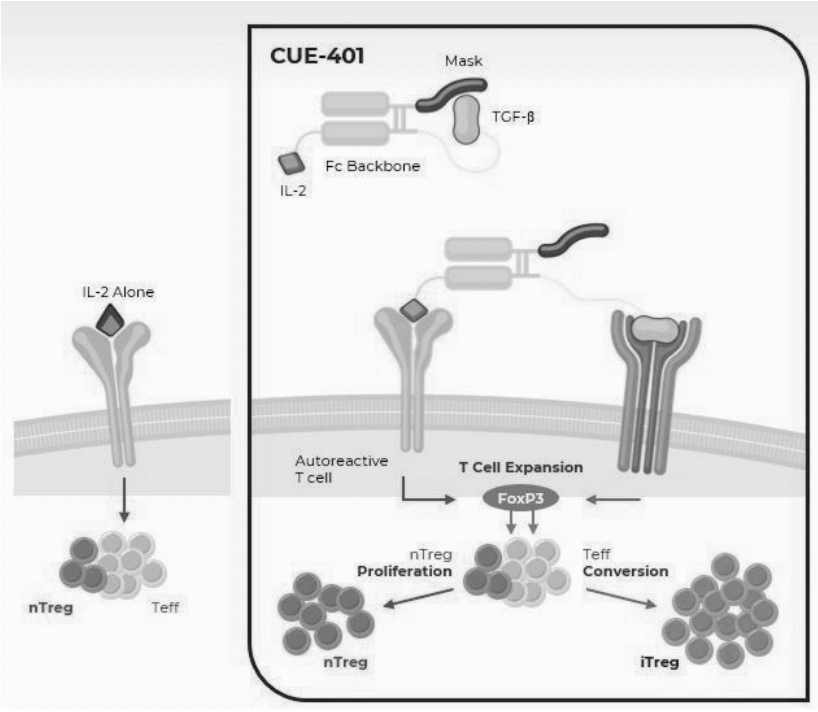
We believe that CUE-401 is a novel approach to not only expand existing Tregs, but also to significantly induce and expand antigen specific Tregs for regulating disease causing autoreactive Teff cells. IL-2 and TGF- β are known to be important signals for promoting expansion and stabilization of existing Tregs in the body, as well as naïve CD4+ T cells undergoing activation resulting in the stable induction of the Foxp3 promoter, present in Tregs. CUE-401 was designed to incorporate the same attenuated IL-2 variant that has been derisked by our CUE-100 series candidates, CUE-101 and CUE-102, as well as a unique and novel, masked TGF-β variant, designed by structure-guided engineering for conditional activation.

CUE-401 Novel and Unique Bi-specific



The mechanism of action of CUE-401, as illustrated below, is significantly differentiated from IL-2 muteins and TNFR2 agonists, providing a unique opportunity to harness the full potential of Treg differentiation and expansion with the qualitative advantages of iTregs.

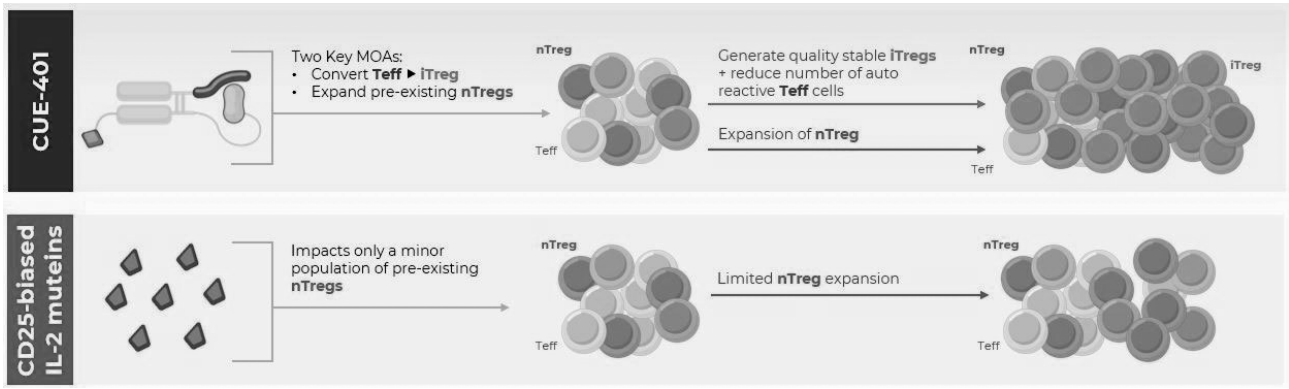
CUE-401 Differentiated Mechanism of Action



T regs act directly on autoreactive T cells, to suppress their activation, proliferation and function, which includes secretion of cytokines known to play an important role in multiple autoimmune diseases. Unlike drugs that only target one predominant cytokine pathway, IL-17 for example, Tregs suppress Teff cell responses of diverse phenotypes, including Th1, Th2 and Th17 responses, which are distinct subsets of T helper cells that underlie autoimmune disease progression. In addition to direct effects on Teff cells, Tregs act on key additional immune compartments to inhibit and resolve self-reactivity and inflammation. Furthermore, Tregs regulate myeloid derived immune cell populations, including macrophages and dendritic cells, which drive inflammation through antigen presentation, cytokine production and T cell stimulation. Given these diverse effects, Tregs represent a promising therapeutics approach for the modulation of inflammation and autoimmune disease.

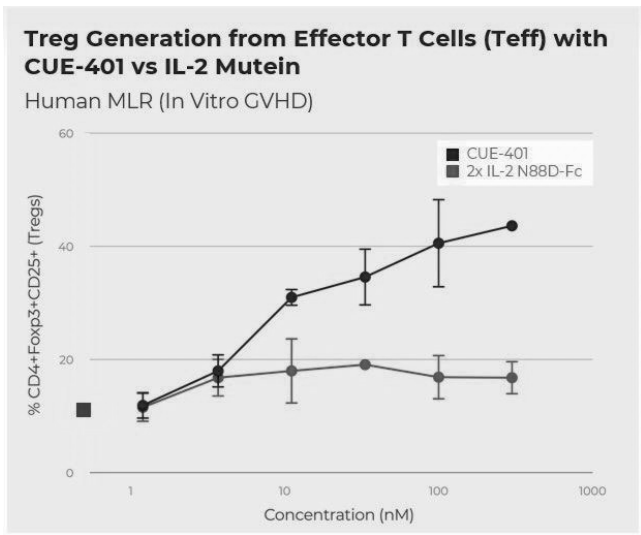
The graphic below highlights the unique and differentiated mechanism of action of CUE-401 as compared to CD25-biased IL-2 muteins, selectively designed for expansion of existing Tregs. As shown below, CUE-401 has shown in preclinical studies that it expanded pre-existing nTregs, as well as converted naïve CD4+ T cells and Teff cells into new Tregs, thereby enhancing the quantitative and qualitative population of Tregs available to control the pathogenic cellular reactions in autoimmune patients and maintain a state of immune balance. The conversion of self-reactive CD4+ T cells into Foxp3-positive Tregs, a specialized subset of CD4+ T cells, decreases the number of pathogenic, autoreactive Teff cells and may also generate antigen-specific Tregs that have enhanced suppressive function.

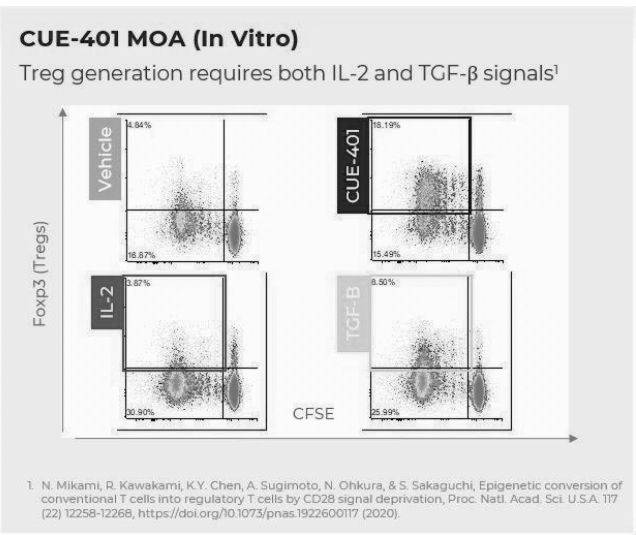
CUE-401 Designed to be Mechanistically Differentiated from IL-2 Muteins



To date, we have made significant progress in the development of CUE-401, including the identification of a lead candidate and initiation of Investigational New Drug, or IND, enabling studies. Preclinical data generated in our labs, as well as in collaboration with Dr. Richard DiPaolo of St. Louis University, supports the premise that CUE-401 selectively expands and induces Tregs (both nTregs and iTregs) that are functionally suppressive and stable. The data shown in the left graph below demonstrated dose-dependent iTreg induction in primary human T cells in a mixed lymphocyte reaction, or MLR, in the presence of CUE-401 treatment. In contrast, treatment of the same T cell MLR with a CD25-biased IL-2 mutein did not result in the generation of iTregs, consistent with the known literature that both IL-2 and TGF-β signals are required for this effect. Further demonstration of this mechanism is shown in the right graph below, where treatment of human T cell MLRs with only the IL-2 or TGF-β domains of CUE-401 did not result in generation of a substantial population of iTregs. In contrast, treatment with the full CUE-401 molecule, containing both the IL-2 and TGF-β domains, demonstrated the generation of a robust population of FOXP3+ iTregs from these primary human T cells.

CUE-401 Preclinical Demonstration of Inducible Treg Expansion from Teff Cells

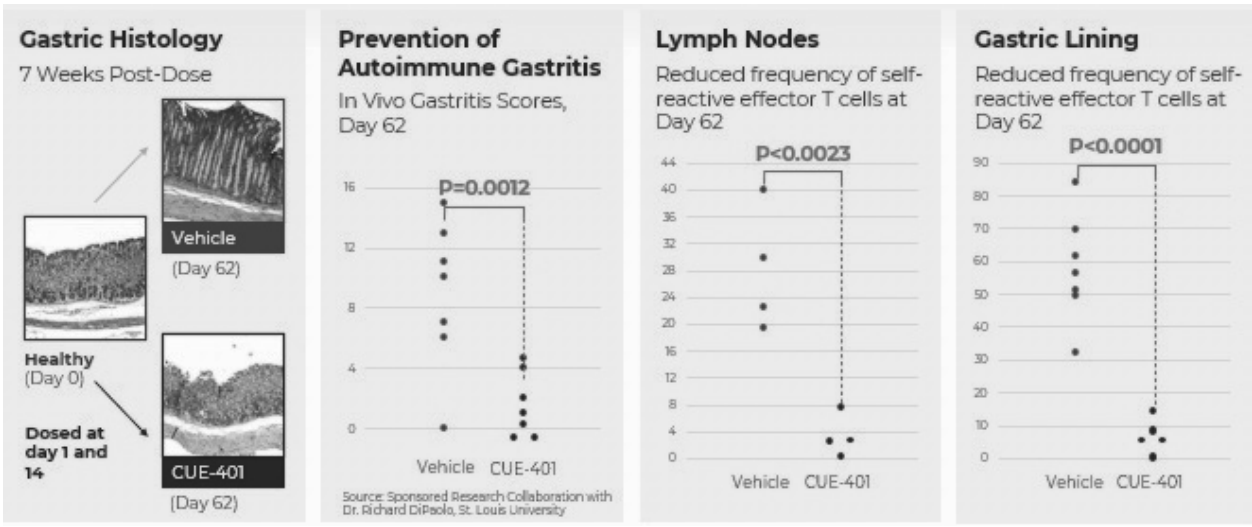




In vivo experiments in mice further demonstrated that treatment with CUE-401 resulted in a significant increase in the frequency of Tregs, as did treatment with IL-2 complexes (a mimic of CD25-biased IL-2; see left graph below). Importantly, treatment with IL-2 complexes also resulted in increased proliferation of Teff cells, while CUE-401 treatment selectively increased Treg frequency without increasing Teff cell proliferation. Teff cells upregulate expression of CD25, the high affinity receptor of IL-2, thus CD25-biased forms of IL-2 can result in stimulation of activated Teff cells, which in the case of autoimmune disease may be the self-reactive Teff cells that are promoting disease. The selectivity of CUE-401 to avoid stimulation of Teff cells and possibly convert Teff cells to iTregs we believe is a competitive advantage of the CUE-401 molecular design.

The expanded Tregs resulting from CUE-401 treatment demonstrated to be functionally suppressive and maintained a stable phenotype, as evidenced by Foxp3+ demethylation, whereby CUE-401 treatment also suppressed the expansion of self-reactive Teff cells in a T cell transfer model of autoimmune gastritis. As shown in the vehicle treated control mice in the figures below, transfer of Treg-depleted T cells into immunocompromised mice in this model resulted in the development of autoimmune gastritis over approximately 9 weeks, where the gastric lining of these mice exhibited histopathological evidence of disease and self-reactive Teff cells were activated and expanded in the gastric lymph node and infiltrated the gastric lining of the stomach. In contrast, treatment of this model with two doses of CUE-401 (Days 1 and 14) resulted in prolonged and durable suppression of Teff self-reactive T cells and significantly reduced pathological evidence of disease in the stomachs of treated mice. The representative histopathology images below and the compiled gastritis pathology scores demonstrate significant, long-term protection from tissue destruction in mice treated with CUE-401.

CUE-401 Reduced Pathologic Autoimmune Teff Cells While Normalizing Histopathologic Gastritis Scores



We have conducted additional preclinical studies to characterize the pharmacokinetics, pharmacodynamics, and tolerability of CUE-401 across multiple animal species providing insights towards potential translation to human clinical studies. These preclinical results, along with advances in the manufacturing of CUE-401, have derisked the development of this asset and identified the lead candidate molecule. Scale-up manufacturing and other IND-enabling studies are ongoing.

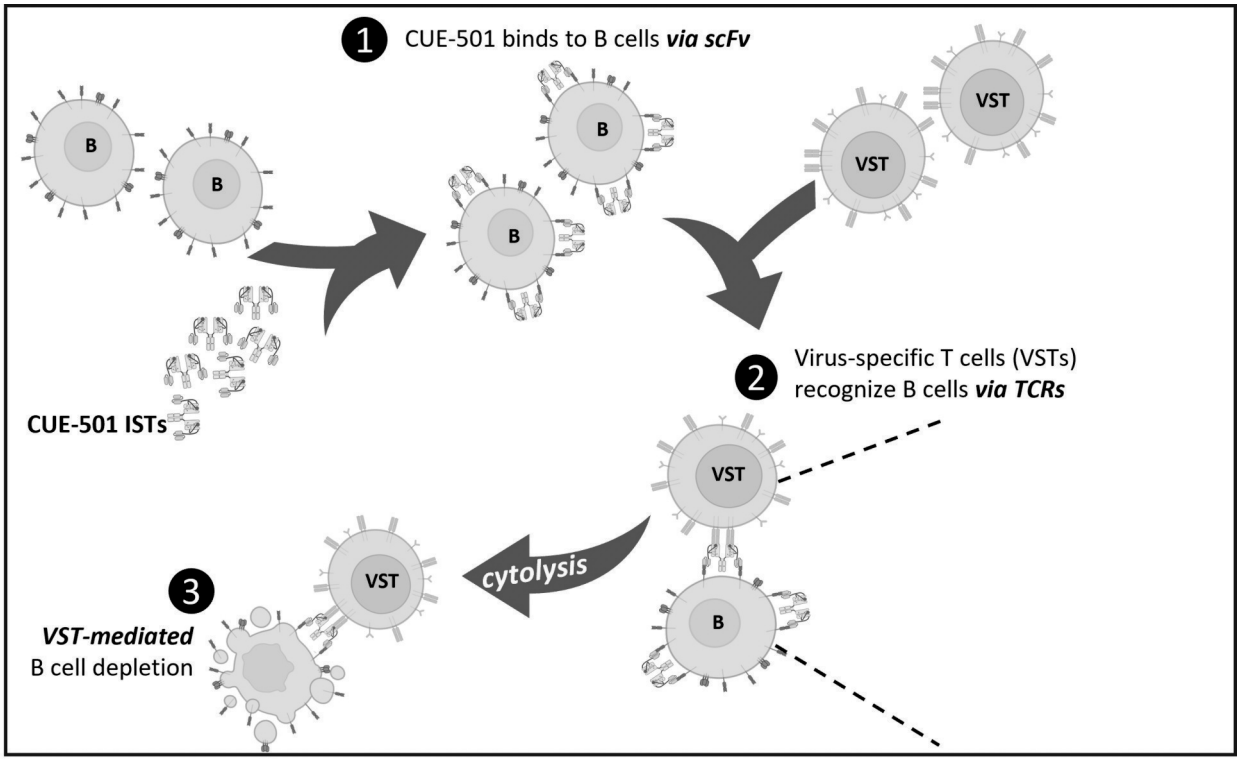
Immuno-STAT Platform for Autoimmune Disease: CUE-500 Series- Exploiting the Natural Anti-viral T Cell Repertoire Against Targeted Tissue

In addition to CUE-401, we are also developing the CUE-500 series for the selective targeting and depletion of pathogenic immune cells with the potential to reset the immune system, which could have the potential to offer more durable and better tolerated therapeutic responses.

We are advancing our CUE-500 series of Immuno-STAT molecules for the depletion of disease-relevant pathogenic cell types. CUE-501 has been specifically designed for the treatment of autoimmune disease via anti-viral T cell-mediated depletion of B cells. We aim to establish a near-term third party development partnership to further pursue this lead program from our CUE-500 series of Immuno-STATs.

The therapeutic concept of the CUE-500 series, as summarized below, builds upon the clinical de-risking accomplished with the CUE-100 series, where the shared constant is the presence of a bivalent peptide-HLA molecule that is designed to selectively engage TCRs of selected T cell populations. Whereas CUE-100 series Immuno-STATs are engineered to selectively engage tumor-specific T cells, in the case of the CUE-500 series, the peptide presented by the HLA is a well characterized virus epitope recognized by virus-specific memory T cells that are present in high frequencies due to our repeated exposures to common viral diseases. Examples of such common viral epitopes would include CMV, EBV, and SARS-CoV-2, each of which are well known to elicit long-lived memory cytotoxic T cells that continually survey our bodies to protect against future exposures to these viruses. In addition to these viral peptide-HLA complexes, each CUE-500 series molecule also contains antibody binding domains directed against unique target proteins expressed on the surface of disease-relevant pathogenic cells. This molecular configuration is designed to allow for CUE-500 molecules to bind target pathologic cells, or "paint" the surface of these cells, making these cells appear as virally infected cells by presenting the viral peptide-HLA complexes that are recognized by naturally occurring virus-specific killer T cells. These targeted pathologic cells can then be recognized and destroyed by our protective anti-viral memory T cell repertoire.

CUE-501 Opportunity for Redirected T Cell Killing



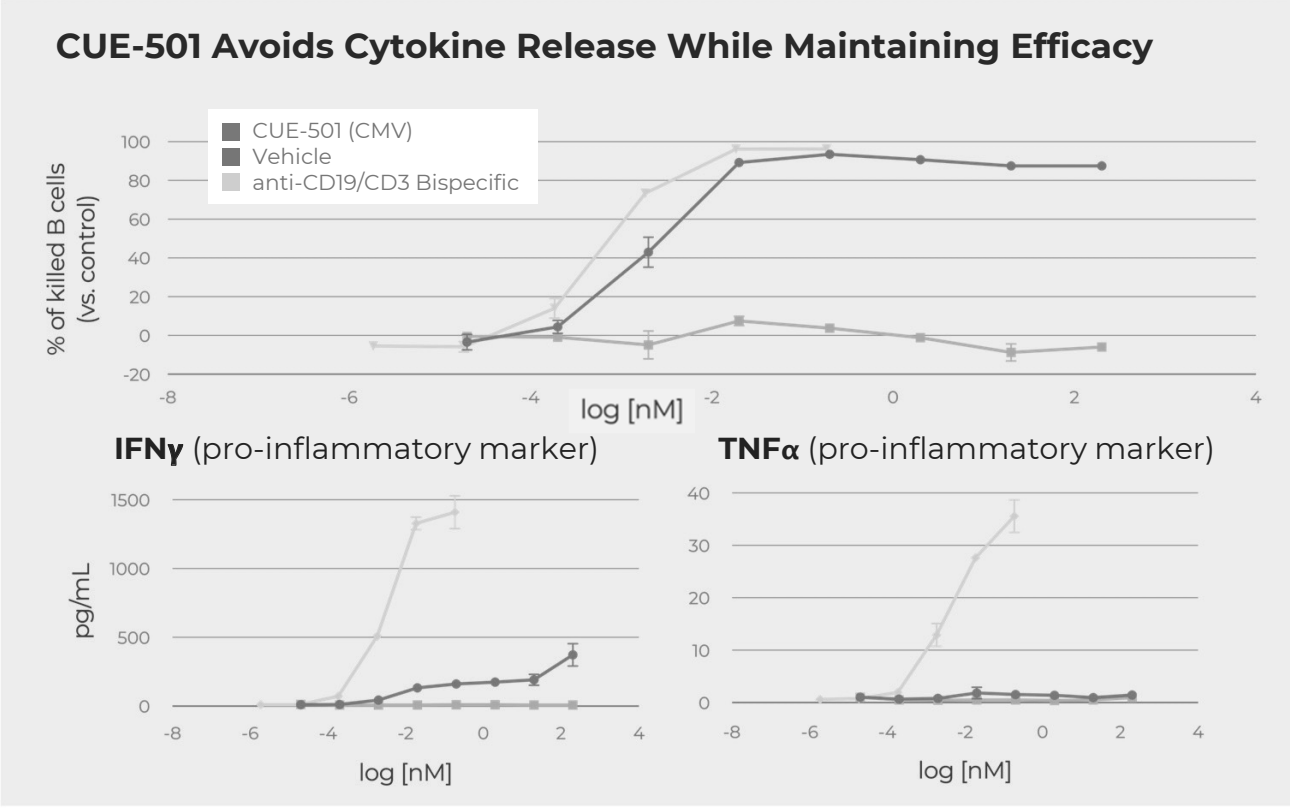
Recently published datasets from small third-party clinical trials have demonstrated evidence of clinical activity in autoimmune patients treated with CAR-T cells and bispecific T cell engagers directed against CD19 for T cell-mediated depletion of B cells, providing strong mechanistic evidence for the superiority of T cell-mediated B cell depletion versus prior approaches with antibody-dependent B cell depletion (such as anti-CD19, anti-CD20 monoclonal antibodies). In many cases, from these third-party clinical trials, long-term ongoing clinical remissions have been noted in patients with lupus and myositis with no concurrent immunosuppressive regimens, which could be early signals of functional cures. However, both of these therapeutic approaches have also exhibited significant safety and tolerability limitations as observed in oncology patients, including cytokine release syndrome, or CRS, and deployment of cellular therapies are in general constrained by a number of challenges associated with manufacturing, logistics, and patient preconditioning requirements.

We see potential for CUE-501, the first asset in our novel CUE-500 series, to enable virus-specific T cell mediated killing of B cells, akin to what CAR-T cellular therapies do, and potentially achieve equivalent B cell killing benefits as an off-the-shelf biologic with a more favorable tolerability profile. This novel mechanism of action is depicted below with an example of a CUE-501 molecule enabling cytomegalovirus-specific T cells, or CMV T cells, to kill primary human B cells. It is well known that CMV-specific T cells are a significant proportion of the protective anti-viral T cell repertoire and are present in a

large portion of the population. This mechanism of natural target recognition via TCRs is of similar sensitivity, if not higher, compared to how a CAR-T cell recognizes its targets via the CAR domain.

In contrast to CAR-T and bispecific T cell engager approaches, CUE-501 was designed to selectively deplete B cells while reducing the risk of CRS by stimulating only a select population of naturally occurring anti-viral T cells. Preclinical evidence for this selective and unique mechanism of action is shown below. As shown in the upper figure above, CUE-501 demonstrated the capacity to deplete CD19 positive B cells from human PBMCs to a similar extent as a CD3-bispecific T cell engager, but in the case of CUE-501, the killing of B cells was specifically mediated by the engagement of only CMV-specific T cells. This specificity of T cell engagement is demonstrated by the lack of killing observed following exposure to a CUE-500 molecule that is identical to CUE-501 except for the presentation of an HIV peptide instead of a CMV peptide. Since HIV-specific T cells are not present in PBMCs of healthy donors, a CUE-500 molecule targeting HIV-specific T cells is not able to cause redirected killing of B cells. While CUE-501 resulted in comparable B cell killing to a CD3-based, pan-T cell engager, the lower panels of this figure show that the bispecific T cell engager also caused significant release of inflammatory cytokines involved in CRS (i.e. interferon gamma, or IFN-g, and tumor necrosis factor alpha, or TNF-a) while CUE-501 did not. This finding suggests that the risk of CRS in patients treated with CUE-501 may be reduced and may provide an advantage over other currently investigated T cell-mediated mechanisms of B cell depletion.

CUE-501 Designed to Direct Selective Memory T Cells to Deplete B Cells to Address Autoimmune and Inflammatory Disease



We believe that our CUE-500 series is capable of selectively redirecting prevalent and naturally occurring anti-viral killer T cells to mediate depletion of pathogenic cell types while avoiding the systemic indiscriminate engagement and activation of T cells. The CUE-500 series is designed with what we believe to be a superior differentiation of the mechanism of action as compared to other competing modalities for target cell depletion, including CAR-T cellular therapy and pan-T cell engagers, including CD3 bi-specifics.

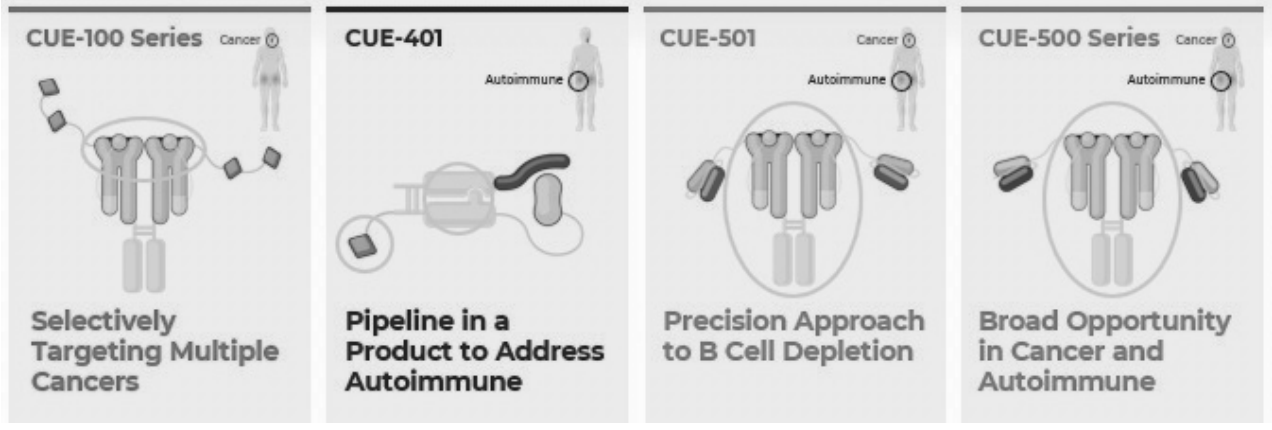
CAR-T approaches face complex manufacturing and supply chains challenge for broad access, as well as patient conditioning regimens, in-patient administration and safety risks including CRS and neurotoxicity that continue to pose challenges. Pan T cell engagers that non-selectively activate T cells via anti-CD3 or CD28 crosslinking are also not favorable for autoimmune applications. These modalities activate all T cells indiscriminately, potentially resulting in CRS and other

toxicities, and we believe therefore may be unsuitable for autoimmune patients. In addition, they pose the risk of further activating and propagating self-reactive T cells that may exacerbate the underlying autoimmune disease. In contrast to these modalities, the CUE-500 series is designed to offer a potential solution for selectively exploiting the long-lasting anti-viral memory T cells to drive pathogenic cell depletion. This off-the-shelf approach therefore offers the potential to achieve CAR-T-like efficacy while avoiding the challenges associated with cell therapy modalities.

Due to its modularity, we believe that the CUE-500 series has therapeutic potential across multiple therapeutic areas. The mode of redirecting a defined population of already existing anti-viral T cells may apply to many pathogenic cell types readily addressed by swapping different cell-targeting antibody domains into the CUE-500 series framework. Lead candidate selection studies are underway for CUE-501, for which we aim to establish a near-term third party partnership to further pursue this preclinical lead program.

As an innovative protein engineering company we aim to fully exploit the modular nature of the Immuno-STAT platform. Building off the design and development of the CUE-100 series associated with demonstrable clinical benefit in clinical trials, we have developed CUE-401 and the CUE-500 series. CUE-401, a potentially first-in-class, masked TGF-β and IL-2v bispecific, incorporates the same IL-2v from our CUE-100 series and offers an opportunity for conversion of antigen-specific Tregs, which have been shown to be more effective at controlling autoreactive T cells, a primary cause of autoimmune disease. The CUE-500 series takes advantage of the peptide-HLA-Fc components of the CUE-100 series to enable targeted cellular depletion in both oncology and immunology. The modularity of the CUE-500 series allows us to utilize the same core framework to target many cell types, including pathogenic immune cells in autoimmune disorders or cancer cells for oncology, thus providing significant efficiencies for the development of additional candidates from this series.

Immuno-STAT Platform a Series of Next Generation Targeted Therapeutic Candidates



Our Business Strategy

Our approach to developing precision immunotherapies has yielded a growing portfolio of novel proteins, addressing multiple unmet needs across autoimmune disease and cancer. We believe that our science is derisked with clinical tolerability and activity from our Phase 1 clinical trials of CUE-101 and CUE-102, with the potential for significant potential market opportunities. As a result of our insights and learnings from our growing body of supportive data, we believe our corresponding strategic plans have us well positioned for optimizing shareholder value. Our pipeline of drug product candidates and programs aims to address significant unmet medical needs for treating serious, life-threatening diseases. To achieve our objectives, we are focused on the following strategy:

Exploring strategic options for our CUE-100 series in oncology, as our clinical data continues to mature

- Continue to assess maturing clinical data to further the potential of establishing strategic development partnerships.
- Fully exploit the potential for the CUE-100 series, e.g. CUE-101 and CUE-102, to address the challenges confronting adoptive cellular therapy, e.g. CAR-T and TCR-T, by enabling durability and persistence.

Optimizing shareholder value by advancing our autoimmune portfolio

- Further position the CUE-401 program as a potentially disruptive, high value opportunity with the potential to address multiple major indications. We believe CUE-401 has the potential to become a new standard of care in the treatment of autoimmune disease.
- The preclinical candidates in our CUE-500 series are precision immune therapeutics, designed to redirect anti-viral killer T cells to eradicate pathogenic cells. By pairing a target cell with a virus-specific epitope, anti-viral killer T cells may be redirected to attack and destroy pathogenic cells. The potential applicability of the CUE-500 series across multiple cell types and indications in both autoimmune and oncology represents an opportunity for strategic collaborations to further advance and validate this novel approach to address multiple high value indications.

We are actively pursuing strategic options, including collaborations across our pipeline. We are seeking development and commercialization partners for our oncology assets, CUE-101 and CUE-102. We are preparing CUE-401 for an IND filing in the third quarter of 2026 with the prospects of early clinical data providing validation of its potential breakthrough mechanism of action. For CUE-501, we intend to establish a third-party partnership to advance the preclinical program, which leverages clinically validated mechanisms for B cell depletion, such as CAR-T or CD3 bispecifics, but with the potential for a more favorable safety profile compared to CAR-T or CD3 bispecifics.

Our License Agreement with Einstein

On January 14, 2015, or the Effective Date, we entered into a license agreement, as amended and restated on July 31, 2017 and as further amended on October 30, 2018 and January 13, 2024, or the Einstein License, with Albert Einstein College of Medicine, or Einstein, for certain patent rights, or the Patents, relating to our core technology platform for the engineering of biologics to control T cell activity, precision, immune-modulatory drug product candidates, and two supporting technologies that enable the discovery of costimulatory signaling molecules (ligands) and T cell targeting peptides. We hold an exclusive worldwide license, with the right to sublicense, import, make, have made, use, provide, offer to sell, and sell all products, processes and services that use the Patents, including certain technology received from Einstein related thereto, which we refer to as the Licensed Products.

The Einstein License is a royalty-bearing license obligating us to pay a percentage of proceeds received from sales of categories of Licensed Products at low single digit rates. We have also agreed to share a portion of our proceeds that we derive from other agreements, like sublicense agreements, that we may enter into relating to the Licensed Products. The percentage of such proceeds that we are required to pay Einstein ranges from the low to mid-teens, depending on how far we have developed a Licensed Product before we enter into an agreement relating to the Licensed Product. These percentages are reduced for sales of Licensed Products in countries where a competing product exists and for products or services involving the use or incorporation of technology received from Einstein relating to synapse for targeted T cell activation molecules, receptor ligand identification or platforms for T cell monitoring. In addition to our obligation to pay royalties based upon a percentage of proceeds from sales of Licensed Products, we have also agreed to pay Einstein annual maintenance fees. The maintenance payments are non-refundable, but are creditable against any royalty payments we pay under the Einstein License. For the year ended December 31, 2024, there were no payments related to Einstein license maintenance fees under the Einstein License, as they were creditable against actual payments owed to Einstein during the twelve-month period.

Under the Einstein License, we are also obligated to make milestone payments corresponding to: (i) approval of the first IND by the FDA or foreign equivalent for a Licensed Product; (ii) approval of any subsequent IND application or foreign equivalent for a “new indication” for a Licensed Product; (iii) initiation of Phase 2 clinical trials or foreign equivalent on a Licensed Product; (iv) initiation of Phase 2 clinical trials or foreign equivalent for a “new indication” for a Licensed Product; (v) initiation of Phase 3 clinical trials or foreign equivalent on a Licensed Product; (vi) initiation of Phase 3 clinical trials or foreign equivalent for a “new indication” for a Licensed Product; (vii) the first commercial sale of a Licensed Product; (viii) the first commercial sale of each “new indication” for one of our previously approved Licensed Products; and (ix) cumulative sales of certain Licensed Products reaching certain threshold amounts. The aggregate amount of milestone payments made under the Einstein License may equal up to $1.85 million for each Licensed Product and up to $1.85 million for each new indication of a Licensed Product. Additionally, the aggregate amount of one-time milestone payments based on cumulative sales of all Licensed Products may equal up to $5.75 million. At December 31, 2024, we have made payments totaling $1.2 million since inception with respect to achievement of these milestones.

In addition to our obligations to make the cash payments to Einstein described above, under the Einstein License we issued Einstein 671,572 shares of our Common Stock immediately prior to completion of the initial public offering of our common stock completed on December 27, 2017.

The Einstein License expires upon the expiration of our last obligation to make royalty payments to Einstein, which may be due with respect to certain Licensed Products, unless terminated earlier under the provisions thereof. Under the Einstein License, we will be obligated to make royalty payments to Einstein, with respect to certain Licensed Products, for the

longer of 15 years from the first sale of such products in each country or for the duration of any market exclusivity period granted by a regulatory agency for such product and, with respect to certain Licensed Products sold by sublicensees, the longer of 10 years from the first sale of such products in each country or for so long as the sublicensee agrees to pay royalties on such products. We have the right to terminate the Einstein License at any time upon 60 days' written notice to Einstein; provided, however, that we will lose intellectual property rights related to the Patents if we choose to terminate the Einstein License in this manner. Each party has the right to terminate the Einstein License if the other party is in default or breach of any condition of the Einstein License with a right to cure any such breach within 60 days from receipt of notice of such default or breach, unless the other party has disputed the alleged breach in good faith. Either party can also terminate the Einstein License if the other party voluntarily files for bankruptcy or other similar insolvency proceedings, makes a general assignment for the benefit of creditors, or is the subject of an involuntary bankruptcy petition that is not dismissed within 90 days. If we fail to pay any sum that is due and payable to Einstein within 30 days after receiving written notice of our default from Einstein, then Einstein has the option of terminating the Einstein License unless we pay within 45 days of such notice all delinquent sums with interest.

The Einstein License also obligates us to meet certain due diligence requirements, or the Diligence Milestones, as follows:

- update our research and development plan annually;
- initiate Phase 1 clinical trials on a Licensed Product within a number of years from the Effective Date;
- initiate Phase 2 clinical trials on a Licensed Product within a number of years from the Effective Date;
- initiate Phase 3 clinical trials on a Licensed Product or an FDA approved clinical trial designed to support a biologics license application, or BLA, within a number of years from the Effective Date;
- submit an application for FDA approval to market and sell a Licensed Product within a number of years from the Effective Date;
- have our first commercial sale of an FDA Licensed Product within a number of years from the Effective Date; and
- spend a minimum amount per year on product development until our first commercial sale of a Licensed Product.

If we fail to meet any of the Diligence Milestones, Einstein will have the right to terminate the Einstein License if such Diligence Milestone is not satisfied within thirty days from receiving a written notice of default from Einstein. Under certain circumstances and upon prior notice to Einstein, we may have the right to an additional extension of our Diligence Milestones if, despite our commercially reasonable efforts we are not able to satisfy the Phase 3 clinical trial Diligence Milestone or any subsequent Diligence Milestone. As of the date of this report, we have met all required Diligence Milestones.

Our Collaboration Agreement with LG Chem

On November 6, 2018, we entered into a Collaboration, License and Option Agreement, or the LG Chem Collaboration Agreement, with LG Chem Ltd., or LG Chem, pertaining to the development of CUE-101 and CUE-102 Immuno-STATs in Australia and in certain countries in Asia, or the LG Chem Territory.

In furtherance of pursuing strategic options pertaining to CUE-101, on March 11, 2025, we regained our rights to the CUE-101 program which had previously been licensed to LG Chem.

LG Chem continues to maintain its interest and rights in the CUE-102 program, targeting WT1 expressing cancers, pursuant to the LG Chem Collaboration Agreement. See discussion of the LG Chem Collaboration Agreement in Note 10 to our consolidated financial statements appearing elsewhere in this Form 10-K.

Our Collaboration and Option Agreement with Ono

Effective March 6, 2025, we regained worldwide development and commercialization rights for CUE-401, which had previously been licensed to Ono Pharmaceutical pursuant to a Collaboration and Option Agreement entered into in February 2023. We are excited to progress CUE-401 through preclinical development and into the clinic.

CUE-401 is currently in IND-enabling studies and we plan to file an IND in the third quarter of 2026. It is our hypothesis that early clinical evidence could demonstrate a mechanistic competitive advantage and may potentially position

CUE-401 as a new standard of care. We intend to disclose CUE-401 preclinical data in the near future. See discussion of the Collaboration and Option Agreement in Note 10 to our consolidated financial statements appearing elsewhere in this Form 10-K.

Our Intellectual Property

We believe that our current patents and patent applications and any future patents and other proprietary rights that we own, or control through licensing, are and will be essential to our business. We believe that these intellectual property rights will affect our ability to compete effectively with others. We also rely and will rely on trade secrets, know-how, continuing technological innovations and licensing opportunities to develop, maintain and strengthen our competitive position. We seek to protect these, in part, through confidentiality agreements with certain employees, consultants, advisors and other parties. Our success will depend in part on our ability, and the ability of our licensors, to obtain, maintain (including making periodic filings and payments) and enforce patent protection for our/their intellectual property, including those patents and patent applications to which we have secured exclusive rights.

As of December 31, 2024, we owned or had licensed 145 issued patents (including 30 issued U.S. patents), 379 pending patent applications (including 79 in the U.S.), 9 pending U.S. provisional patent applications, 18 pending PCT (international) applications, and 282 pending foreign patent applications.

Our patent applications describe certain features of our technologies, including our Immuno-STAT platform, our Neo-STAT platform, CAR-T and ex-vivo applications of our Immuno-STAT platform, our RDI-STAT platform, our CUE-300 Series platform, including CUE-301, our CUE-400 Series platform, including CUE-401, as well as specific biologic molecules, drug product candidates and methods of treatment using our Immuno-STATs. In addition, we have pending applications that cover CUE-501 and the CUE-500 series and their use in oncology and autoimmune indications. We plan to spend considerable resources and focus in the future on obtaining U.S. and foreign patents. We have and will continue to actively protect our intellectual property. No assurances can be given that any of our patent applications will result in the issuance of a patent or that the examination process will not require us to narrow our claims. In addition, any issued patents may be contested, circumvented, found unenforceable or invalid, and we may not be able to successfully enforce our patent rights against third parties. No assurance can be given that others will not independently develop a similar or competing technology or design around any patents that may be issued to us. We intend to expand our international operations in the future and our patent portfolio, copyright, trademark and trade secret protections may not be available or may be limited in foreign countries.

Each of our patents, if and when granted, will generally have a term of 20 years from its respective U.S. or international non-provisional priority filing date, subject to available extensions. They are thus set to expire no earlier than dates ranging from 2033 to 2045, although patents that specifically cover our drug product candidates will expire no earlier than December 2037, subject to available extensions.

Competition

Our Immuno-STAT platform offers a differentiated approach by targeting disease-relevant T cells without inducing systemic toxicity seen in traditional immunotherapies. While we believe that our drug product candidates, technology, knowledge and experience provide us with significant competitive advantages, we face competition from established and emerging pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others, who may have drug product candidates in further stages of development than ours.

Autoimmune Competition

We compete with other companies working to develop cytokines to restore immune balance, as well as those developing other therapeutic modalities, including monoclonal antibodies, bi-specific antibodies, cell therapies, and vaccines with application in treating patients living with autoimmune disease. Potential competitors in the cytokine-based therapy space include Amgen, Bristol-Myers Squibb, Merck & Co., Nektar Therapeutics, Sanofi S.A., TRex Bio, and RegCell. In the regulatory T cell therapies space, potential competitors include Abata Therapeutics, Coya Therapeutics, Quell Therapeutics, Sangamo Therapeutics, and Sonoma Biotherapeutics.

We believe that our approach provides us with a superior competitive advantage and differentiation, with a potentially first-in-class, masked TGF-β and IL-2v designed to address the underlying mechanism of disease by rebalancing the Treg and effector cell ratio.

Oncology Competition

We compete with other companies working to develop cytokines as cancer immunotherapies, as well as those developing other immunotherapeutic modalities, including monoclonal antibodies, bi-specific antibodies, antibody-drug conjugates, cell therapies, oncolytic viruses, and vaccines with application in treating patients living with cancer. Potential competitors in the cytokine-based therapy space include Asher Bio, Aulos Bio, BioNTech SE, Medicenna Therapeutics, Moderna, Inc., Mural Oncology, Roche Holding AG, Synthekine, Werewolf Therapeutics, and Xilio Therapeutics. In the cell therapy space, potential competitors include Adaptimmune Therapeutics, Bristol-Myers Squibb, Iovance Biotherapeutics, Gilead Sciences, Janssen Pharmaceuticals, and Novartis AG. In the checkpoint inhibitor, or CPI, space, potential competitors include AstraZeneca, Bristol-Myers Squibb, Merck & Co., and Roche Holding AG.

We believe that our approach provides us with a competitive advantage through selective delivery of immune activating signals, coupling engineered cytokines (i.e., IL-2) to a targeting moiety (i.e., peptide-MHC complex) for enhanced activation of cancer-specific CD8+ T cells.

Many of our competitors have greater financial, technical and human resources than we do. Additionally, many competitors have greater experience in product discovery and development, obtaining FDA and other regulatory approvals, and commercialization capabilities, which may provide them with a competitive advantage.

We expect any drug product candidate that we commercialize, either independently or with our strategic partners, will compete with existing, market-leading products and believe that our ability to compete will depend on our ability to execute on the following objectives:

- design, develop and commercialize products that are superior to other products in the market in terms of, among other things, safety, efficacy, convenience, or price;
- obtain patent and/or other proprietary protection for our processes and drug product candidates;
- obtain required regulatory approvals;
- obtain favorable reimbursement, formulary and guideline status; and
- collaborate with others in the design, development and commercialization of our products.

Established competitors may invest heavily to discover and develop novel compounds that could make our drug product candidates obsolete. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and/or safety in order to obtain approval, to overcome price competition and to be commercially successful. If we are not able to compete effectively, our business will not grow and our financial condition and operations will suffer.

Government Regulation and Licensure of Products

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, or EU, extensively regulate, among other things, the research, development, testing, manufacture, pricing, reimbursement, sales, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products, including biological products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources and may have a significant impact on our business.

Licensure and Regulation of Biologics in the United States

In the United States, our drug product candidates are regulated as biological products, or biologics, under the Public Health Service Act, or the PHSA, and the Federal Food, Drug and Cosmetic Act, or the FDCA, and their implementing regulations and guidance. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. The failure to comply with the applicable U.S. requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may subject a sponsor to delays in the conduct of the study, regulatory review and approval, and/or administrative or judicial sanctions. A sponsor seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's

Good Laboratory Practice, or GLP, regulations and standards and other applicable regulations;

- completion of the manufacture, under current Good Manufacturing Practices, or GMP, conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;

- design of a clinical protocol and submission to the FDA of an investigational new drug application, or IND, application for human clinical testing, which must become effective before human clinical trials may begin;

- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with current Good Clinical Practices, or GCP;

- preparation and submission to the FDA of a BLA for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product in clinical development and proposed labelling;

- review of the product by an FDA advisory committee, where appropriate or if applicable;

- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with GMP requirements and to assure that the chemistry, methods, and controls, or CMC, for the product are adequate to preserve the product's identity, strength, quality, and purity, and, if applicable, the FDA's current good tissue practice for the use of human cellular and tissue products;

- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCPs and the integrity of clinical data in support of the BLA;

- payment of substantial application and program fees pursuant to the Prescription Drug User Free Act, or PDUFA;

- securing FDA approval of the BLA and licensure of the new biologic product allowing marketing in the United States for particular indications and under certain conditions; and

- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and any post-approval studies required by the FDA.

Preclinical Studies

Before testing any biologic product candidate in humans, a product candidate must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animal studies. These studies are generally referred to as IND-enabling studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application.

The IND Process

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin or recommence.

As a result, submission of the IND may result in the FDA not allowing the trials to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this

initial 30-day period or following commencement of the clinical trial, it may choose to impose a partial or complete clinical hold. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or CMC. This order issued by the FDA would delay either a proposed clinical study or cause suspension of an ongoing study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. This could cause significant delays or difficulties in completing planned clinical studies in a timely manner.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational products for patients who may benefit from investigational therapies. FDA regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or treatment IND application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or the Cures Act, passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests, it must make that policy publicly available. Although these requirements were rolled out over time, they have now come into full effect. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its investigational products available to eligible patients as a result of the Right to Try Act.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

Each clinical trial must be reviewed and approved by an IRB either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects, and the possible liability of the institution. An IRB must operate in compliance with FDA regulations. The IRB or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data monitoring committee, or DMC. This group may recommend continuation of the study as planned, changes in study conduct, or cessation of the study at designated check points based on certain available data from the study to which only the DMC has access. Finally, research activities involving infectious agents, hazardous chemicals, recombinant DNA, and genetically altered organisms and agents may be subject to review and approval of an Institutional Biosafety Committee in accordance with U.S. National Institutes of Health, or NIH, Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- *Phase 1* clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, on occasion, in patients, such as cancer patients.

- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.

- *Phase 3* clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy, and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic; such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such trials are typically referred to as post-approval clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any post-approval clinical trial requirement or to request a change in the product labeling. Failure to exhibit due diligence with regard to conducting post-approval clinical trials could result in withdrawal of approval for products.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In March 2022, the FDA released final guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology biological product development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by the FDA. Expansion cohort trials can potentially bring efficiency to product development and reduce developmental costs and time.

In December 2022, with the passage of the Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan, or DAP, for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, DAPs must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directed the FDA to issue new guidance on DAPs. In June 2024, the FDA issued draft guidance

setting out its policies for the collection of race and ethnicity data in clinical trials. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. The implications of this action are not yet known.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the International Council for Harmonisation's recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although the FDA has historically not enforced these reporting requirements due to the U.S. Department of Health and Human Services', or HHS's, long delay in issuing final implementing regulations, those regulations have now been issued. With those regulations now in place, the FDA has issued, as of December 19, 2024, six notices of non-compliance, thereby signaling the government's willingness to begin enforcing these requirements against non-compliant clinical trial sponsors. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

Clinical Studies Outside the United States in Support of FDA Approval

In connection with our clinical development program, we may conduct trials at sites outside the United States. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, or IEC, and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

The acceptance by the FDA of study data from clinical trials conducted outside the United States in support of US approval 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 marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through 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, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-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 approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Interactions with FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. Progress reports detailing the results of clinical trials must be submitted annually within 60 days of the anniversary dates that the IND went into effect and more frequently if serious adverse events occur. These reports must include a development safety update report, or DSUR. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other trials or animal or *in vitro* testing that

suggest a significant risk in humans exposed to the product; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Meetings at other times may also be requested. There are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-BLA meetings, as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including for example meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. A Type D meeting is focused on a narrow set of issues, which should be limited to no more than two focused topics and should not require input from more than three disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product.

At the conclusion of these meetings, the FDA will typically provide its responses to questions posed by the sponsor regarding the clinical development program. The FDA will not indicate whether a BLA will be approved, but it will provide guidance to the sponsor on various questions, including whether an application should be submitted in the first place on the basis of the studies and data proposed by the sponsor. The agency may also generally express support for the sponsor's approach in the clinical development program but indicate that questions concerning whether the data support approval will be subject to review by the agency following its acceptance for filing of the BLA. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, a BLA or supplement thereto must contain data that are adequate to assess the safety, potency and purity of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

For products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The FDA is required to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although the FDA has taken steps to limit what it considers abuse of this statutory exemption in PREA. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

Compliance with GMP Requirements

The FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with GMPs. The GMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process.

Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with GMPs and other laws. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from GMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

Submission and Filing for Review of a BLA

The results of product candidate development, preclinical testing, and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting a license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee. Under federal law, the submission of most BLAs is subject to an application user fee, which for federal fiscal year 2025 is $4,310,002 for an application requiring clinical data. The sponsor of a licensed BLA is also subject to an annual program fee, which for federal fiscal year 2025 is $403,889. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In the event that the FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor. The FDA may request additional information and studies, and the application must be resubmitted with the additional information. The resubmitted application is subject to review before the FDA accepts it for filing.

Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the sponsor, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

The FDA seeks to meet these timelines for review of an application but its ability to do so may be affected by a variety of factors. While the costs associated with review of an application are typically covered by the PDUFA user fee program, other activities, including government budget and funding levels, the ability to hire and retain key personnel and statutory, regulatory and policy changes, may impact the FDA's review and approval of marketing applications. Average review times at the agency have fluctuated in recent years, as a result. For example, during the past decade, the U.S. government has shut down several times and certain regulatory agencies, including the FDA, have had to furlough critical employees and stop critical activities. Further, there is substantial uncertainty as to how measures currently being implemented by the new Trump Administration across the government will impact the FDA and other federal agencies with jurisdiction over biologics.

In connection with its review of an application, the FDA will typically submit information requests to the applicant and set deadlines for responses thereto. The FDA will also inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with a submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application

unless it determines that the manufacturing processes and facilities are in compliance with current GMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an application, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the data submitted in support of the application. With passage of FDORA, Congress clarified FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to FDA as well as other persons holding study records or involved in the study process.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the BLA. That is because, under certain circumstances, principal investigators at a clinical trial site may also serve as scientific advisors or consultants to a sponsor and receive compensation in connection with such services. Depending on the level of that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of safety and efficacy of the investigational product.

The FDA may also refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Decisions on BLAs

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter, or CRL, or an approval letter. To reach this determination, the FDA must determine whether there is substantial evidence that the product is effective and that expected benefits of the proposed product outweigh its potential risks to patients. This assessment is informed by the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks.

If the application is not approved, the FDA will issue a CRL, which will contain the conditions that must be met in order to secure final approval of the application, and, when possible, will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a CRL may submit to the FDA information that represents a complete response to the issues identified by the FDA. Such resubmissions are classified under PDUFA as either Class 1 or Class 2. The classification of a resubmission is based on the information submitted by a sponsor in response to an action letter. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has two months to review a Class 1 resubmission and six months to review a Class 2 resubmission. The FDA will not approve an application until issues identified in the complete response letter have been addressed. For those seeking to challenge FDA's CRL decision, the agency has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications.

The FDA may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may call for post-approval studies, including post-approval clinical trials, to further assess the product's safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patent registries.

The FDA may prevent or limit further marketing of a product based on the results of post-approval studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications,

manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Expedited Review Programs

The FDA is authorized to expedite the review of applications in several ways. Under the Fast Track program, the sponsor of a product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Product candidates are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.

Any product candidate submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, priority review and accelerated approval.

- *Breakthrough therapy designation.* To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.

- *Priority review.* A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. The FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.

- *Accelerated approval.* Biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.

  With passage of FDORA, in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval trial of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner of Food and Drugs, or the Commissioner, or the Commissioner's designee and a written appeal, among other things.

  In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The agency indicated that the accelerated approval pathway is commonly used for approval of oncology

drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidances relating to accelerated approval. These guidances describe FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

- *Regenerative advanced therapy.* With passage of the Cures Act in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

None of these expedited programs changes the standards for approval but each may help expedite the development or approval process governing product candidates.

Project Optimus

Project Optimus is an initiative of the Oncology Center of Excellence, or OCE, at the FDA. This project focuses on dose optimization and dose selection in oncology drug development, and whether the current paradigm based on cytotoxic chemotherapeutics leads to doses and schedules of molecularly targeted therapies that provide more toxicity without additional efficacy, among other things. In Project Optimus, drug developers have the opportunity to meet with the FDA's Oncology Review Divisions early in their development programs, well before conducting trials intended for registration, to discuss dose-finding and dose optimization. The program thus allows sponsors to develop strategies for dose finding and dose optimization that leverages nonclinical and clinical data in dose selection, including randomized evaluations of a range of doses in trials, with the objective of performing these studies as early as possible in the development program to bring promising new therapies to patients. In August 2024, the FDA issued final guidance concerning optimizing the dosage of biologics and drugs for the treatment of oncologic diseases.

Real-Time Oncology Review of Supplemental NDAs

Through its OCE, the FDA has established two pilot programs allowing for real-time review of supplemental applications for previously approved oncology products. This approach will allow FDA to evaluate clinical data as soon as the results of a clinical trial become available with the objective of reviewing and approving a new indication soon after a sponsor files the application. The first of these pilot programs, Real-Time Oncology Review, or RTOR, focuses on early submission of data that are the most relevant to assessing the product's safety, potency and purity. RTOR allows the FDA to review much of the data earlier, after the clinical trial results become available and the database is locked, but before the information is formally submitted to the agency.

The FDA has established several criteria to determine whether a supplemental application may be selected for RTOR. Those criteria include whether: the investigational product is likely to demonstrate substantial improvements over available therapy; the study design is straight forward, as determined by the review division and the OCE; the endpoints can be easily interpreted. Applications with chemistry, manufacturing and control formulation changes and supplements with pharmacology/toxicology data are excluded from RTOR. In addition, submissions with greater complexity, including those with companion diagnostics, may also be excluded for the purposes of the pilot program. On the basis of these criteria, the appropriate FDA review division and OCE management will jointly decide whether the application can be selected for the RTOR pilot program.

If the FDA determines that RTOR is an appropriate review pathway, the sponsor can send pre-submission data to the agency under the original application two to four weeks after all patient data have been entered and locked in the database, and the sponsor is ready to request FDA approval. The package should also include key raw and derived datasets, including safety/efficacy tables and figures, study protocol and amendments, and a draft of the package insert. The sponsor must also submit key results, analysis, and datasets for other disciplines, if applicable. The FDA will then evaluate these materials for sufficiency and integrity so that it can analyze the data to properly address key regulatory questions. By the time the sponsor submits the application to the FDA, the review team will have completed the analysis and be familiar with the data, and can conduct a more efficient, timely, and thorough review.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA have imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including GMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with GMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the 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 post-market studies or clinical trials to assess new safety risks; or imposition of distribution 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 holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. Although health care providers may prescribe products for off-label uses in their professional judgment, drug manufacturers are prohibited from soliciting, encouraging or promoting unapproved uses of a product. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a biologic.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the U.S. Department of Justice, or the Office of the Inspector General of HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws. The Prescription Drug Marketing Act, or PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. In November 2013, the federal Drug Supply Chain Security Act, or DSCSA, became effective in the United States, mandating an industry-wide, electronic, interoperable system to trace prescription drugs through the pharmaceutical distribution supply chain with a ten-year phase-in process. Manufacturers were required by November 2023 to have such systems and processes in place. So as not to disrupt supply chains, the FDA has granted certain exemptions from enhanced drug distribution security requirements for eligible trading partners for particular periods of time.

Orphan Drug Designation and Exclusivity

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product

generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same indication for seven years, except in certain limited circumstances. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

The period of exclusivity begins on the date that the marketing application is approved by the FDA. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if the company with orphan drug exclusivity is not able to meet market demand or the subsequent product is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care. Under Omnibus legislation signed by the then President of the United States on December 27, 2020, the requirement for a product to show clinical superiority applies to drug products that received orphan drug designation before enactment of amendments to the FDCA in 2017 but have not yet been approved by FDA.

In September 2021, the Court of Appeals for the 11th Circuit, in *Catalyst Pharms, Inc. v. Becerra*, or Catalyst, held that, for the purpose of determining the scope of orphan drug exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of the Catalyst court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug is approved. More recently however, on February 14, 2025, a federal district court in Washington, D.C. fully embraced the reasoning of the Catalyst decision in another decision challenging the scope of orphan drug exclusivity. The implications of this decision, and its impact on the FDA's implementation of the Orphan Drug Act, are unclear at this point.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of regulatory exclusivity to the term of any existing regulatory exclusivity, including orphan exclusivity, for biologic products. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Biosimilars and Regulatory Exclusivity

The 2010 Patient Protection and Affordable Care Act, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or the BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. A biosimilar is a biological product that is highly similar to an existing FDA-licensed "reference product." To date, the FDA has licensed a number of biosimilar products and interchangeable biosimilar products.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. In December 2022, Congress clarified through FDORA that FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the first day on which such a product is approved as interchangeable with the reference product.

An application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the

sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. There have been recent government proposals to reduce the 12-year reference product exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products.

Patent Term Restoration and Extension

A patent claiming a new biologic product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of the IND clearing the clinical investigation involving human beings and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

FDA Approval of Companion Diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products.

The 2014 guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a biologic product candidate 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 generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a product 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 the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE.

In April 2020, the FDA issued additional guidance which describes considerations for the development and labeling of companion diagnostic devices to support the indicated uses of multiple biological oncology products, when appropriate. The 2020 guidance expands on the policy statement in the 2014 guidance by recommending that companion diagnostic developers consider a number of factors when determining whether their test could be developed, or the labeling for approved companion diagnostics could be revised through a supplement, to support a broader labeling claim such as use with a specific group of oncology therapeutic products (rather than listing an individual therapeutic product(s)).

Under the FDCA, *in vitro* diagnostics, including 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 FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic product candidate. 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 sponsor 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. PMA applications are subject to an application fee. For federal fiscal year 2025, the standard fee is $540,783 and the small business fee is $135,196.

A clinical trial is typically required for a PMA application and, in a small percentage of cases, the FDA may require a clinical study in support of a 510(k) submission. A manufacturer that wishes to conduct a clinical study involving the device is subject to the FDA's IDE regulation. The IDE regulation distinguishes between significant and non-significant risk device studies and the procedures for obtaining approval to begin the study differ accordingly. Also, some types of studies are exempt from the IDE regulations. A significant risk device presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices are devices that are substantially important in diagnosing, curing, mitigating, or treating disease or in preventing impairment to human health. Studies of devices that pose a significant risk require both FDA and an IRB approval prior to initiation of a clinical study. Non-significant risk devices are devices that do not pose a significant risk to the human subjects. A non-significant risk device study requires only IRB approval prior to initiation of a clinical study.

After a device is placed on the market, 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 Quality System Regulation, which covers 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.

It is possible that an in vitro companion diagnostic device could be subject to FDA enforcement discretion from compliance with the FDCA if it meets the definition of a Laboratory Developed Test, or LDT. However, the FDA issued a final rule in April 2024 to end enforcement discretion for LDTs and actively regulate such products as medical devices. Under this final rule, LDTs are required to come into compliance with the FDA's medical device regulatory requirements in a staged approach over the course of four years. The implementation of this LDT final rule could potentially be affected by the Executive Order, Regulatory Freeze Pending Review, issued by President Trump on January 20, 2025 and/or the anticipated change in leadership at the FDA under the new administration. Further, while the final regulation is set to take effect on May 6, 2025, a number of parties have challenged the legality of the LDT regulation in a federal district court. That court held a hearing on this matter on February 19, 2025, and is expected to issue a ruling soon.

Federal and State Data Privacy and Security Laws

Under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, HHS has issued regulations to protect the privacy and security of protected health information used or disclosed by covered entities including certain healthcare providers, health plans, and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes, and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their regulations, including the omnibus final rule published on January 25, 2013, also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that are applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. Accordingly, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. New laws and regulations governing privacy and security may be adopted in the future as well.

In addition to potential enforcement by HHS, we are also potentially subject to privacy enforcement from the Federal Trade Commission, or FTC. The FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the Federal Trade Commission Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate

any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements. Finally, both the FTC and HHS's enforcement priorities (as well as those of other federal regulators) may be impacted by the change in administration and new leadership. These shifts in enforcement priorities may also impact our business.

There are also increased restrictions at the federal level relating to transferring sensitive data outside of the United States to certain foreign countries. For example, in 2024, Congress passed H.B. 815, which included the Protecting Americans' Data from Foreign Adversaries Act of 2024. This law creates certain restrictions for entities that disclose sensitive data (including potential health data) to countries such as China. Failure to comply with these rules can lead to a potential FTC enforcement action. Additionally, the U.S. Department of Justice recently finalized a rule implementing Executive Order 14117, which creates similar restrictions related to the transfer of sensitive U.S. data to countries such as China. These data transfer restrictions (and others that may pass in the future) may create operational challenges and legal risks for our business.

Additionally, California recently enacted legislation that has been dubbed the first "GDPR-like" (referring to the EU General Data Protection Regulation, or GDPR) law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. The CCPA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, a number of other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime over the next several years. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws that will go into effect over the next several years. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business.

Regulation and Procedures Governing Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, a sponsor will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy

of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Non-clinical Studies

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical Trial Approval

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014, or CTR, became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union, or EU Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the European Medicines Agency, or EMA, and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU Portal and Database"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted, or concerned member states. Part II is assessed separately by each concerned member state. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned member state. However, overall related timelines will be defined by the CTR.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

As of January 31, 2025, all clinical trials (including those which are ongoing) are subject to the provisions of the CTR. The failure to transition ongoing clinical trials to the CTR can result in corrective measures under Article 77 of the CTR, including revocation of the authorization of the clinical trial or suspension of the clinical trial as well as criminal sanctions and fines under national law of EU Member States.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation

In March 2016, the EMA, launched an initiative to facilitate development of drug product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority Medicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of drug product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated EMA contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies are appointed early in the PRIME scheme

facilitating increased understanding of the product at the EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Pediatric Studies

Sponsors developing a new medicinal product must agree upon a Pediatric Investigation Plan, or PIP, with the EMA's pediatric committee, or PDCO, and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies (e.g., because the relevant disease or condition occurs only in adults). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date.

Marketing Authorization

To obtain a marketing authorization for a product under the EU regulatory system, a sponsor must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in EU Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to a sponsor established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, a sponsor must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU Member States. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. Manufacturers must demonstrate the quality, safety, and efficacy of their products to the EMA, which provides an opinion regarding the MAA. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting an initial assessment of a product. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Conditional Marketing Authorization

In particular circumstances, EU legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables sponsors to obtain a "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive; and (5) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing

authorization holder, including obligations with respect to the completion of ongoing or new clinical trials and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Exceptional Circumstances

A marketing authorization may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This marketing authorization is close to the conditional marketing authorization as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a marketing authorization However, unlike the conditional marketing authorization, the applicant does not have to provide the missing data and will never have to. Although the marketing authorization "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the marketing authorization is withdrawn in case the risk-benefit ratio is no longer favorable. Under these procedures, before granting the marketing authorization, the EMA or the competent authorities of the member states make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety, and efficacy. Except conditional marketing authorizations, marketing authorizations have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

Regulatory Data Protection in the European Union

In the EU, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

The EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products was published in April 2023 and includes, among other things, provisions that would potentially reduce the duration of regulatory data protection. The European Parliament requested several amendments in April 2024. At this time, the proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry in the long term, if and when adopted.

Patent Term Extensions in the European Union and Other Jurisdictions

The European Union also provides for patent term extension through Supplementary Protection Certificates, or SPCs. The rules and requirements for obtaining a SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. These periods can be extended for six additional months if pediatric exclusivity is obtained, which is described in detail below. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EU market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities, and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83EC, as amended.

Orphan Drug Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the sponsor must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized European Union marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the European Commission or the member states can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity.

Pediatric Exclusivity

Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) even where the trial results are negative. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Approval of Companion Diagnostic Devices

In the European Union, medical devices such as companion diagnostics must comply with the General Safety and Performance Requirements, or SPRs, detailed in Annex I of the EU Medical Devices Regulation (Regulation (EU) 2017/745), or MDR, which came into force on May 26, 2021 and replaced the previously applicable EU Medical Devices Directive (Council Directive 93/42/EEC). Compliance with SPRs and additional requirements applicable to companion medical devices is a prerequisite to be able to affix the CE Mark of Conformity to medical devices, without which they cannot be marketed or sold. To demonstrate compliance with the SPRs, a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. The MDR is meant to establish a uniform, transparent, predictable, and sustainable regulatory framework across the EU for medical devices.

Separately, the regulatory authorities in the EU also adopted a new In Vitro Diagnostic Regulation, or IVDR, (EU) 2017/746, which became effective in May 2022. The new regulation replaces the In Vitro Diagnostics Directive (IVDD) 98/79/EC. Manufacturers wishing to apply to a notified body for a conformity assessment of their in vitro diagnostic medical device had until May 2022 to update their Technical Documentation to meet the requirements and comply with the new, more stringent Regulation. The regulation will, among other things: strengthen the rules on placing devices on the market and reinforce surveillance once they are available; establish explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance, and safety of devices placed on the market; improve the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number; set up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the European Union; and strengthen rules for the assessment of certain high-risk devices, such as implants, which may have to undergo an additional check by experts before they are placed on the market.

The IVDR became effective in May 2022. However, it became clear in 2021 that that EU Member States, health institutions and economic operators were not ready to apply the IVDR as from that date. The European Commission therefore proposed a progressive or staggered roll-out of the rules of the IVDR. The current transition periods range from May 26, 2025 for high risk in vitro diagnostics, or IVDs, to May 26, 2027 for lower risk IVDs. Certain provisions for devices manufactured and used in health institutions, would have to apply as from May 26, 2028. These transition periods only apply to so called "legacy device", meaning devices covered by a certificate or declaration of conformity issued under the previous legal framework (notably, the IVDD).

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom's, or UK's, withdrawal from the EU, commonly referred to as Brexit, took place on January 31, 2020. The EU and the UK reached an agreement on their new partnership in the Trade and Cooperation Agreement, which entered into force on May 1, 2021. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol, as amended by the so-called Windsor Framework agreed in February 2023. As of January 1, 2025, the changes introduced by the Windsor Framework resulted in the MHRA being responsible for approving all medicinal products destined for the UK market (Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. The MHRA relies on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that existed prior to the UK's withdrawal from the EU.

As of January 1, 2024, a new international recognition procedure, or IRP, applies which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include the EMA and regulators in the EEA member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). The RR assessment must have undergone a full and standalone review. RR assessments based on reliance or recognition cannot be used to support an IRP application. A CHMP positive opinion or a Mutual Recognition/Decentralised Reliance Procedure positive end of procedure outcome is an RR authorization for the purposes of IRP.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing

information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States.

Following the CJEU decision, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The European Union initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022, and the European Commission adopted the adequacy decision in July 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the European Union to the United States. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business.

On June 23, 2016, the electorate in the UK voted in favor of leaving the EU, commonly referred to as Brexit. As with other issues related to Brexit, there are open questions about how personal data will be protected in the UK and whether personal information can transfer from the EU to the UK. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. While the Data Protection Act of 2018 in the UK that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the UK, it is unclear whether transfer of data from the EEA to the UK will remain lawful under the GDPR, although these transfers currently are permitted by an adequacy decision from the European Commission. The UK government has already determined that it considers all European Union 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the UK to the EU/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the UK as being "essentially adequate" for purposes of data transfer from the EU to the UK, although this decision may be re-evaluated in the future. The UK and the U.S. have also agreed to a U.S.-UK "Data Bridge," which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the United States. In addition to the UK, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the United States). Any changes or updates to these developments have the potential to impact our business.

Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any drug product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such drug product candidates. Even if any drug product candidates we may develop are approved, sales of such drug product candidates will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such drug product candidates. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, drug product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any drug product candidates we may develop could reduce physician utilization of such drug product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

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

Outside the United States, ensuring adequate coverage and payment for any drug product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any drug product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so called health technology assessments) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any

good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent or knowingly making, using, or causing to made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

- the federal civil monetary penalty and false statement laws and regulations relating to pricing and submission of pricing information for government programs, including penalties for knowingly and intentionally overcharging 340b eligible entities and the submission of false or fraudulent pricing information to government entities;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits 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 health care benefits, items or services;

- the Foreign Corrupt Practices Act, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, or PPACA, as amended by the Health Care Education Reconciliation Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within HHS information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the PPACA, which, among other things, includes changes to the coverage and payment for products under government health care programs.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act.

The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our drug product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the TCJA, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the PPACA brought by several states without specifically ruling on the constitutionality of the PPACA. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

During the first Trump Administration, the Congress and administration sought to overturn the PPACA and related measures. Shortly after taking office in January 2025, President Trump revoked numerous executive orders issued by President Biden, including at least two executive orders (e.g., EO 14009, Strengthening Medicaid and the Affordable Care Act, and EO 14070, Continuing to Strengthen Americans' Access to Affordable, Quality Health Coverage) which were designed to further implement the PPACA. There may be similar efforts to undermine the PPACA, and the accompanying uncertainty, for the foreseeable future.

Pharmaceutical Price Initiatives

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Seven states (Colorado, Florida, Maine, New Hampshire, New Mexico, Texas and Vermont) have passed laws allowing for the importation of drugs from Canada. North Dakota and Virginia have passed legislation establishing workgroups to examine the impact of a state importation program. As of May 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) had submitted SIP proposals to the FDA and, on January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. That state now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current safe harbor for Medicare drug rebates and create

new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the Inflation Reduction Act of 2022, or IRA, has been delayed by Congress to January 1, 2032.

On August 16, 2022, the IRA was signed into law by the President of the United States. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap, and it replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). In addition, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. In addition to the drug price negotiation program, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs. The new law also caps Medicare out-of-pocket drug costs at $2,000 a year.

The IRA includes a provision, known as the orphan drug exclusion, that excludes from price negotiations those orphan drugs that have been designated for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition. Thus, as CMS stated in final guidance in July 2023, a drug or biologic that is designated for more than one rare disease or condition will not qualify for the orphan drug exclusion, even if it is not approved for any indications for the additional diseases or conditions. Further, CMS will only consider active designations/approvals when evaluating a drug or biologic for the orphan drug exclusion. CMS has also clarified that, if a drug loses its orphan drug status, the agency will use the earliest date of approval/licensure to determine whether the product is a qualifying single source drug subject to price negotiations.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On January 17, 2025, shortly before the new administration took office, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. There has been uncertainty about the extent to which the new administration would support the price negotiation program. Following the change in administrations, CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. The second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

The IRA includes a provision, known as the orphan drug exclusion, that excludes from price negotiations those orphan drugs that have been designated for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition. Thus, as CMS stated in final guidance in July 2023, a drug or biologic that is designated for more than one rare disease or condition will not qualify for the orphan drug exclusion, even if it is not approved for any indications for the additional diseases or conditions. Further, CMS will only consider active designations/approvals when evaluating a drug or biologic for the orphan drug exclusion. CMS has also clarified that, if a drug loses its orphan drug status, the agency will use the earliest date of approval/licensure to determine whether the product is a qualifying single source drug subject to price negotiations.

On June 6, 2023, Merck & Co. filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, or Chamber, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional health care 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 health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug product candidates or additional pricing pressures. This may be increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval.

Additional Regulations

In addition to the foregoing, state, and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act, and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling, and disposal of various biologic, chemical, and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in foreign countries that impose similar obligations.

Human Capital

As of December 31, 2024, we had 41 full time employees. Substantially all of our employees are located in Massachusetts. None of our employees are represented by a labor union or covered by a collective bargaining agreement, and we believe our relationship with our employees is good. Additionally, we utilize independent contractors and other third parties to assist with various aspects of our drug and product development.

We recognize the value of our employees and are committed to being a workplace that encourages respect, collaboration, communication, transparency, and integrity. We seek to hire employees with diverse backgrounds and perspectives. Our success starts and ends with having the best talent, and as a result, we are focused on attracting, developing and retaining our employees. We offer employees a competitive and comprehensive benefits package. The principal purposes of our incentive plans are to attract, retain and motivate selected employees, consultants, advisors and directors through the granting of stock-based compensation awards and cash-based performance bonus awards, as applicable. We support employees attending industry conferences and obtaining professional licenses. We use a variety of human capital measures in managing our business, including: workforce demographics; inclusion; and employee health and safety.

Corporation Information

Our website address is www.cuebiopharma.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K or any other report or document we file with the Securities and Exchange Commission, or the SEC, and any reference to our website address is intended to be an inactive textual reference only.

Item 1A. Risk Factors

We are subject to various risks that may materially harm our business, prospects, financial condition and results of operations. This discussion highlights some of the risks that may affect our future operating results. These are the risks and uncertainties we believe are most important for you to consider. We cannot be certain that we will successfully address these risks. If we are unable to address these risks, our business may not grow, our stock price may suffer, and we may be unable to stay in business. Additional risks and uncertainties not presently known to us, which we currently deem immaterial or which are similar to those faced by other companies in our industry or business in general, may also impair our business, prospects, results of operations and financial condition. The risks discussed below include forward-looking statements, and our actual results may differ substantially from those discussed in these forward-looking statements.

Risks Related to Our Business

Our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern.

We have incurred significant losses since our inception and have never generated revenue or profit from product sales, and it is possible we will never generate revenue or profit from product sales. As of December 31, 2024, we had cash and cash equivalents of $22.5 million. Based on our current operating plans, we believe we will have sufficient funds to meet our obligations into the fourth quarter of 2025. However, we will need to raise additional capital to fund our future operations and remain as a going concern. There can be no assurance that we will be able to obtain additional funding, including through a combination of equity offerings, collaborations, and other strategic alliances, or other sources on acceptable terms, if at all. To the extent that we raise additional capital through future equity offerings, the ownership interest of common stockholders will be diluted, which dilution may be significant. We cannot guarantee that we will be able to obtain any or sufficient additional funding or that such funding, if available, will be obtainable on terms satisfactory to us. In the event that we are unable to obtain any or sufficient additional funding, there can be no assurance that we will be able to continue as a going concern, and we will be forced to delay, reduce or discontinue our product development programs or consider other various strategic alternatives.

Moreover, these factors raise substantial doubt about our ability to continue as a going concern. Substantial doubt about our ability to continue as a going concern may materially and adversely affect the price per share of our common stock, and it may be more difficult for us to obtain financing. If existing or potential collaborators decline to do business with us or potential investors decline to participate in any future financings due to such concerns, our ability to increase our cash position may be limited. The perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

We are a clinical-stage biopharmaceutical company, have no history of generating commercial revenue, have a history of operating losses and may never achieve or maintain profitability.

We are a clinical-stage biopharmaceutical company. We have a limited operating history, have never generated revenue from product sales, and have a history of losses from operations. As of December 31, 2024, we had an accumulated deficit of $340.9 million. Our ability to achieve commercial revenue-generating operations and, ultimately, achieve profitability will depend on whether we can obtain additional capital when we need it, complete the development of our technology, receive regulatory approval of our drug product candidates, successfully commercialize our drug product candidates and/or find strategic collaborators that can incorporate our drug product candidates into new or existing drugs which can be successfully commercialized together. There can be no assurance that we will ever generate commercial revenues or achieve or maintain profitability.

We currently do not have, and may never develop, any FDA-approved or commercialized products.

We currently do not have any products approved by the FDA or any other regulatory agency or any commercialized products and thus have never generated commercial revenue from product sales. We have not yet sought to obtain any regulatory approvals for any drug product candidates in the United States or any foreign market. Therefore, any estimated timing for our drug product candidates to be commercialized would be highly speculative.

To date, we have invested substantial resources in an exclusive license with Albert Einstein College of Medicine, or Einstein, that forms the foundation for certain of our drug product candidates and potential applications. For us to develop any products that might ultimately be commercialized, we will have to invest further time and capital in research and product

development, regulatory compliance and market development. We and our licensor, prospective business partners and other collaborators may never develop any products that can be commercialized. All of our development efforts will require substantial additional funding, none of which may result in any commercial revenue. Our efforts may not lead to commercially successful products for a number of reasons, including:

- we and our licensor, prospective business partners and other collaborators may not be able to complete research regarding, and nonclinical and clinical development of, our drug product candidates;
- regulatory approvals and marketing authorizations may not be achieved for our drug product candidates, or the scope of the approved indication may be narrower than sought;
- we and our licensor, prospective business partners and other collaborators may experience delays in our development programs, clinical trials and the regulatory approval process;
- our technology may not prove to be safe and effective in clinical trials or preclinical studies and our drug product candidates may have adverse side effects which outweigh any potential benefit to patients;
- we may not be able to identify suitable collaborators to complete development or commercialization of our potential products;
- we may not be able to maintain, protect or expand our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- any future products that are ultimately approved by the FDA or other regulatory bodies may not be commercially accepted in the marketplace by physicians or patients;
- any future products that are ultimately approved by the FDA or other regulatory bodies may not be able to be manufactured in commercial quantities or at an acceptable cost;
- physicians may not receive any reimbursement from third-party payors, or the level of reimbursement may be insufficient to support widespread adoption of any of our future products once approved by the FDA or other regulatory bodies; and
- rapid technological change may make our technology and drug product candidates obsolete.

Moreover, in July 2024, we determined to prioritize and strategically focus on our autoimmune programs, including CUE-401 and CUE-501, which are currently at a preclinical stage. We are actively seeking third party support through partnerships and collaborations, or alternative funding structures, to further develop the CUE-100 series and CUE-500 series programs, including CUE-101, CUE-102 and CUE-501, and there is no guarantee that we will be able to do so on favorable terms or at all.

We are substantially dependent on the success of our drug product candidates, only two of which are currently being tested in clinical trials, and significant additional research and development and clinical testing will be required before we can potentially seek regulatory approval for or commercialize any of our drug product candidates.

Historically, our main focus and the investment of a significant portion of our efforts and financial resources has been in the development of our most advanced clinical stage asset, CUE-101, for which we are currently completing an ongoing Phase 1 clinical trial, and CUE-102, for which we are also completing an ongoing Phase 1 clinical trial. Our other drug product candidates, including CUE-401 and CUE-501, are all at a preclinical stage. In July 2024, we determined to prioritize and strategically focus on our autoimmune programs, including CUE-401 and CUE-501. We are actively seeking third party support through partnerships and collaborations, or alternative funding structures, to further develop the CUE-101 and CUE-102 oncology programs in our CUE-100 series. Even if we are successful in obtaining third party support to develop the CUE-100 series, we expect that additional trials of CUE-101 and CUE-102 will be required in order to gain approval by the FDA. We also aim to establish a near-term third party development partnership to further pursue CUE-501 from our CUE-500 series of Immuno-STATs, which series is at the preclinical stage. Therefore, significant additional research and development activity and clinical testing are required before we and our collaborators will have a chance to achieve a commercially viable product from CUE-101, CUE-102, CUE-401, CUE-501 or our other drug product candidates. Our research and development efforts remain subject to all of the risks associated with the development of new biopharmaceutical products and treatments based on

immune modulation. Development of the underlying technology may be affected by unanticipated technical or other problems, among other research and development issues, and the possible insufficiency of funds needed in order to complete development of these drug product candidates. Safety, regulatory and efficacy issues, clinical hurdles or other challenges may result in delays and cause us to incur additional expenses that would increase our losses. If we and our collaborators cannot complete, or if we experience significant delays in developing, our potential drug product candidates or products for use in potential commercial applications, particularly after incurring significant expenditures, our business may fail and investors may lose the entirety of their investment.

We have limited experience in conducting clinical trials and no history of commercializing biologic products, which may make it difficult to evaluate the prospects for our future viability.

Our operations to date have been limited to financing and staffing our company, conducting research and developing our core technologies, and identifying and optimizing our lead drug product candidates. Additionally, we have conducted limited clinical testing of two of our drug product candidates. Although we have recruited a team that has experience with clinical trials in the United States, as a company, we have limited experience conducting clinical trials and have not had previous experience commercializing drug product candidates or submitting a Biologic License Application, or BLA, to the FDA or similar submissions to initiate clinical trials or obtain marketing authorization to foreign regulatory authorities. We cannot be certain that our current or any future clinical trials will begin or be completed on time, if at all, or that our planned development programs would be acceptable to the FDA or other regulatory authorities, or that, if regulatory approval is obtained, our drug product candidates can be successfully commercialized. Clinical trials and commercializing our drug product candidates will require significant additional financial and management resources, and reliance on third-party clinical investigators, contract research organizations, or CROs, contract manufacturing organization, or CMOs, consultants and collaborators. Relying on third-party clinical investigators, CROs, CMOs or collaborators may result in delays that are outside of our control.

Furthermore, we may not have the financial resources to continue development of, or to enter into collaborations for, a product candidate if we experience any problems or other unforeseen events that delay or prevent regulatory approval of, or our ability to commercialize, drug product candidates, including:

- negative or inconclusive results from our IND-enabling studies, clinical trials or the clinical trials of other drug product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- delays in submitting INDs or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or a foreign regulatory authority regarding the number, scope or design of our clinical trials;
- delays in enrolling patients in clinical trials;
- high drop-out rates of patients;
- inadequate supply or quality of clinical trial materials or other supplies necessary to conduct our clinical trials;
- greater than anticipated clinical trial costs;
- poor effectiveness or unacceptable side effects of our drug product candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- difficulty in establishing or managing relationships with CROs, CMOs, and clinical investigators;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;

- serious and unexpected drug-related side effects or other safety issues experienced by participants in our clinical trials or by individuals using drugs similar to our drug product candidates;

- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or

- varying interpretations of data by the FDA and foreign regulatory authorities.

In addition, policies of the FDA and other regulatory authorities with respect to clinical trials may change and additional government regulations may be enacted. For example, in December 2022, with the passage of the Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan, or DAP, for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directed the FDA to issue new guidance on DAPs. In June 2024, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. The implications of this action are not yet known.

Similarly, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

Our current or any future clinical trials or those of our collaborators may reveal significant adverse events, toxicities or other side effects not seen in our preclinical studies and may result in a safety profile that could inhibit or prevent regulatory approval or market acceptance of any of our drug product candidates.

In order to obtain marketing approval for any of our biologic drug product candidates, we must demonstrate the safety, purity, and efficacy of the product candidate for the relevant clinical indication or indications through preclinical studies and clinical trials as well as additional supporting data. If our drug product candidates are associated with undesirable side effects in preclinical studies or clinical trials or have characteristics that are unexpected, we may need to interrupt, delay or abandon their development or limit 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.

We are completing Phase 1 clinical trials for our most advanced clinical stage asset, CUE-101, and a Phase 1 clinical trial for CUE-102, but otherwise we have not conducted any clinical trials. We have conducted various preclinical studies of our drug product candidates, but we do not know the predictive value of these studies for humans, and we cannot guarantee that any positive results in preclinical studies will successfully translate to human patients. It is not uncommon to observe results in human clinical trials that are unexpected based on preclinical testing, and many drug product candidates fail in clinical trials despite promising preclinical results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their products. Human patients in clinical trials may suffer significant adverse events or other side effects not observed in our preclinical studies, including, but not limited to, immunogenic responses, organ toxicities such as liver, heart or kidney or other tolerability issues or possibly even death. The observed potency and kinetics of our drug product candidates in preclinical studies may not be observed in human clinical trials. If clinical trials of our drug product candidates fail to demonstrate efficacy to the satisfaction of

regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug product candidates.

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

Further, if any of our drug product candidates obtains marketing approval, toxicities associated with our drug product candidates may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional warnings being added to the labeling, significant restrictions on the use of the product or the withdrawal of the product from the market. We cannot predict whether our drug product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or clinical testing. However, any such event, were it to occur, would cause substantial harm to our business and financial condition and would result in the diversion of our management's attention.

Success in preclinical studies or early clinical trials may not be indicative of results obtained in later trials.

Results from preclinical studies or early clinical trials are not necessarily predictive of future clinical trial results, and interim results of a clinical trial are not necessarily indicative of final results. Our drug product candidates may fail to show the desired safety and efficacy in clinical development despite demonstrating positive results in preclinical studies or having successfully advanced through initial clinical trials or preliminary stages of clinical trials. There can be no assurance that the results seen in preclinical studies for any of our drug product candidates ultimately will result in success in clinical trials or that results seen in Phase 1 or 2 trials will be replicated in Phase 3 trials.

There is a high failure rate for drugs and biologic products proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy or requirements during the period of our drug product candidate development. Any such delays could materially and adversely affect our business, financial condition, results of operations and prospects.

We plan to continue to seek collaborations or strategic alliances. However, we may not be able to establish such relationships, and relationships we have established may not provide the expected benefits.

On November 6, 2018, we entered into a Collaboration, License and Option Agreement, or the LG Chem Collaboration Agreement, with LG Chem Ltd., or LG Chem, for the development of CUE-101 and CUE-102 Immuno-STATs. Pursuant to the LG Chem Collaboration Agreement, we have granted certain exclusive license rights to LG Chem in Australia and in certain countries in Asia and LG Chem has agreed to provide certain services to us and to make payments to us that include licensing fees, milestone payments and sales royalties. This agreement does not commit LG Chem to a long-term relationship, and LG Chem may disengage with us at any time.

In furtherance of pursuing strategic options pertaining to CUE-101, on March 11, 2025, we regained our rights back to the CUE-101 program which had previously been licensed to LG Chem. LG Chem continues to maintain its interest and rights in the CUE-102 program, targeting WT1 expressing cancers, pursuant to the LG Chem Collaboration Agreement.

In July 2024, we determined to prioritize and strategically focus on our autoimmune programs, including CUE-401 and CUE-501. We are actively seeking third party support through partnerships and collaborations, or alternative funding structures, to further develop our CUE-101 and CUE-102 oncology programs in our CUE-100 series and our CUE-501 preclinical autoimmune program in our CUE-500 series, and there is no guarantee that we will be able to do so on favorable terms or at all.

In addition, on February 22, 2023, we entered into a strategic collaboration agreement, or the Ono Collaboration and Option Agreement, with Ono Pharmaceutical Co., Ltd., or Ono, to further develop CUE-401 and provide dedicated resources and capabilities to help advance CUE-401 toward the clinic. On March 11, 2025, we and Ono agreed to terminate the Ono Collaboration and Option Agreement, effective as of March 6, 2025 . Effective upon termination, we regained worldwide development and commercialization rights for CUE-401 from Ono. At such time, the agreement had no further force or effect with the exception of certain customary provisions which are intended to survive termination and expiration of the agreement.

We plan to also seek additional strategic alliances or collaborations with other third parties that we believe will complement or augment our development and commercialization efforts with respect to our drug product candidates and any future drug product candidates that we may develop. In addition, we currently do not have sales, marketing, manufacturing or distribution capabilities or arrangements. In order to commercialize our potential products, we plan to seek development and marketing partners or sublicensees to obtain necessary marketing, manufacturing and distribution capabilities.

Any of these relationships may require us to incur non-recurring and other charges, give up certain rights relating to our intellectual property and research and development activities, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, issue debt which may require liens on our assets and which will increase our monthly expense obligations, or disrupt our management and business. Moreover, we may not be successful in our efforts to establish additional strategic partnerships or collaborations for our drug product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our drug product candidates as having the requisite clinical and/or commercial potential based on current or future demonstrated safety, purity, and efficacy. If we are unable to establish additional strategic partnerships or collaborations to develop our drug product candidates, the costs for us to independently develop our drug product candidates may be higher than we currently anticipate, which could materially harm our business prospects, financial condition and results of operation.

Further, collaborations involving our drug product candidates are subject to numerous risks, which may include the following:

- our collaborators may have significant discretion in determining the efforts and resources that they will apply to our collaboration as compared to their other then-existing collaborations;

- our collaborators may not pursue development and commercialization of our drug product candidates or may elect not to continue or renew development or commercialization of our programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;

- our collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;

- our collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our drug product candidates;

- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of each of our potential products;

- our collaborators may not properly maintain or defend our intellectual property rights in accordance with the terms of our contractual arrangements with them or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to other potential liability;

- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our drug product candidates, or that result in costly litigation or arbitration that diverts our management's attention and our other resources;

- collaborations have been, and in the future, additional collaborations may be, terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable drug product candidates; and

- our collaborators may own or co-own intellectual property covering our potential products that results from our collaboration with them, and in such case, we would not have the exclusive right to commercialize such intellectual property without our collaborators' involvement and consent.

As a result, we may not be able to realize the benefit of collaboration agreements, strategic partnerships or licenses of our technology or potential products, which could delay our product development timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve sufficient revenue, net income or other benefits to justify such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to our drug product candidates could delay the development and commercialization of our drug product candidates, which would harm our business prospects, financial condition, and results of operations.

Our collaboration agreement with LG Chem contains exclusivity provisions that restrict our research and development activities.

We have granted to LG Chem under the LG Chem Collaboration Agreement an exclusive license to develop, manufacture and commercialize CUE-102 in the LG Chem Territory. Under the LG Chem Collaboration Agreement, we will engineer the selected Immuno-STAT for up to three alleles, which are expected to include the predominant alleles in the LG Chem Territory, while LG Chem will establish a chemistry, manufacturing and controls, or CMC, process for the development and commercialization of Drug Product Candidates.

These restrictions on our development, manufacturing, and commercialization activities could impact our ability to successfully develop certain drug product candidates, which could harm our future business prospects for commercializing drugs for those drug product candidates.

We may not be successful in our efforts to identify additional drug product candidates. Due to our limited resources and access to capital, we must prioritize the development of certain drug product candidates; these decisions may prove to be wrong and may adversely affect our business.

In July 2024, we decided to strategically focus on our autoimmune programs, including CUE-401 and CUE-501. We are actively seeking third party support through partnerships and collaborations, or alternative funding structures, to further pursue our CUE-501 preclinical autoimmune program in our CUE-500 series and further develop our CUE-101 and CUE-102 oncology programs in our CUE-100 series, and there is no guarantee that we will be able to do so on favorable terms or at all.

Although we may explore other therapeutic opportunities, in addition to the drug product candidates that we are currently developing, we may fail to identify successful drug product candidates for clinical development for a number of reasons. If we fail to identify additional potential drug product candidates, our business could be materially harmed.

Research programs to pursue the development of our drug product candidates for additional indications and to identify new drug product candidates and disease targets require substantial technical, financial and human resources whether or not they are ultimately successful. Our research programs may initially show promise in identifying potential indications and/or drug product candidates, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or drug product candidates;

- our key platform technology, Immuno-STAT Biologics™, may not adequately enable us to design, discover and validate drug product candidates;

- potential drug product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective drugs; or

- it may take greater human and financial resources than we possess to identify additional therapeutic opportunities for our drug product candidates or to develop suitable potential drug product candidates through internal research programs, thereby limiting our ability to develop, diversify and expand our drug portfolio.

Because we have limited financial and human resources, we intend to initially focus on research programs and drug product candidates for a limited set of indications. As a result, we may forego or delay pursuit of opportunities with other drug product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of

success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

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

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results than our drug product candidates.

The biotechnology and pharmaceutical industries are characterized by intense competition and rapid innovation. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results than our drug product candidates. Our competitors may include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources than we have, such as a larger research and development staff and experienced marketing and manufacturing organizations, established relationships with CROs and other collaborators, as well as established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our drug product candidates or may develop proprietary technologies or secure patent protection and, in turn, exclude us from technologies that we may need for the development of our technologies and potential products.

Immunotherapy technologies are advancing at a rapid pace and we anticipate competing with companies developing cytokine-based therapies (e.g., Amgen, Bristol-Myers Squibb, Merck, Nektar Therapeutics, Sanofi S.A, TRex Bio and RegCell), regulatory T cell therapies (e.g., Abata Therapeutics, Coya Therapeutics, Quell Therapeutics, Sangamo Therapeutics and Sonoma Biotherapeutics), cell therapies (e.g., Adaptimmune, Bristol-Myers Squibb, Gilead Sciences, Iovance Biotherapeutics, Janssen Pharmaceuticals, and Novartis AG), immune checkpoint inhibitors (e.g., AstraZeneca, Bristol-Myers Squibb, Merck and Roche Holding AG), and targeted cytokines (e.g., Asher Bio, Aulos Bio, BioNTech SE, Medicenna Therapeutics, Moderna, Mural Oncology, Roche Holding AG, Synthekine, Werewolf Therapeutics and Xilio Therapeutics) many of which have significantly greater financial and other resources than we currently have.

Even if we obtain regulatory approval of any of our drug product candidates, we may not be the first to market, and that may negatively affect the price or demand for our drug product candidates. Additionally, we may not be able to implement our business plan if the acceptance of our drug product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our drug product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our drug product candidates for use in limited circumstances. Furthermore, a competitor could obtain orphan product exclusivity from the FDA with respect to such competitor's product. If such competitor product is determined to be the same product as one of our drug product candidates, we may be prevented from obtaining approval from the FDA for such product candidate for the same indication for seven years, except in limited circumstances, and we may be subject to similar restrictions under non-U.S. regulations.

If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to identify and develop new or next generation drug product candidates will be impaired, could result in loss of markets or market share and could make us less competitive.

We are highly dependent upon the principal members of our management team and other members of our scientific and clinical advisory team. Our team has significant experience and knowledge of oncology drug discovery and development, T cell modulation, protein biochemistry and immunological assays, and the loss of any current or future team member could impair our ability to design, identify, and develop new intellectual property and drug product candidates and new scientific or product ideas. Additionally, if we lose the services of any of these persons, we would likely be forced to expend significant time and money in the pursuit of replacements, which may result in a delay in the development of our drug product candidates and the implementation of our business plan and plan of operations and diversion of our management's attention. We can give

no assurance that we could find satisfactory replacements for our current and future key scientific and management employees on terms that would not be unduly expensive or burdensome to us.

To induce valuable personnel to remain at our company, in addition to salary and cash incentives, we have granted stock options and restricted stock units that vest over time. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that these employees could leave our employment at any time, for or without cause. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical and scientific personnel.

Our internal computer systems, or those used by third-party CROs, manufacturers or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our future CROs, manufacturers and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures, cyberattacks or cyber-intrusions, loss of funds or information from phishing or other fraudulent schemes, attachments to emails, persons inside our organization, or persons with access to systems inside our organization or those with whom we do business. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Increased security threats and more sophisticated cybercrimes and cyberattacks pose a potential risk to the security and availability of our internal computer systems, networks and services, including those used by third-party CROs, manufacturers or other contractors or consultants, as well as the confidentiality, availability and integrity of our data and the data of potential trial participants or patients, employees and others. Although to our knowledge we have not experienced any such material system failure or security breach to date, if such an event were to occur, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information (such as individually identifiable health information), we could incur significant liabilities and the further development and commercialization of our drug product candidates could be delayed. In addition, the foreign, federal and state regulatory environment surrounding information security and privacy is increasingly demanding, with frequent imposition of new and changing requirements. Compliance with changes in privacy and information security laws and standards may result in significant expense due to increased investment in technology and the development of new operational processes.

War, terrorism, other acts of violence, or natural or manmade disasters may affect the markets in which we operate, our patients and resources required in our research and development activities.

Our business may be adversely affected by political instability, disruption or destruction in a geographic region in which we operate, regardless of cause, including war, terrorism, riot, civil insurrection or social unrest, and natural or manmade disasters, including famine, flood, fire, earthquake, storm or pandemic events and spread of disease, and geopolitical conflicts. Such events may affect our business by increasing prices for resources required in our research and development activities or limiting our access to patients for our clinical trials which may delay our progress on one or more of our clinical or preclinical drug product candidates.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to successfully complete development of, obtain regulatory approval for, or commercialize our drug product candidates and our business could be substantially harmed.

We rely upon and plan to continue to rely upon third-party CROs for execution of our clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs, including our CMO Catalent Pharma Solutions, LLC, or Catalent, are required to comply with FDA laws and regulations regarding current good clinical practice, or GCP, for all of our

products in clinical development. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot be certain that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or GMP, regulations. While we work closely with our CMOs on the manufacturing process for our drug product candidates, including quality audits, we generally do not control the implementation of the manufacturing process of, and are completely dependent on, our CMOs for compliance with GMP regulatory requirements and for manufacture of both active drug substances and finished drug products. In addition, portions of the clinical trials for our drug product candidates may be conducted outside of the United States, which will make it more difficult for us to monitor CROs and perform visits of our clinical trial sites and will force us to rely heavily on CROs to ensure the proper and timely conduct of our clinical trials and compliance with applicable regulations, including GCP. Failure to comply with applicable regulations in the conduct of the clinical trials for our drug product candidates may require us to repeat clinical trials, which would delay the regulatory approval process.

Some of our CROs have an ability to terminate their respective agreements with us if, among other reasons, it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated. If any of our relationships with these third-party CROs terminate for any reason, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our preclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our drug product candidates. Consequently, our results of operations and the commercial prospects for our drug product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, 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 completely on third parties to manufacture our preclinical and clinical drug supplies for our drug product candidates.

We rely completely on third parties to manufacture clinical drug supplies for our drug product candidates. If we were to experience an unexpected loss of supply of our drug product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience disruptions in supply or delays, suspensions or terminations of clinical trials or regulatory submissions. We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our preclinical and clinical drug supplies and we lack the resources and the capability to manufacture any of our drug product candidates on a clinical or commercial scale. The facilities used by our contract manufacturers or other third-party manufacturers to manufacture our drug product candidates, including Catalent and Ajinomoto, must obtain and maintain approval by the FDA. While we work closely with our third-party manufacturers on the manufacturing process for our drug product candidates, including quality audits, we generally do not control the implementation of the manufacturing process of, and are completely dependent on, our contract manufacturers or other third-party manufacturers for compliance with GMP regulatory requirements and for manufacture of both active drug substances and finished drug products. If our contract manufacturers or other third-party manufacturers cannot successfully manufacture material that conforms to applicable specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities and we may not have sufficient access to supplies, which could significantly and adversely affect our operations.

In addition, we have no control over the ability of our contract manufacturers or other third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve, or withdraws approval for, these facilities for the manufacture of our products and drug product candidates, we may need to find alternative manufacturing facilities, which would significantly impact our ability to commercialize, develop, or obtain or maintain regulatory approval for our products and drug product candidates.

We also rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our drug product candidates for our clinical trials. There are a limited number of suppliers for raw materials that we use to manufacture

our products and drug product candidates and we may need to assess alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our drug product candidates for our clinical trials. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a contract manufacturer or other third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our drug product candidates.

Reliance on third-party manufacturers entails additional risks, including the possible breach of manufacturing agreements by the third party, the possible misappropriation of our proprietary information and the possible termination or non-renewal of an agreement by a third party at a time that is costly or inconvenient for us.

We expect to continue to depend on contract manufacturers or other third-party manufacturers for the foreseeable future. We may, however, be unable to enter into agreements or do so on commercially reasonable terms for potential future drug product candidates, which could have a material adverse impact upon our business.

We rely on certain sole or limited sources of supply for our drug product candidates and disruptions in the chain of supply have in the past, and may in the future, cause delays in developing, obtaining approval for, and commercializing our drug product candidates.

Currently, we use Catalent and Ajinomoto as our source of supply for manufacturing clinical supply of our most advanced clinical stage assets, CUE-101 and CUE-102. If we experience multiple successive batch failures, or if supply from Catalent and Ajinomoto is otherwise interrupted, there could be a significant disruption in our drug product candidates supply. Any alternative vendor would need to be qualified through an IND supplement, which could result in delay of our clinical trials of CUE-101 and CUE-102. On December 18, 2024, Novo Holdings announced that it had completed its acquisition of Catalent and sold three Catalent sites in Italy, the United States and Belgium to Novo Nordisk. While we have been in communications with Catalent, and as of the filing of this report we are not aware of any delays or interruptions related to our agreements with Catalent as a result of the merger, we cannot guarantee that there will not be delays or interruptions in the future.

The manufacturing processes for CUE-101, CUE-102, CUE-401, CUE-501 and our other drug product candidates are complex, and it may be difficult or impossible to finalize appropriate processes for the scaled manufacture of the drug product candidates. These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of any of our drug product candidates; cause us to incur higher costs; or prevent us from commercializing them successfully. Furthermore, if our suppliers fail to deliver the required clinical or commercial quantities of active pharmaceutical ingredient on a timely basis and at commercially reasonable prices and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed.

Risks Related to Intellectual Property and Other Legal Matters

If we or our licensor(s) are unable to protect our or its intellectual property, then our financial condition, results of operations and the value of our technology and potential products could be adversely affected.

Patents and other proprietary rights are essential to our business, and our ability to compete effectively is dependent upon the proprietary nature of our technologies. We also rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop, maintain and strengthen our competitive position. We seek to protect these, in part, through confidentiality agreements with certain employees, consultants and other parties. Our success will depend in part on the ability of ourselves and our licensor(s) to obtain, to maintain (including making periodic filings and payments) and to enforce patent protection for its intellectual property, particularly those patent applications and other intellectual property to which we have secured exclusive rights. We and our licensor(s) may not successfully prosecute or continue to prosecute the patent applications which we have licensed. Even if patents are issued in respect of pending patent applications, we or our licensor(s) may fail to maintain these patents, may determine not to pursue litigation against entities that are infringing upon these patents, or may pursue such enforcement less aggressively than we ordinarily would. Without adequate protection for the intellectual property that we own or license, others may be able to offer substantially identical products for sale, which could unfavorably affect our competitive business position and harm our business prospects. Even if issued, patents may be challenged, invalidated, or circumvented, which could limit our ability to stop competitors from marketing similar products or limit the length of the term of patent protection that we may have for our potential products.

Filing, prosecuting, maintaining and defending patents on drug product candidates in all countries throughout the world could be prohibitively expensive for us, and our intellectual property rights in some non-U.S. countries can have a

different scope and strength than do those in the United States. In addition, the laws of certain non-U.S. countries do not protect intellectual property rights to the same extent as U.S. federal and state laws do. 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 drugs made using our inventions in and into the United States or non-U.S. jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and further, may export otherwise infringing drugs to non-U.S. jurisdictions where we have patent protection, but where enforcement rights are not as strong as those in the United States. These drugs may compete with our drug product candidates and our patent rights or other intellectual property rights may not be effective or adequate to prevent them from competing.

Many U.S.-based companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of some countries do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to biopharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or misappropriation of our patents or other intellectual property rights, or the marketing of competing drugs in violation of our proprietary rights. Proceedings to enforce our patent and other intellectual property rights in non-U.S. jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business.

Furthermore, such proceedings could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims of infringement or misappropriation 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 rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and potential products could be adversely affected.

In addition to our licensed technology, we rely, and will continue to rely, upon, among other things, unpatented proprietary technology, processes, trade secrets, trademarks, and know-how. Any involuntary disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to duplicate or surpass our technological achievements, potentially eroding our competitive position in our market. We seek to protect confidential or proprietary information in part by confidentiality agreements with our employees, consultants and third parties. While we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information and technology to enter into confidentiality agreements, we cannot be certain that this know-how, information and technology will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. These agreements may be terminated or breached, and we may not have adequate remedies for any such termination or breach. Furthermore, these agreements may not provide meaningful protection for our trade secrets and know-how in the event of unauthorized use or disclosure. To the extent that any of our staff was previously employed by other pharmaceutical, medical technology or biotechnology companies, those employers may allege violations of trade secrets and other similar claims in relation to their former employee's therapeutic development activities for us. Any dispute involving such employees may result in liabilities to us.

If we fail to comply with our obligations in the agreements under which we license development or commercialization rights to products or technology from third parties, we could lose license rights that are important to our business.

We hold an exclusive license from Einstein to intellectual property relating to certain patent rights, relating to our core technology platform for the engineering of biologics to control T cell activity, precision, immune-modulatory drug product candidates, and two supporting technologies that enable the discovery of costimulatory signaling molecules (ligands) and T cell targeting peptides. This license imposes various developmental milestone obligations on us. If we fail to comply with any obligations under the license agreement and fail to cure such noncompliance, Einstein will have the right to terminate the agreement and our license. The existing patent applications or future patents to which we have rights based on our agreements with Einstein may be too specific and narrowly construed to prevent third parties from developing or designing around the protection provided by these patents. Additionally, we may lose our rights to the patents and patent applications we license in the event of termination of the license agreement. There is no assurance that we will be successful in meeting all of the milestones in the future on a timely basis or that this license agreement will not be terminated for other reasons, depriving us of significant rights. The termination of this license agreement would have a material adverse effect on our financial condition, results of operations, and prospects.

If we are unable to patent and protect the intellectual property used in our potential products, others may be able to copy our innovations, which may impair our ability to compete effectively in our markets.

The strength of our anticipated patents will involve complex legal and scientific matters and can be uncertain. As described above under "Business – Our Intellectual Property," we own or license a number of pending patent applications. Our anticipated patents may be challenged or fail to result in issued patents and anticipated patents may be too specific and narrowly construed to prevent third parties from developing or designing around the protections provided by our intellectual property and in that event we may lose competitive advantage and our business may suffer. Further, the patent and patent applications that we license or have filed may fail to result in issued patents or the claims may need to be amended. Even after amendment, a patent may not issue. In that event, we may not obtain the exclusive use of the intellectual property that we seek, and we may lose competitive advantage, which could result in harm to our business.

Litigation or third-party claims of intellectual property infringement or challenges to the validity of our anticipated patents would require us to use resources to protect our technology and may prevent or delay our development, regulatory approval or commercialization of our drug product candidates.

If we are the target of claims by third parties asserting that our potential products or intellectual property infringe upon the rights of others, we may be forced to incur substantial expenses or divert substantial employee resources from our business.

If successful, those claims could result in our having to pay substantial damages or could prevent us from developing one or more drug product candidates. Further, if a patent infringement suit is brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit.

If we or our collaborators experience patent infringement claims, or if we elect to avoid potential claims others may be able to assert, we or our collaborators may choose to seek, or be required to seek, a license from the third party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our collaborators were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we or our collaborators are unable to enter into license agreements on acceptable terms or at all. This could harm our business significantly. The cost to us of any litigation or other proceeding, regardless of its merit, and even if resolved in our favor, could be substantial. Some of our competitors may be able to bear the costs of such litigation or proceedings more effectively than we can because of their greater financial and human resources. 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. Intellectual property litigation and other proceedings may, regardless of their merit, also absorb significant management time and employee resources.

Although we are not currently aware of any litigation or other proceedings or third-party claims of intellectual property infringement, the biotechnology and pharmaceutical industries are characterized by many suits regarding patents and other intellectual property rights. Other parties may in the future allege that our activities infringe upon their patents or that we are employing their proprietary technology without authorization. We may not have identified all the patents, patent applications or published literature that affect our business either by blocking our ability to commercialize our potential products, by preventing the patentability of one or more aspects of our potential products or those of our licensor or by covering the same or similar technologies that may affect our ability to market our potential products. In addition, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our drug product candidates, and we have done so from time to time. We may fail to obtain future licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be unable to further develop and commercialize one or more of our drug product candidates, which could harm our business significantly.

Some intellectual property that we have in-licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.

The majority of the intellectual property rights we have licensed are generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to

intellectual property embodied in our current or future drug product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

Patent terms may be inadequate to protect our competitive position on our drug product candidates for an adequate amount of time.

Patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the normal statutory term of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Further, normal statutory patent terms may be limited in the U.S. in the event there is a determination that the claims in different patents are directed to obvious variants of the same invention, which can negatively impact the normal statutory patent term. Even if patents covering our drug product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new drug product candidates, patents protecting such drug product candidates might expire before or shortly after such drug product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drug product candidates similar or identical to ours.

Depending upon the timing, duration and conditions of any FDA marketing approval of our drug product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union, or EU. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. Only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14 years from approval, and the scope of protection is not the full scope of the claims but is instead limited to the approved drug, a method for using it or a method for manufacturing it may be extended. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for the applicable product candidate will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case, and our competitive position, business, financial condition, results of operations, and prospects could be materially harmed.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our drug product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our drug product candidates and will face an even greater risk if we commercialize any drugs. For example, we may be sued if our drug product candidates cause or are perceived to cause injury or death or are found to be otherwise unsuitable during clinical 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 drug, negligence, strict liability or a breach of warranties. Claims could also be asserted under state or foreign consumer protection laws. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our drug product candidates. 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 potential drugs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- financial cost;
- exhaustion of any available insurance and our capital resources; and
- the inability to commercialize any product candidate.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of drugs we develop, alone or with collaborators. Our insurance policies may 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 insurance 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. Even if our agreements with any future collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Risks Related to Government Regulation

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of any of our drug product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our drug product candidates, and our ability to generate revenue will be materially impaired.

Any of our drug product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any drug product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and

supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any of our drug product candidates may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

Further, the process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. For example, in December 2022, with the passage of FDORA, Congress required sponsors to develop and submit a DAP for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Further, on January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. We have not previously secured authorization to conduct clinical studies in the EU pursuant to this new regulation and, accordingly, there is a risk that we may be delayed in commencing such studies.

In addition, under the Pediatric Research Equity Act of 2003, a BLA or supplement to a BLA for certain biological products must contain data to assess the safety and effectiveness of the biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The applicable legislation in the EU also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the European Medicines Agency, or EMA, or to obtain a waiver or deferral from the conduct of these studies by the Pediatric Committee of the EMA. For any of our drug product candidates for which we are seeking regulatory approval in the U.S. or the EU, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

Finally, the FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

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

We are subject to regulation in respect of our research and federal funding.

Because our licensor has conducted research under federal grants and we may conduct further research under federal grants, we will be subject to federal regulation in how we conduct our research and the agreement terms relating to those grants. There are also ethical guidelines promulgated by various governments and research institutions that we are required to follow in respect of our research. These guidelines are orientated towards research and experimentation involving humans and animals. Failure to follow the regulations, agreement terms and accepted scientific practices would jeopardize our grants and our results and the use of the results in further research and approval circumstances. Because our licensor has used federal funding, the government retains a "march-in" right in connection with these grants, which is the right to grant additional licenses to practice inventions developed from grant funding.

In December 2023, the National Institute of Standards and Technology, or NIST, released for public comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights, or the Draft Framework. The Draft Framework sets forth the factors that an agency may consider when deciding whether to exercise march-in rights pursuant to the Bayh-Dole Act and includes a first-ever specification that price can be a factor in determining that a drug or other taxpayer-

funded invention is not accessible to the public. NIST is currently seeking public comments on the proposed Draft Framework. The potential inclusion of price as a factor in a march-in determination and the exercise of "march-in" rights by the federal government could result in decreased demand for our future products, which could have a material adverse effect on our results of operations and financial condition. In addition, any failure to comply with applicable laws or regulations could harm our business and divert our management's attention.

Failure to obtain marketing approval in foreign jurisdictions would prevent any of our drug product candidates from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell any of our drug product candidates in the European Union and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the same or similar risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our drug product candidates in any jurisdiction, which would materially impair our ability to generate revenue.

Additionally, we could face heightened risks with respect to obtaining marketing authorization in the UK as a result of the withdrawal of the UK from the EU, commonly referred to as Brexit. The UK is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency, or MHRA, is responsible for approving all medicinal products destined for the United Kingdom market (i.e., Great Britain and Northern Ireland). At the same time, a new international recognition procedure, or IRP, will apply, which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the EU/European Economic Area, or EEA, member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the UK for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products, which may reduce the duration of regulatory data protection and exclusivity periods for orphan drugs, and revise the eligibility for expedited pathways in addition to other changes, was published on April 26, 2023. On April 10, 2024 the European Parliament adopted a position on the proposal requesting several amendments to the package. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term.

We expect that we will be subject to additional risks in commercializing any of our drug product candidates that receive marketing approval outside the United States, including 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; and workforce uncertainty in countries where labor unrest is more common than in the United States.

We may seek orphan drug designation for one or more of our drug product candidates, but even if such designation is granted, we may be unable to maintain any benefits associated with orphan drug designation, including market exclusivity that prevents the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the European Union. Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021. In Catalyst Pharms, Inc. v. Becerra, or Catalyst, that court held that, for the purpose of determining the scope of orphan drug exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the approved "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of the Catalyst court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug is approved. More recently however, on February 14, 2025, a federal district court in Washington, D.C. fully embraced the reasoning of the Catalyst decision in another decision challenging the scope of orphan drug exclusivity. The implications of this decision, and its impact on the FDA's implementation of the Orphan Drug Act, are unclear at this point.

If approved, our drug product candidates that are licensed and regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the PPACA, to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product In addition, the licensure of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still develop and receive approval of a competing biologic, so long as its BLA does not reply on the reference product, sponsor's data or submit the application as a biosimilar application.

We believe that any of the product candidates we develop as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing. Nonetheless, the approval of a biosimilar to our drug product candidates would have a material adverse impact on our business due to increased competition and pricing pressure.

We may seek fast track designation or breakthrough therapy and priority review programs for our drug product candidates. Even if our drug product candidates receive one or more of these designations, the product candidate may not be subject to a faster review process nor does any such designation assure approval of our drug product candidates.

We aim to benefit from the FDA's fast track, breakthrough therapy and priority review programs. However, our drug product candidates may not receive an FDA fast track designation, breakthrough therapy designation, or priority review. Without fast track designation, submitting a BLA, and getting through the regulatory process to gain marketing approval is a lengthy process. Under fast track designation, the FDA may initiate review of sections of a fast track drug's BLA before the application is complete. However, the FDA's time period goal for reviewing an application does not begin until the last section of the BLA is submitted. On October 3, 2022, we received fast track designation for CUE-101 for the treatment of R/M HPV+ HNSCC as a monotherapy and in combination with KEYTRUDA.

The FDA has also established breakthrough therapy designation, which is for a product that is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product 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 FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner. We may seek breakthrough therapy designation for one or more of our drug product candidates, but there can be no assurance that we will receive such designation.

Under the FDA's policies, a product candidate is eligible for priority review, or review within a six-month time frame from the time a complete BLA is accepted for filing, if the product candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A fast track or breakthrough therapy designated drug product candidate would ordinarily meet the FDA's criteria for priority review.

The FDA has broad discretion with respect to whether or not to grant these designations to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, any such designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to licensure compared to conventional FDA procedures. As a result, while we may seek and receive these designations for our drug product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw these designations if it believes that the designation is no longer supported by data from our clinical development program. A delay in the review process or in the approval of our potential products would delay revenue, if any, from their potential sales and would increase the capital necessary to fund these product development programs.

We are also currently participating in Project Optimus, an initiative of the Oncology Center of Excellence at the FDA. This project focuses on dose optimization and dose selection in oncology drug development, and whether the current paradigm based on cytotoxic chemotherapeutics leads to doses and schedules of molecularly targeted therapies that provide more toxicity without additional efficacy, among other things. By participating in Project Optimus, we have the opportunity to meet with the FDA's Oncology Review Divisions early in our development programs, well before conducting trials intended for registration, to discuss dose-finding and dose optimization. The program thus allows us to develop strategies for dose finding and dose optimization that leverages nonclinical and clinical data in dose selection, including randomized evaluations of a range of doses in trials, with the objective of performing these studies as early as possible in the development program to bring promising new therapies to patients. There is no assurance, however, that our involvement in this program will lead to early discussions with the FDA or expedited studies leading to optimization of dose selection for our candidate products.

We may seek approval from the FDA or comparable foreign regulatory authorities to use accelerated development pathways for our drug product candidates. If we are not able to use such pathways, we may be required to conduct additional clinical trials beyond those that are contemplated, which would increase the expense of obtaining, and delay the receipt of, necessary marketing approvals, if we receive them at all. In addition, even if an accelerated approval pathway is available to us, it may not lead to expedited approval of our drug product candidates, or approval at all.

Under the Federal Food, Drug and Cosmetic Act, or the FDCA, and implementing regulations, the FDA may grant accelerated approval to a product candidate to treat a serious or life-threatening condition that provides meaningful therapeutic

benefit over available therapies, upon a determination that the product 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 is a 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 measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug. 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.

Prior to seeking such accelerated approval, we will continue to seek feedback from the FDA or comparable foreign regulatory agencies and otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that the FDA or foreign regulatory agencies will agree with our surrogate endpoints or intermediate clinical endpoints in any of our clinical trials, or that we will decide to pursue or submit any additional applications for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from the FDA or comparable foreign regulatory agencies, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval. Furthermore, for any submission of an application for accelerated approval or application under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted for filing or that any expedited development, review or approval will be granted on a timely basis, or at all.

Finally, there can be no assurance that we will satisfy all FDA requirements, including new provisions that govern accelerated approval. For example, with passage of the FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner of Food and Drugs, or the Commissioner, or the Commissioner's designee and a written appeal, among other things. We will need to fully comply with these and other requirements in connection with the development and approval of any product candidate that qualifies for accelerated approval.

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidances relating to accelerated approval. These guidances describe FDA's views on what it means to conduct a confirmatory trial with due diligence and how the agency plans to interpret whether such a study needs to be underway at the time of approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

Accordingly, a failure to obtain and maintain accelerated approval or any other form of expedited development, review or approval for our drug product candidates, or withdrawal of a product candidate, would result in a longer time period until commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

We may in the future, conduct clinical trials for certain of our drug product candidates at sites outside the United States. The FDA may not accept data from trials conducted in such locations and the conduct of trials outside the United States could subject us to additional delays and expense.

We may in the future conduct one or more of our clinical trials with trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and

performed by qualified investigators in accordance with good clinical practice. The FDA must be able to validate the data from the trial through an onsite inspection if necessary. The trial population must also have a similar profile to the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the United States. In addition, while these clinical trials are subject to the applicable local laws, the FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from clinical trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our drug product candidates.

In addition, the conduct of clinical trials outside the United States could have a significant adverse impact on us or the trial results. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange rate fluctuations; and
- diminished protection of intellectual property in some countries.

To obtain the necessary approval of our potential products, as a precondition, we will need to conduct various preclinical and clinical tests, all of which will be costly and time consuming, and may not provide results that will allow us to seek regulatory approval.

The number of preclinical and clinical tests that will be required for regulatory approval varies depending on the disease or condition to be treated, the method of treatment, the nature of the drug, the jurisdiction in which approval is sought and the applicable regulations. Regulatory agencies can delay, limit or deny approval of a product for many reasons. For example, regulatory agencies may:

- not deem a product candidate to be safe or effective;
- interpret data from preclinical and clinical testing differently than we do;
- not approve the manufacturing processes;
- conclude that our drug product candidate does not meet quality standards for durability, long-term reliability, biocompatibility, compatibility, or safety; and
- change their approval policies or adopt new regulations.

The FDA may make requests or suggestions regarding conduct of any clinical trials, resulting in an increased risk of difficulties or delays in obtaining regulatory approval in the United States. Foreign regulatory agencies may similarly have the ability to influence any clinical trials occurring outside the United States. Any of these occurrences could prove materially harmful to our operations and business.

Even if we, or any collaborators we may have, obtain marketing approvals for any of our drug product candidates, the terms of approvals and ongoing regulation of our products could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, GMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of

approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more of our drug product candidates, we, and such collaborators, and our and their contract manufacturers will continue to need to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to generate revenue and achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

If we receive regulatory approval for any product candidate, we will be subject to ongoing obligations and continuing regulatory review, which may result in significant additional expense. Our drug product candidates, if approved, could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our drug product candidates, when and if approved.

Any drug product candidate for which we obtain marketing approval will also be subject to ongoing regulatory requirements for labeling, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post marketing information. For example, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to GMPs. As such, we and our contract manufacturers will be subject to continual review and periodic inspections to assess compliance with GMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and to comply with requirements concerning advertising and promotion for our products.

In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, may be subject to significant conditions of approval or may impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA may also require a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval of our drug product candidates, 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.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us. In addition, if any product fails to comply with applicable regulatory requirements, a regulatory agency may:

- issue fines, warning letters, untitled letters or impose holds on clinical trials if any are still ongoing;
- mandate modifications to promotional materials or require provision of corrective information to healthcare practitioners;
- impose restrictions on the product or its manufacturers or manufacturing processes;
- impose restrictions on the labeling or marketing of the product;
- impose restrictions on product distribution or use;
- require post-marketing clinical trials;
- require withdrawal of the product from the market;
- refuse to approve pending applications or supplements to approved applications that we submit;
- require recall of the product;
- require entry into a consent decree, which can include imposition of various fines (including restitution or disgorgement of profits or revenue), reimbursements for inspection costs, required due dates for specific actions and penalties for non-compliance;

- suspend or withdraw marketing approvals;
- refuse to permit the import or export of the product;
- seize or detain supplies of the product; or
- issue injunctions or impose civil or criminal penalties.

Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA's approval of another company's drug product. In April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious. In June 2024, the Supreme Court reversed that decision after unanimously finding that the plaintiffs (anti-abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11, 2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in the district court in Texas challenging FDA's actions. On January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation.

In addition, we could be adversely affected by several significant administrative law cases decided by the U.S. Supreme Court in 2024. In Loper Bright Enterprises v. Raimondo, for example, the court overruled Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc., which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U.S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act, or the APA. Additionally, in Corner Post, Inc. v. Board of Governors of the Federal Reserve System, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, Securities and Exchange Commission v. Jarkesy, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any approval that we may have obtained and we may not achieve or sustain profitability. Further, any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize any drug product candidates we develop and adversely affect our business, financial condition, results of operations, and prospects.

Similar restrictions apply to the approval of our products in the EU. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the EU's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the EU and are also subject to EU Member State laws. The failure to comply with these and other EU requirements can also lead to significant penalties and sanctions.

Any regulatory approval to market our products will be limited by indication. If we fail to comply or are found to be in violation of FDA regulations restricting the promotion of our products for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA, EMA, MHRA and other government agencies. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. Physicians may nevertheless prescribe our products off-label to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our products for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product.

In addition, under some relatively recent guidance from the FDA and the Pre-Approval Information Exchange Act, or PIE Act, signed into law as part of the Consolidated Appropriations Act of 2023, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We may engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.

In recent years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the U.S. Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of HHS, the FDA, the Federal Trade Commission, or the FTC, and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the False Claims Act, the Prescription Drug Marketing Act and anti-kickback laws and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "*qui tam*" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim or caused a false claim to be submitted to the government for payment. The person bringing a *qui tam* suit is entitled to a share of any recovery or settlement. *Qui tam* suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a *qui tam* suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a *qui tam* suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

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

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes, which has caused average review times at the agency to fluctuate in recent years. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of

the Securities and Exchange Commission, or SEC, and other government agencies on which our operations may rely, including those that fund research and development activities or enable capital raising activities, is subject to the political process, which is inherently fluid and unpredictable. Further, while the FDA's review of BLAs and other applications is funded through the user fee program established under the Prescription Drug User Fee Act, the Trump Administration has indicated that it will be reviewing that program and its implementation.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In addition, disruptions may result from events similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

There is also substantial uncertainty as to how measures being implemented by the new Trump Administration across the government will impact the FDA, CMS and other federal agencies with jurisdiction over our activities. For example, since taking office, President Trump has issued a number of executive orders, which could have a significant impact on the manner in which the FDA conducts its operations and engages in regulatory and oversight activities. These include E.O. 14192, "Unleashing Prosperity Through Deregulation," January 31, 2025; E.O. 14212, "Establishing the President's Make America Healthy Again Commission," February 13, 2025; and E.O. 14219, "Ensuring Lawful Governance and Implementing the President's 'Department of Government Efficiency' Deregulatory Initiative," February 19, 2025.

If these or other orders or executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. In addition, the loss of FDA personnel could lead to further disruptions and delays in FDA review and oversight of our product candidates. Similarly, efforts by the new administration to substantially reduce or delay research funding by the National Institutes of Health of medical research could have substantial direct or indirect impacts on our research activities.

Accordingly, if a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

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

Healthcare providers, physicians, and third-party payors play a primary role in the recommendation and prescription of any of our drug product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;

- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid, or other government payors that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;

- the federal Health Insurance Portability and Accountability Act of 1996, as further amended by the Health Information Technology for Economic and Clinical Health Act, which imposes certain requirements, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses, and health care providers;

- the federal false statements statute, which prohibits 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;

- the federal transparency requirements under the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report to HHS information related to payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations; and

- analogous state 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, and certain state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If commercial third-party payors or government payors fail to provide coverage or adequate reimbursement, our revenue and prospects for profitability would be harmed.

There is increasing pressure on biotechnology and pharmaceutical companies to reduce healthcare costs. In the United States, these pressures come from a variety of sources, such as managed care groups and institutional and government purchasers. Increased purchasing power of entities that negotiate on behalf of federal healthcare programs and private sector beneficiaries could increase pricing pressures in the future. Such pressures may also increase the risk of litigation or investigation by the government regarding pricing calculations. The biotechnology and pharmaceutical industries will likely face greater regulation and political and legal actions in the future.

There is increased uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within HHS, as CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement. Adverse pricing limitations may hinder our ability to recoup our investment in one or more future drug product candidates, even if our future drug product candidates obtain regulatory approval. Adverse pricing limitations prior to approval will also adversely affect us by reducing our commercial potential. Our ability to commercialize any potential products successfully also will depend in part on the extent to which reimbursement for these products and related treatments becomes available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers, pharmacy benefit managers, and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

A significant trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize in the future and, if reimbursement is available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, any product for which we obtain marketing approval in the future. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

There may be significant delays in obtaining reimbursement for approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable payment rates from both government funded and private payors for future products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize potential products and our overall financial condition.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our drug product candidates and affect the prices we may obtain for any products that are approved in the United States or foreign jurisdictions.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our drug product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any drug product candidates for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and have been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA approved product.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, the PPACA was signed into law. In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 pursuant to the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act.

The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our drug product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Act delays the 4% Statutory Pay-As-You-Go Act of 2010, or PAYGO, sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Act's healthcare offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the TCJA, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on June 17, 2021, the U.S. Supreme Court dismissed an action challenging the PPACA after finding that the plaintiffs did not have standing to challenge the constitutionality of the law. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

During the first Trump Administration, the Congress and administration sought to overturn the PPACA and related measures. Shortly after taking office in January 2025, President Trump revoked numerous executive orders issued by President Biden, including at least two executive orders (e.g., EO 14009, Strengthening Medicaid and the Affordable Care Act, and EO 14070, Continuing to Strengthen Americans' Access to Affordable, Quality Health Coverage) where were designed to further implement the PPACA. We anticipate similar efforts to undermine the PPACA, and the accompanying uncertainty, for the foreseeable future.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if approved.

The prices of prescription pharmaceuticals have been the subject of considerable legislative and executive actions in the United States. There have been U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Seven states have passed laws allowing for the importation of drugs from Canada. Three states have passed legislation establishing workgroups to examine the impact of a state importation program. As of May 2024, five states had submitted Section 804 Importation Program proposals to the FDA and, on January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. That state now has authority to import certain drugs from Canada for a period of two years once

certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the Inflation Reduction Act of 2022, or IRA, has been delayed by Congress to January 1, 2032.

More recently, on August 16, 2022, the IRA was signed into law by the President of the United States. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap, and it replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). In addition, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On January 17, 2025, CMS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. Thereafter, following the change in administrations, CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program. The second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027.

On June 6, 2023, Merck & Co. filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

In addition, we will need to carefully navigate the IRA and its provisions governing orphan drugs. Specifically, the IRA includes a provision, known as the orphan drug exclusion, that excludes from price negotiations those orphan drugs that have been designated for only one rare disease or condition and for which the only approved indication (or indications) is for such disease or condition. Thus, as CMS stated in final guidance in July 2023, a drug or biologic that is designated for more than one rare disease or condition will not qualify for the orphan drug exclusion, even if the drug or biologic is not approved for any indications for the additional diseases or conditions. While there is Congressional support for expanding the orphan drug exclusion to include orphan drugs with more than one approved indication, no legislation has been enacted. Accordingly, if one of our product candidates is designated and approved as an orphan drug for one disease or condition, and we subsequently receive approval of that product for a different disease or condition, the product will no longer be excluded from the IRA price negotiation provision under the orphan drug exclusion and that could impact our revenues and business.

The legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. In addition to the drug price negotiation program, the IRA established inflation rebate programs under Medicare Part B and Part D. These programs require manufacturers to pay rebates to Medicare if they raise their prices for certain Part B and Part D drugs faster than the rate of inflation. On December 9, 2024, with issuance of its 2025 Physician Fee Schedule final regulation, CMS finalized its rules governing the IRA inflation rebate programs. The new law also caps Medicare out-of-pocket drug costs at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and placing price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

While it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care organizations 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 health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug product candidates or additional pricing pressures. This may be increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval.

In countries outside of the United States, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Compliance with the HIPAA security, privacy and breach notification regulations may increase our costs.

The HIPAA privacy, security and breach notification regulations, including the expanded requirements under HITECH, establish comprehensive federal standards with respect to the uses and disclosures of protected health information, or PHI, by health plans, healthcare providers and healthcare clearinghouses, in addition to setting standards to protect the

confidentiality, integrity and security of PHI. The regulations establish a complex regulatory framework on a variety of subjects, including:

- the circumstances under which uses and disclosures of PHI are permitted or required without a specific authorization by the patient, including but not limited to treatment purposes, activities to obtain payments for our services, and our healthcare operations activities;
- a patient's rights to access, amend and receive an accounting of certain disclosures of PHI;
- requirements to notify individuals if there is a breach of their PHI;
- the contents of notices of privacy practices for PHI;
- administrative, technical and physical safeguards required of entities that use or receive PHI; and
- the protection of computing systems maintaining electronic PHI.

We have implemented practices intended to meet the requirements of the HIPAA privacy, security and breach notification regulations, as required by law. We are required to comply with federal privacy, security and breach notification regulations as well as varying state privacy, security and breach notification laws and regulations, which may be more stringent than federal HIPAA requirements. In addition, for healthcare data transfers from other countries relating to citizens of those countries, we must comply with the laws of those countries. The federal privacy regulations restrict our ability to use or disclose patient identifiable data, without patient authorization, for purposes other than payment, treatment, healthcare operations and certain other specified disclosures such as public health and governmental oversight of the healthcare industry.

HIPAA provides for significant fines and other penalties for wrongful use or disclosure of PHI, including potential civil and criminal fines and penalties. Computer networks are always vulnerable to breach and unauthorized persons may in the future be able to exploit weaknesses in the security systems of our computer networks and gain access to PHI. Additionally, we share PHI with third parties who are legally obligated to safeguard and maintain the confidentiality of PHI. Unauthorized persons may be able to gain access to PHI stored in such third-parties computer networks. Any wrongful use or disclosure of PHI by us or such third parties, including disclosure due to data theft or unauthorized access to our or our third-parties computer networks, could subject us to fines or penalties that could adversely affect our business and results of operations. Although the HIPAA statute and regulations do not expressly provide for a private right of damages, we could also incur damages under state laws to private parties for the wrongful use or disclosure of confidential health information or other private personal information.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the EEA in May 2018. In the UK, the GDPR is retained in domestic law as the UK GDPR and sits alongside an amended version of the UK Data Protection Act of 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors.

The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require

destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues of the respective group of companies or €20 million, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

The GDPR places restrictions on the cross-border transfer of personal data from the EU to countries that have not been found by the European Commission to offer adequate data protection legislation. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the EU, or the CJEU, invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for international transfers of personal data from the EEA. This CJEU decision resulted in increased scrutiny on data transfers and increased our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

In October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which serves as a replacement to the EU-U.S. Privacy Shield. The European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business. Following the withdrawal of the UK from the EU, the UK Data Protection Act of 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the UK and the EU have determined, through separate "adequacy" decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act of 2018 and the GDPR, respectively. The UK and the U.S. have also agreed to a U.S.-UK "Data Bridge", which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the U.S. In addition to the UK, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the U.S.). Any changes or updates to these developments have the potential to impact our business.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions.

While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the U.S. regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

We are subject to stringent federal and state privacy laws, information security laws, regulations, policies, and contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations at the federal and state levels of government that apply to the collection, transmission, storage and use of personally identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information. Failure to comply with any of these laws and regulations could result in enforcement actions against us, including fines, claims for damages by affected

individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and to ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

In 2018, California passed into law the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020, and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements.

In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, several other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are considering or have already passed comprehensive privacy laws during the 2023 legislative sessions that will go into effect in the next several years. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington recently passed a health privacy law that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities, and could lead to government enforcement actions, private litigation and significant fines and penalties against us, all of which could increase our cost of doing business and have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws

regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Further, we cannot assure you that our third-party service providers with access to our or our customers', suppliers', trial patients' and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage and transmission of such information.

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

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants, and partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, 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 government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. 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, financial condition, results of operations, and prospects, including the imposition of significant fines or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain drug product candidates outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the U.S. Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

On February 10, 2025, President Trump issued an Executive Order directing the Attorney General to review the guidelines and policies governing FCPA investigations and enforcement actions. Per the Executive Order, this review will result in new U.S. Department of Justice FCPA guidelines intended to enhance American economic competitiveness and to safeguard national security interests. During the 180-day review period, any new FCPA investigations and enforcement actions

are to be suspended absent authorization from the Attorney General, and all existing FCPA investigations and enforcement actions will be reviewed. Additionally, after the Attorney General issues revised guidelines, the Executive Order directs her to assess whether "remedial measures" related to past FCPA actions are warranted. We will need to carefully navigate these developments.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and drug product candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

Our business operations will subject us to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also may produce hazardous waste products. We expect to generally contract with third parties for the disposal of these materials and wastes. However, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. In addition, we may be required to incur substantial costs to comply with current or future environmental, health and safety laws and regulations. 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 and we may not have sufficient (or any) insurance to cover any such costs.

Risks Related to Our Financial Results, Our Need for Financing and Owning Our Common Stock

We anticipate future losses and negative cash flow, and it is uncertain if or when we will become profitable.

We do not expect to generate any commercial revenues until we successfully complete development of one or more potential products and we are able to successfully commercialize them through sales and licensing, which we expect will take a number of years, if ever. We have not yet demonstrated our ability to generate commercial revenue, and we may never be able to produce commercial revenues or operate on a profitable basis. As a result, we have incurred losses since our inception and expect to experience operating losses and negative cash flow for the foreseeable future. Our drug product candidates may never be approved or become commercially viable. Even if we and our collaborators are able to commercialize our technology, which may include licensing, we may never recover our research and development expenses.

We will need substantial additional financing to support our growth and ongoing operations. Additional capital may be difficult to obtain, restrict our operations, require us to relinquish rights to our technologies or drug product candidates, encumber our assets and result in ongoing debt service cost, or result in additional dilution to our stockholders.

Our business will require additional capital for implementation of our long-term business plan and product development and commercialization. As we require additional funds, we may seek to fund our operations through the sale of additional equity securities, debt financing and/or strategic collaboration agreements. We cannot be sure that additional financing from any of these sources will be available when needed or that, if available, the additional financing will be obtained on favorable terms. Our ability to raise additional funds may be adversely impacted by general economic conditions, both inside and outside the U.S., including disruptions to, and instability and volatility in, the credit and financial markets in the U.S. and worldwide, heightened inflation, interest rate and currency rate fluctuations, the implementation of trade barriers and tariffs and economic slowdown or recession as well as concerns related to pandemic events, spread of disease and geopolitical events, including civil or political unrest. In addition, market instability and volatility, high levels of inflation and interest rate fluctuations may increase our cost of financing or restrict our access to potential sources of future liquidity.

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

- the progress, timing, scope and costs of our clinical trials, including the ability to timely enroll patients in our current and any future clinical trials;
- the outcome, timing and cost of regulatory approvals by the FDA and comparable regulatory authorities, including the potential that the FDA or comparable regulatory authorities may require that we perform more studies than those that we currently expect;
- the number and characteristics of drug product candidates that we may in-license and develop;
- our ability to successfully commercialize our drug product candidates, if approved;
- the amount of sales and other revenues from drug product candidates that we may commercialize, if any, including the selling prices for such potential products and the availability of adequate third-party reimbursement;
- selling and marketing costs associated with our potential products, including the cost and timing of expanding our marketing and sales capabilities;
- the terms and timing of any potential future collaborations, licensing or other arrangements that we may establish;
- cash requirements of any future acquisitions and/or the development of other drug product candidates;
- the costs of operating as a public company;
- the cost and timing of completion of commercial-scale, outsourced manufacturing activities;
- the time and cost necessary to respond to technological and market developments;
- any disputes which may occur between us and our employees, collaborators, including Einstein, LG Chem and Ono, or other prospective business partners; and

- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

If we raise additional funds by selling shares of our common stock or other equity-linked securities, the ownership interest of our current stockholders will be diluted. We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or drug product candidates or to grant licenses on terms that may not be acceptable to us. If we raise additional funds through debt financing, we may have to grant a security interest on our assets to the future lenders, our debt service costs may be substantial, and the lenders may have a preferential position in connection with any future bankruptcy or liquidation involving the company. Our pledge of our assets as collateral to secure our obligations under our loan and security agreement, as amended, or the Loan Agreement, with Silicon Valley Bank, or SVB, a division of First Citizens Bank (as defined below), may limit our ability to obtain additional debt financing. Under the Loan Agreement, we are also restricted from incurring future debt, granting liens, making investments, making acquisitions, distributing dividends on our common stock and selling assets and making certain other uses of our cash, without SVB's consent, subject in each case to certain exceptions.

If we are unable to raise additional capital when needed, we may be required to curtail the development of our technology or materially curtail or reduce our operations. We could be forced to sell or dispose of our rights or assets. Any inability to raise adequate funds on commercially reasonable terms could have a material adverse effect on our business, results of operation and financial condition, including the possibility that a lack of funds could cause our business to fail and the Company to dissolve and liquidate with little or no return to investors.

We hold a portion of our cash and cash equivalents that we use to meet our working capital and operating expense needs in deposit accounts, and our liquidity and operations could be adversely affected if a financial institution holding such funds fails.

We hold a portion of our cash and cash equivalents that we use to meet our working capital and operating expense needs in deposit accounts at multiple financial institutions. The balances held in these accounts typically exceed the Federal Deposit Insurance Corporation, or FDIC, standard deposit insurance limit of $250,000 per depositor and per institution. If a financial institution in which we hold such funds fails or is subject to significant adverse conditions in the financial or credit markets, we could be subject to a risk of loss of all or a portion of such uninsured funds or be subject to a delay in accessing all or a portion of our funds. Any such loss or lack of access to these funds could adversely impact our short-term liquidity and ability to meet our operating expense obligations, including payroll obligations.

For example, on March 10, 2023, SVB was closed and the FDIC was appointed receiver for the bank. The FDIC created a successor bridge bank, and all deposits and loans of SVB were transferred to the bridge bank under a systemic risk exception approved by the United States Department of the Treasury, the Federal Reserve and the FDIC. On March 27, 2023, First Citizens Bank & Trust Company, or First Citizens Bank, assumed all of SVB's deposits and certain other liabilities and acquired substantially all of SVB's loans and certain other assets from the FDIC. Access to and availability of deposits was delayed, though ultimately, in that case, restored. If financial institutions in which we may hold funds for working capital and operating expenses were to fail, we cannot provide any assurances that the applicable governmental agencies would take action to protect our uninsured deposits or make deposits available in a similar manner.

We also maintain investment accounts with financial institutions in which we hold our marketable securities and, if access to the funds we use for working capital and operating expenses is impaired, we may not be able to open new operating accounts or to sell investments or transfer funds from our investment accounts to new operating accounts in a timely manner sufficient to meet our operating expense obligations. In addition, to the extent that the financial institutions with which we hold securities fail or are associated with banks that fail, there may be delays or other access restrictions with respect to such securities, similar to those described above for deposit accounts.

We have a loan agreement that requires us to meet certain operating covenants and place restrictions on our operating and financial flexibility.

On February 15, 2022, we entered into the Loan Agreement with SVB, which has been assumed by First Citizens Bank, pursuant to which we have borrowed $10.0 million. The Loan Agreement was amended in April 2023 and October 2024. The outstanding principal amount under the Loan Agreement as of December 31, 2024 is $4.0 million. The Loan Agreement is secured by substantially all of our properties, rights and assets, except for our intellectual property, which is subject to a

negative pledge, and certain other customary exclusions. Because of the security interest, SVB's rights to repayment from a liquidation of the assets subject to that security interest would be senior to the rights of other creditors.

The Loan Agreement, as amended, includes customary covenants including covenants requiring us to maintain our corporate existence and governmental approvals, deliver certain financial reports and maintain insurance coverage. It also requires us to have at all times on deposit in our accounts maintained with SVB, unrestricted and unencumbered cash in an amount equal to the lesser of (i) 100% of the dollar value of our consolidated cash, in the aggregate, at all financial institutions and (ii) $20,000,000. As of December 31, 2024, we had unrestricted and unencumbered cash and cash equivalents totaling $22.5 million. Additionally, we are restricted in our ability to transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay dividends or make other distributions, make investments, create liens, sell assets and agree to a change in control. Upon the occurrence of an event of default, which includes our failure to satisfy our payment obligations under the Loan Agreement, the breach of certain of these covenants under the Loan Agreement, or the occurrence of a material adverse change in our business, SVB is entitled to accelerate amounts due under the Loan Agreement and dispose the collateral as permitted under applicable law. Any declaration by SVB of an event of default and its exercise of its remedies in the event of such declaration of an event of default, such as acceleration of the amounts due under the Loan Agreement, would adversely impact the amount of cash we have available to fund our operations, could significantly harm our business and prospects and could cause the price of our common stock to decline.

For a further description of the Loan Agreement, please refer to Note 5 of the Notes to the Consolidated Financial Statements included in this Annual Report on Form 10-K.

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

We are a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting shares of common stock held by non-affiliates is $250 million or more measured on the last business day of our second fiscal quarter, or our annual revenues are less than $100 million during the most recently completed fiscal year and our voting and non-voting shares of common stock held by non-affiliates is $700 million or more measured on the last business day of our second fiscal quarter. Smaller reporting companies have reduced disclosure obligations, such as an ability to provide simplified executive compensation information and only two years of audited financial statements.

We have elected to take advantage of certain of the reduced reporting obligations. Investors may find our common stock less attractive as a result of our reliance 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 more volatile.

Our stock price can be volatile and fluctuate significantly, and our stockholders may have difficulty selling their shares and/or suffer substantial losses.

Our common stock is currently listed on the Nasdaq Capital Market under the symbol "CUE." The price of our common stock has fluctuated, and is likely to continue to fluctuate, significantly in response to market and other factors, some of which are beyond our control, including those listed in this "Item 1A. Risk Factors" section and other, unknown factors. Our stock price may be affected by many factors, including:

- setbacks with respect to our research and development programs;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials;
- any adverse changes to our relationship with collaborators;
- results of internal and external studies and clinical trials;
- results of our business development efforts;

- variations in the level of expenses related to our existing drug product candidates or preclinical and clinical development programs;
- any intellectual property infringement actions in which we may become involved;
- variations in our results of operations;
- press reports, whether or not true, about our business;
- additions to or departures of our management;
- sales or perceived potential sales of additional shares of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future; and
- general economic and market conditions, including recent adverse changes in the domestic and international financial markets, the impacts of inflation and the implementation of trade barriers and tariffs and government action in response thereto.

Any of these factors may result in large and sudden changes in the volume and trading price of our common stock. In addition, the stock market, in general, and small pharmaceutical and biotechnology companies have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors beyond our control may negatively affect the market price of our common stock, regardless of our actual operating performance, and cause the price of our common stock to decline rapidly and unexpectedly.

If we fail to comply with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

We are required to comply with the continued listing requirements of the Nasdaq Stock Market LLC, or Nasdaq, including, among other things, maintaining a minimum closing bid price of at least $1.00 per share, or shares of our common stock may be subject to delisting, which would have a material adverse effect on our business. Any potential delisting of our common stock could have a material adverse effect on the market for, and liquidity and price of, our common stock and would adversely affect our ability to raise capital on terms acceptable to us, or at all. Delisting from Nasdaq could also have other negative results, including, without limitation, the potential loss of confidence by investors, customers and employees and fewer business development opportunities. Any delisting of our common stock from Nasdaq would also make it more difficult for our stockholders to sell their shares of our common stock in the public market.

On August 15, 2024, we received a deficiency letter from Nasdaq indicating that we failed to comply with the minimum bid price requirement. Subsequently, on October 18, 2024, we received a letter from Nasdaq notifying us that we had regained compliance with the minimum bid price requirement and were in compliance with the listing requirements. Our common stock will continue to be listed and traded on the Nasdaq Capital Market. However, there can be no assurance that we will be able to continue to comply with the Nasdaq listing requirements.

We may be subject to securities litigation, which is expensive and could divert management attention.

The price of our common stock can be volatile, and in the past companies that have experienced volatility in the market price of their common stock have been subject to an increased incidence of securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

If securities or industry analysts do not publish research reports about our business, or if they issue an adverse opinion about our business, the price of our securities and trading volume could decline.

The trading market for our securities is influenced by the research and reports that industry or securities analysts publish about us or our business. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. Although we have obtained analyst coverage, if one or more of the analysts who cover us issues an adverse opinion about our company, the price of our securities would likely decline. If one or more of these analysts ceases research coverage of us or fails to regularly

publish reports on us, we could lose visibility in the financial markets, which in turn could cause the price of our securities or trading volume to decline.

We have not paid dividends in the past and have no immediate plans to pay dividends.

We plan to reinvest all of our earnings, to the extent we have earnings, in order to further develop our technology and drug product candidates and to cover operating costs. We do not plan to pay any cash dividends with respect to our securities in the foreseeable future. We cannot assure you that we would, at any time, generate sufficient surplus cash that would be available for distribution to the holders of our common stock as a dividend. In addition, our ability to pay cash dividends is currently restricted by the terms of the Loan Agreement, and future debt financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock.

Our ability to use net operating loss carryforwards and research and development tax credits to reduce future tax payments may be limited or restricted.

We have generated significant net operating loss carryforwards, or NOLs, and research and development tax credits, or R&D credits, as a result of our incurrence of losses and our conduct of research activities since inception. We generally are able to carry NOLs and R&D credits forward to reduce our tax liability in future years. However, our ability to utilize the NOLs and R&D credits is subject to the rules of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, respectively. Those sections generally restrict the use of NOLs and R&D credits after an "ownership change." An ownership change occurs if, among other things, the stockholders (or specified groups of stockholders) who own or have owned, directly or indirectly, 5% or more of a corporation's common stock or are otherwise treated as 5% stockholders under Section 382 of the Code and the United States Treasury Department regulations promulgated thereunder increase their aggregate percentage ownership of that corporation's stock by more than 50 percentage points over the lowest percentage of the stock owned by these stockholders over the applicable testing period. In the event of an ownership change, Section 382 imposes an annual limitation on the amount of taxable income a corporation may offset with NOL carryforwards and Section 383 imposes an annual limitation on the amount of tax a corporation may offset with business credit (including the R&D credit) carryforwards.

We may have experienced an "ownership change" within the meaning of Section 382 in the past and there can be no assurance that we will not experience additional ownership changes in the future. As a result, our NOLs and business credits (including the R&D credit) may be subject to limitations and we may be required to pay taxes earlier and in larger amounts than would be the case if our NOLs or R&D credits were freely usable. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs and R&D credit carryforwards could expire or otherwise become unavailable to offset future income tax liabilities. In addition, state NOLs generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

We incur significant costs as a result of being a public company and our management is required to devote substantial time to meet compliance obligations.

As a public company, and particularly as we are no longer an emerging growth company, we incur significant legal, accounting and other expenses. We are subject to reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC that impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. In addition, there are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Wall Street Reform and Protection Act that increase public companies' legal and financial compliance costs, make some activities more difficult, time-consuming or costly and may also place undue strain on personnel, systems and resources. Our management and other personnel devote a substantial amount of time to these compliance initiatives. In addition, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers.

Our charter documents and Delaware law may inhibit a takeover that stockholders consider favorable.

Provisions of our amended and restated certificate of incorporation, or the Certificate of Incorporation, and our amended and restated bylaws, or the Bylaws, and applicable provisions of Delaware law may delay or discourage transactions involving an actual or potential change in control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. The provisions in our Certificate of Incorporation and Bylaws:

- authorize our board of directors to issue preferred stock without stockholder approval and to designate the rights, preferences and privileges of each class; if issued, such preferred stock would increase the number of outstanding shares of our common stock and could include terms that may deter an acquisition of us;

- limit who may call stockholder meetings;

- do not provide for cumulative voting rights;

- provide that all vacancies on our board of directors may be filled only by the affirmative vote of a majority of directors then in office, even if less than a quorum, or by a sole remaining director;

- provide that stockholders must comply with advance notice procedures with respect to stockholder proposals and the nomination of candidates for director;

- provide that stockholders may only amend our Certificate of Incorporation and Bylaws upon a supermajority vote of stockholders; and

- provide that the Court of Chancery of the State of Delaware will be the exclusive forum for certain legal claims.

In addition, Section 203 of the Delaware General Corporation Law may limit our ability to engage in any business combination with a person who beneficially owns 15% or more of our outstanding voting stock unless certain conditions are satisfied. This restriction lasts for a period of three years following the time such person came to beneficially own 15% or more of our outstanding voting stock. These provisions may have the effect of entrenching our management team and may deprive you of the opportunity to sell your shares to potential acquirers at a premium over prevailing prices. This potential inability to obtain a control premium could reduce the price of our common stock.

Our Certificate of Incorporation provides, subject to certain exceptions, that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for certain stockholder litigation matters, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or stockholders.

Our Certificate of Incorporation provides that, subject to limited exceptions and unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for all "internal corporate claims." "Internal corporate claims" mean claims, including claims in the right of the corporation, (i) that are based upon a violation of a duty by a current or former director or officer or stockholder in such capacity or (ii) as to which Title 8 of the Delaware Code confers jurisdiction upon the Court of Chancery, except for, as to each of (i) through (ii) above, any claim as to which the Court of Chancery determines that there is an indispensable party not subject to the jurisdiction of the Court of Chancery (and the indispensable party does not consent to the personal jurisdiction of the Court of Chancery within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery, or for which the Court of Chancery does not have subject matter jurisdiction.

The choice of forum provisions will not apply to claims arising under the Securities Act of 1933, as amended, or the Securities Act, the Exchange Act, or any other claim for which federal courts have exclusive jurisdiction.

Any person or entity purchasing or otherwise acquiring any interest in shares of our common stock shall be deemed to have notice of and to have consented to the provisions of our Certificate of Incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provision that will be contained in our 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 materially adversely affect our business, financial condition and results of operations.

If we are unable to implement and maintain effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our securities may decrease.

As a public company, we are required to maintain internal control over financial reporting and to report any material weaknesses in such internal controls. Section 404 of the Sarbanes-Oxley Act requires that we evaluate and determine the effectiveness of our internal control over financial reporting and provide a management report on our internal control over financial reporting. Until such time as we are no longer a "smaller reporting company" with less than $100 million in annual revenue, our auditors will not be required to attest as to our internal control over financial reporting.

If we are unable to comply with the requirements of Section 404 in a timely manner, if we are unable to assert that our internal control over financial reporting is effective or, once required, provide an attestation report from our independent registered public accounting firm, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could decrease. We could also become subject to stockholder or other third-party litigation as well as investigations by the stock exchange on which our securities are listed, the SEC or other regulatory authorities, which could require additional financial and management resources and could result in fines, trading suspensions or other remedies.

If a significant number of our total outstanding shares are sold into the market, the market price of our common stock could drop significantly, even if our business is performing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act or to the extent such shares have already been registered under the Securities Act and are held by non-affiliates of ours .

Additionally, in September 2024, we completed an underwritten public offering of (i) 11,564,401 shares, or the Shares, of our common stock, $0.001 par value per share, and accompanying common stock warrants, or the Common Stock Warrants, to purchase 2,891,100 shares of our common stock, and (ii) to certain investors in lieu of common stock, pre-funded warrants, or the Pre-Funded Warrants, to purchase 12,435,599 shares of our common stock and accompanying Common Stock Warrants to purchase 3,108,900 shares of common stock.

We currently have on file with the SEC a universal shelf registration statement which allows us to offer and sell up to $300 million of registered common stock, preferred stock, debt securities, warrants, subscription rights and/or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. In addition, we have also entered into an open market sales agreement with Jefferies LLC, as sales agent, or the ATM Sales Agreement, pursuant to which we may offer and sell shares of our common stock under such registration statement for aggregate gross proceeds of up to $80.0 million under an “at-the-market” offering program. To date, we have sold $40.4 million of securities, net of commission paid, but excluding transaction expenses, pursuant to the ATM Sales Agreement.

In addition, we have filed registration statements registering all shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to black-out periods and volume limitations applicable to affiliates.

The number of shares of common stock underlying our outstanding warrants is significant in relation to our currently outstanding common stock, which could have a negative effect on the market price of our common stock and make it more difficult for us to raise funds through future equity offerings. In addition, in connection with any merger, consolidation or sale of all or substantially all of our assets, holders of our outstanding warrants would be entitled to receive consideration in excess of their reported beneficial ownership of our common stock and this could adversely impact the consideration our other stockholders would receive.

As part of our private placement of common stock in November 2022, we issued common stock warrants to purchase an aggregate of 9,188,406 shares of our common stock, and pre-funded warrants to purchase up to an aggregate of 1,531,440 shares of our common stock. Each pre-funded warrant has an exercise price per share of common stock equal to $0.0001 per share. Each pre-funded warrant is exercisable from the date of issuance. Each common stock warrant has an exercise price per share of common stock equal to $3.93, or if exercised for a pre-funded warrant in lieu thereof, $3.9299 per pre-funded warrant. Each common stock warrant is exercisable from the date of issuance until November 16, 2027. Holders of pre-funded warrants and common stock warrants may not exercise any portion of their warrants to the extent that they would beneficially own more

than 4.99% of our outstanding common stock immediately after exercise, which limitation we refer to as the November 2022 Beneficial Ownership Limitation. The holders may increase or decrease their November 2022 Beneficial Ownership Limitation to a percentage not in excess of 19.99% by giving notice to us.

As part of our registered offering of common stock in September 2024, we issued common stock warrants to purchase an aggregate of 2,891,100 shares of our common stock, and pre-funded warrants to purchase up to an aggregate of 12,435,599 shares of our common stock. Each pre-funded warrant has an exercise price per share of common stock equal to $0.001 per share. Each pre-funded warrant is exercisable from the date of issuance until exercised in full. Each common stock warrant has an exercise price per share of common stock equal to $0.50. Each common stock warrant is exercisable from the date of issuance until September 30, 2029. Holders of pre-funded warrants and common stock warrants may not exercise any portion of their warrants to the extent that they would beneficially own more than 4.99% or 9.99%, as elected by the holder, of our outstanding common stock immediately after exercise, which limitation we refer to as the September 2024 Beneficial Ownership Limitation. The holders may increase or decrease their September 2024 Beneficial Ownership Limitation to a percentage not in excess of 19.99% by giving notice to us.

Although the warrants issued in November 2022 and September 2024 are subject to beneficial ownership limitations, upon exercise in full of the warrants, the shares issuable upon exercise would represent a significant portion of our outstanding common stock. As a result, the holders of these warrants may be able to exert substantial influence over our business. The concentration of voting power resulting from the exercise of the warrants could delay, defer or prevent a change of control, entrench our management and our board of directors or delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire. In addition, conflicts of interest could arise in the future between us, on the one hand, and the holders of these warrants, concerning potential competitive business activities, business opportunities, the issuance of additional securities and other matters. In addition, sales of these shares could cause the market price of our common stock to decline significantly. We have registered the issuance of shares upon exercise of these warrants under registration statements. As a result, the shares issuable upon exercise of these warrants can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. Sales of these shares could cause the market price of our common stock to decline significantly. Furthermore, if our stock price rises, the holders of these warrants may be more likely to exercise their warrants and sell a large number of shares, which could negatively impact the market price of our common stock and reduce or eliminate any appreciation in our stock price that might otherwise occur. Given the amount and terms of these warrants, we may find it more difficult to raise additional equity capital on favorable terms or at all while these warrants are outstanding.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We have policies, procedures, and processes for assessing, identifying, and managing cybersecurity risks, which are built into our overall information technology function and are designed to help protect our information assets and operations from internal and external cyber threats as well as secure our networks and systems. Such processes include procedural and technical safeguards, response plans, and routine review of our policies and procedures to identify risks and improve our practices. Our security incident response plan is designed to help coordinate our response to, and recovery from, any cybersecurity incidents, and includes processes to assess the severity of, escalate, contain, investigate, and remediate such incidents as well as to comply with applicable legal obligations.

In response to the complexity and evolving nature of cybersecurity threats, incidents and risks, we engage with a range of third-party experts, including cybersecurity penetration testers, data protection services, security awareness and training, and AI based security services in evaluating and supporting our risk management. Our collaboration with these third parties includes regular independent audits, threat assessments, and consultation on security enhancements. Depending on the nature of the services provided, the sensitivity and quantity of information processed, and the identity of the service provider, we evaluate the security and risk posture of third-party service providers according to the perceived level of risk and benchmarked against industry standard best practices.

The Audit Committee of the board of directors provides direct oversight over cybersecurity risk and provides regular updates to the board of directors regarding such oversight. The Audit Committee regularly meets with members of

management responsible for data privacy, technology, and information security risks to discuss these risks, risk management activities, incident response plans, best practices, the effectiveness of our security measures, and other related matters.

Our Information Technology and Cyber Security Manager, who reports to our Chief Financial Officer, leads the operational oversight of company-wide cybersecurity strategy, policy, standards, and processes and works across relevant departments to assess and help prepare us and our employees to address cybersecurity risks. Specific cybersecurity related responsibilities of the Information Technology and Cyber Security Manager include overseeing our processes and strategies for the detection, mitigation, and remediation of cybersecurity incidents. Our Information Technology and Cyber Security Manager has over 17 years of experience in information technology and cybersecurity, enabling him to effectively oversee cybersecurity risks and threats. He helped design and implement our initial cybersecurity infrastructure.

In an effort to deter and detect cyber threats, we provide all employees, including any part-time employees, with a data protection, cybersecurity, and incident response and prevention training program designed to educate employees on the importance of identifying and reporting all potential data security incidents immediately. The training covers timely and relevant topics, including social engineering, phishing, password protection, confidential data protection, asset use, and mobile security. We also use technology-based tools to mitigate cybersecurity threats and risks and to bolster our employee-based cybersecurity programs.

We do not believe that there are currently any risks from known cybersecurity threats that have materially affected or are reasonably likely to materially affect us or our business strategy, results of operations or financial condition. Despite our cybersecurity efforts, we may not be successful in preventing or mitigating a cybersecurity incident that could have a material adverse effect on us. See Part I, Item 1A, Risk Factors, in this Annual Report for a discussion of cybersecurity risks. We maintain cyber insurance coverage; however, such insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks, and other related breaches.

Item 2. Properties

Our principal office is located in Boston, Massachusetts. In March 2022, we entered into a License Agreement pursuant to which we relocated our corporate headquarters from Cambridge, Massachusetts to Boston, Massachusetts. We currently lease approximately 13,000 square feet of office and laboratory space under a lease that expires in April 2026. We use this space as our principal executive offices and for general office, research and development, and laboratory uses. The monthly rental rate was $209,700 until April 2023, when it increased to $218,088. In April 2024, it increased to $226,812 and in April 2025 it will increase to $235,884 for the remainder of the term through April 2026. We also lease additional laboratory space consisting of one procedure and two holding rooms. The monthly payments due under this lease agreement were $59,153 until November 2023, when they increased to $61,519 for the remainder of the lease term which expired on December 1, 2024. On November 20, 2024, we extended the lease for the additional laboratory space through July 14, 2026. The monthly rental rate is $61,519 through November 30, 2025 and $63,979 for the remainder of the term until July 14, 2026.

Item 3. Legal Proceedings

We are not currently a party to any pending legal proceedings that we believe will have a material adverse effect on our business or financial conditions. We may, however, be subject to various claims and legal actions arising in the ordinary course of business from time to time.

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

Common Stock

Our shares of common stock have been listed on the Nasdaq Capital Market under the symbol "CUE" since January 2, 2018. Prior to that date, there was no public trading market for our common stock.

As of March 27, 2025, there were approximately 85 registered holders of our common stock.

Dividend Policy

We have never paid cash dividends on our securities and we do not anticipate paying any cash dividends on our shares of common stock in the foreseeable future. In addition, our ability to pay cash dividends is currently restricted by the terms of the Loan Agreement, and future debt financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. We intend to retain any future earnings for reinvestment in our business. Any future determination to pay cash dividends will be at the discretion of our board of directors, and will be dependent upon our financial condition, results of operations, capital requirements and such other factors as our board of directors deems relevant.

Recent Sales of Unregistered Securities

Other than as set forth below, during the period covered by this Annual Report on Form 10-K, we did not issue any unregistered equity securities other than pursuant to transactions previously disclosed in our Current Reports on Form 8-K.

On November 25, 2024, we granted to an employee an option to purchase 200,000 shares of our common stock. This option was made as an inducement material to such individual's acceptance of an offer of employment with us in accordance with Nasdaq Listing Rule 5635(c)(4). We intend to file a registration statement on a Form S-8 to register the shares of common stock underlying this inducement award prior to the time at which the award becomes exercisable.

Item 6. [Reserved]

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

The following discussion of our financial condition and results of operations should be read in conjunction with the financial statements and the related notes thereto included elsewhere in this Annual Report on Form 10-K.

Overview

We are a clinical-stage biopharmaceutical company with a novel class of injectable therapeutics engineered to selectively engage and modulate targeted, disease-relevant T cells. Through our approach, we aim to establish a new standard of care for diseases that cause human suffering and mortality, with an initial focus on cancer and autoimmune disease, by selectively modulating the immune system to restore function and re-establish immune balance. We believe our proprietary Immuno-STAT™ (Selective Targeting and Alteration of T Cells) platform, as described below, will enable us to therapeutically enhance a patient's own immune system to potentially restore health.

A key factor in the susceptibility to cancer is inadequate immunity against malignant cancer cells and inversely, autoimmune disease is caused by excessive immune activation against self-tissue. T cells are central to enhancing tumor-immunity as well as maintaining tolerance against self-tissue antigens and are regulated with a highly selective "command and control" instruction process through interactions with antigen-presenting cells, or APCs. We have designed and engineered our Immuno-STAT platform to mimic nature's "command and control" system to restore immune balance.

The immune system's specificity of T cell engagement is achieved through the T cell receptor, or TCR, binding to a highly specific, targeted peptide segment, referred to as an "epitope". The epitope is presented by a specialized protein scaffold, referred to as HLA molecules, present on the surface of APCs. TCR engagement along with "command" secondary signals, such as interleukin 2, transforming growth factor beta, or TGF-β, PD-1, determines the activation state and effector function of T cells. These "cues", or signals, when engaged at the same time, as is the case with our Immuno-STATs, are able to "dial-in" selective activation of targeted tumor-specific T cells to attack cancer while avoiding potentially harmful broad immune activation of T cells. Conversely, in autoimmunity, our autoimmune drug product candidates are designed to deploy signals to generate Tregs to selectively inhibit, or dampen, autoreactive T cells while avoiding broad immune suppression that can increase susceptibility to other diseases. It is through the specificity of the TCR and the simultaneous delivery of "co-stimulatory" signals, that we aim to "command and control" disease-relevant T cells with necessary precision for the treatment of cancer and autoimmune disease.

The Immuno-STAT framework is engineered to be highly flexible and modular, enabling us to deploy the same or similar core functional elements to restore immune balance across diverse therapeutic approaches. In the case of oncology, Immuno-STATs can selectively engage and activate tumor-specific T cells while avoiding systemic immune activation. In contrast, for autoimmune diseases, CUE-401 has been designed to induce and proliferate Tregs to selectively down regulate autoreactive T cells, referred to as Teff cells, while avoiding broad immuno-suppression.

Our drug product candidates are in various stages of clinical and preclinical development. The clinical data generated to date for CUE-101 and CUE-102 as well as the preclinical data supporting the advancement of our CUE-400 and CUE-500 series for autoimmune disease bolsters our belief that we have developed a potential breakthrough approach for the treatment of cancer and autoimmune disease. However, our activities are also subject to significant risks and uncertainties. We have not yet commenced any commercial revenue-generating operations, have limited cash flows from operations, and will need to access substantial additional capital to fund our growth and ongoing business operations.

Plan of Operation and Events that Raise Substantial Doubt About Our Ability to Continue as a Going Concern

Our technology is in the development phase. We believe that our platforms have the potential for creating a diverse pipeline of promising drug product candidates addressing multiple medical indications. We intend to maximize the value and probability of commercialization of our Immuno-STAT drug product candidates by focusing on researching, testing, optimizing, conducting pilot studies, performing early-stage clinical development and potentially partnering, where appropriate, for more extensive, later stages of clinical development, as well as seeking extensive patent protection and intellectual property development.

Since we are a development-stage company, the majority of our business activities to date have been, and our planned future activities will be, devoted to furthering research and development.

A fundamental part of our corporate development strategy is to establish strategic partnerships with leading pharmaceutical or biotechnology organizations that will allow us to more fully exploit the potential of our technology platform

in the areas of oncology and autoimmune disease and accelerate and expand our CUE-100 series pipeline, such as our collaborations described below under the headings “Collaboration Agreement with LG Chem" and "Collaboration and Option Agreement with Ono."

We will need to raise additional capital to fund our future operations and remain as a going concern. We expect to finance our future cash needs through a combination of equity offerings, collaborations, and other strategic alliances. Volatility in capital markets and general economic conditions in the U.S. may be a significant obstacle to raising the required funds and, as a result, we may be unable to secure the necessary funding on acceptable terms. This raises substantial doubt about our ability to continue as a going concern.

Critical Accounting Estimates and Significant Judgments

Our management’s discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or U.S. GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements, and the reported revenue and expenses during the reported periods. We evaluate these estimates and judgments, including those described below, on an ongoing basis. We base our estimates on historical experience, known trends and events, contractual milestones 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 value 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 more fully described in Note 2 to our consolidated financial statements appearing elsewhere in this Form 10-K, we believe that the estimates, assumptions and judgments involved in the following accounting policies may have the greatest potential impact on the financial statements, so we consider these to be our critical accounting policies and estimates. There were no material changes to our critical accounting policies and estimates during the year ended December 31, 2024.

Revenue Recognition

We recognize collaboration revenue under certain of our license and collaboration agreements that are within the scope of Accounting Standards Codification, or ASC, Topic 606, *Revenue from Contracts with Customers*. Our contracts with customers typically include promises related to licenses to intellectual property and research and development services. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. Our contracts may include options to acquire additional goods and/or services.

The terms of our arrangements with customers typically include the payment of one or more of the following: (i) non-refundable, up-front payment, and pass through costs related to research activities, (ii) development, regulatory and commercial milestone payments, (iii) future options and (iv) royalties on net sales of licensed products. Accordingly, the transaction price is generally comprised of a fixed fee due at contract inception and variable consideration in the form of pass through costs and milestone payments due upon the achievement of specified events and tiered royalties earned when customers recognize net sales of licensed products. We measure the transaction price based on the amount of consideration to which we expect to be entitled in exchange for transferring the promised goods and/or services to the customer. We utilize the “expected value method” method to estimate the amount of variable consideration, to predict the amount of consideration to which we will be entitled for our one open contract. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. Milestone payments that are not within our control or the licensee's control, such as those dependent upon receipt of regulatory approval, are not considered to be probable of achievement until the triggering event occurs. At the end of each reporting period, we reevaluate the probability of achievement of each milestone and any related constraint, and, if necessary, adjust its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment.

For arrangements that include sales-based royalties, including milestone payments based upon the achievement of a certain level of product sales, we recognize revenue upon the later of: (i) when the related sales occur or (ii) when the performance obligation to which some or all of the payment has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any development, regulatory or commercial milestones or royalty revenue resulting from any of our collaboration arrangements. Consideration that would be received for optional goods and/or services is excluded from the transaction price at contract inception.

Research and Development Costs

Research and development expenses consist primarily of compensation costs, fees paid to consultants, outside service providers and organizations (including research institutes at universities), facility costs, and development and clinical trial costs with respect to our drug product candidates. We utilize our employee and infrastructure resources across multiple research and development programs, and do not track these costs by project. We believe the attempted allocation of these costs by project would be arbitrary and not meaningful.

Research and development expenses incurred under contracts are expensed ratably over the life of the underlying contracts, unless the achievement of milestones, the completion of contracted work, or other information indicates that a different pattern of performance is more appropriate. Other research and development expenses are charged to operations as incurred.

Nonrefundable advance payments are recognized as an expense as the related services are performed. We evaluate whether we expect the services to be rendered at each quarter end and year end reporting date. If we do not expect the services to be rendered, the advance payment is recorded as expense. Nonrefundable advance payments for research and development services are included in prepaid and other current assets on the balance sheet. To the extent that a nonrefundable advance payment is for contracted services to be performed within 12 months from the reporting date, such advance is included in current assets; otherwise, such advance is included in non-current assets.

We evaluate the status of our research and development agreements and contracts, and the carrying amount of the related assets and liabilities, at each quarter end and year end reporting date, and adjust the carrying amounts and their classification on the balance sheet as appropriate.

The following table summarizes our research and development expenses by category for the years ended December 31, 2024 and 2023 (in millions):

	December 31,	
	2024	**2023**
Employee compensation	$ 13.1	$ 14.4
Clinical trial costs	7.1	9.6
Facilities and overhead	5.2	5.0
Contract manufacturing costs	5.4	8.1
Lab costs	4.9	2.9
Professional fees	0.6	0.8
Total	$ 36.3	$ 40.8

Income Taxes

We account for income taxes under an asset and liability approach for financial accounting and reporting for income taxes. Accordingly, we recognize deferred tax assets and liabilities for the expected impact of differences between the financial statements and the tax basis of assets and liabilities.

We account for uncertainties in income tax law under a comprehensive model for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns as prescribed by GAAP. The tax effects of a position are recognized only if it is “more-likely-than-not” to be sustained by the taxing authority as of the reporting date. If the tax position is not considered “more-likely-than-not” to be sustained, then no benefits of the position are recognized.

We record a valuation allowance to reduce our deferred tax assets to the amount that is more likely than not to be realized. In the event we were to determine that we would be able to realize our deferred tax assets in the future in excess of its recorded amount, an adjustment to the deferred tax assets would be credited to operations in the period such determination was made. Likewise, should we determine that we would not be able to realize all or part of our deferred tax assets in the future, an adjustment to the deferred tax assets would be charged to operations in the period such determination was made.

We are subject to U.S. federal and Massachusetts state income taxes. As our net operating losses have yet to be utilized, all previous tax years remain open to examination by federal and state taxing authorities in which we currently operate.

We recognize interest accrued relative to unrecognized tax benefits in interest expense and penalties in operating expense.

For the years ended December 31, 2024 and 2023, there is no provision for income taxes in the U.S. because we have historically incurred net operating losses and maintain a full valuation allowance against our net deferred assets. The reported amount of income tax expense for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of changes in valuation allowance.

We recognize interest accrued relative to unrecognized tax benefits in interest expense and penalties in operating expense. During the years ended December 31, 2024 and 2023, we did not recognize any income tax related interest and penalties. We did not have any accruals for income tax related interest and penalties at December 31, 2024 and 2023.

Recent Accounting Pronouncements and Adopted Standards

A discussion of recent accounting pronouncements is included in Note 2 to the consolidated financial statements in this Annual Report on Form 10-K.

Significant Contracts and Agreements Related to Research and Development Activities

Einstein License Agreement

On January 14, 2015, we entered into a license agreement, as amended and restated on July 31, 2017, and as further amended on October 30, 2018 and January 13, 2024, or the Einstein License, with Albert Einstein College of Medicine, or Einstein, for certain patent rights, or the Patents, relating to our core technology platform for the engineering of biologics to control T cell activity, precision, immune-modulatory drug product candidates, and two supporting technologies that enable the discovery of costimulatory signaling molecules (ligands) and T cell targeting peptides.

We hold an exclusive worldwide license, with the right to sublicense, import, make, have made, use, provide, offer to sell, and sell all products, processes and services that use the Patents, including certain technology received from Einstein related thereto, which we refer to as the Licensed Products. Under the Einstein License, we are required to:

- Pay royalties and amounts based on a certain percentage of proceeds, as defined in the Einstein License, from sales of Licensed Products and sublicense agreements.
- Pay escalating annual maintenance fees, which are non-refundable, but are creditable against the amount due to Einstein for royalties.
- Make significant payments based upon the achievement of certain milestones, as defined in the Einstein License. As of December 31, 2024, two of these milestones had been achieved, as we had filed an investigational new drug application, or IND, in 2019, and initiated the investigator sponsored Phase 1b neoadjuvant clinical trial for CUE-101 in 2021.
- Incur minimum product development costs per year and meet certain diligence obligations until the first commercial sale of the first Licensed Product.

We were in compliance with our obligations under the Einstein License at December 31, 2024 and 2023.

The Einstein License expires upon the expiration of the last obligation to make royalty payments to Einstein which may be due with respect to certain Licensed Products, unless terminated earlier under the provisions thereof. The Einstein License includes certain termination provisions that will be triggered if we fail to meet our obligations thereunder.

We account for the costs incurred in connection with the Einstein License in accordance with ASC 730, *Research and Development*. For the years ended December 31, 2024 and 2023, costs incurred with respect to the Einstein License were $0.1 million and $7,000, respectively. Such costs are included in research and development costs in our consolidated statements of operations and comprehensive loss.

Pursuant to the Einstein License, we issued to Einstein 671,572 shares of our common stock in connection with the consummation of the initial public offering of our common stock on December 27, 2017.

See "Our License Agreement with Einstein" under Part I, Item 1 of this Annual Report on Form 10-K for additional discussion of the Einstein License.

Collaboration Agreement with LG Chem

On November 6, 2018, we entered into a Collaboration, License and Option Agreement, or the LG Chem Collaboration Agreement, with LG Chem Ltd., or LG Chem, pertaining to the development of CUE-101 and CUE-102 Immuno-STATs focused in the field of oncology.

Pursuant to the LG Chem Collaboration Agreement, we granted LG Chem an exclusive license to develop, manufacture and commercialize CUE-101, as well as Immuno-STATs that target T cells against two additional cancer antigens, or the Drug Product Candidates, in Australia, Japan, Republic of Korea, Singapore, Malaysia, Vietnam, Thailand, Philippines, Indonesia, China (including Macau and Hong Kong) and Taiwan, which we refer to collectively as the LG Chem Territory. In June 2021, after ongoing discussions regarding the selection of the second of the two additional cancer antigens, LG Chem and the Company agreed to let the selection period expire without a second antigen being selected. We retain rights to develop and commercialize all assets included in the LG Chem Collaboration Agreement in the United States and in global markets outside of the LG Chem Territory. Under the LG Chem Collaboration Agreement, we will engineer the selected Immuno-STATs for up to three alleles, which are expected to include the predominant alleles in the LG Chem Territory, thereby enhancing our market reach by providing for greater patient coverage of populations in global markets, while LG Chem will establish a chemistry, manufacturing and controls, or CMC, process for the development and commercialization of selected Drug Product Candidates. In addition, LG Chem has the option to select one additional Immuno-STAT for an oncology target, or an Additional Immuno-STAT, for an exclusive worldwide development and commercialization license. On December 18, 2019, we and LG Chem entered into a global license and collaboration agreement, which was amended on November 5, 2020. We refer to such agreement, as amended, as the Global License and Collaboration Agreement. The Global License and Collaboration Agreement supersedes the provisions of the LG Chem Collaboration Agreement related to LG Chem's option for an Additional Immuno-STAT, which agreement provided for effectiveness if and when LG Chem exercised its option, other than certain select provisions including the length of the option period and representations, warranties and covenants of the parties. On April 30, 2021, LG Chem's option pursuant to the Global License and Collaboration Agreement expired.

Under the terms of the LG Chem Collaboration Agreement, LG Chem paid us a $5.0 million non-refundable, non-creditable upfront payment and purchased $5.0 million of shares of our common stock at a price per share equal to a 20% premium to the volume weighted-average closing price per share over the 30 trading day period immediately prior to the effective date of the LG Chem Collaboration Agreement. We are also eligible to receive additional aggregate payments of up to $400.0 million if certain research, development, regulatory and commercial milestones are successfully achieved. On May 16, 2019, we earned a $2.5 million milestone payment for the FDA's acceptance of the IND for our lead drug product candidate, CUE-101, pursuant to the LG Chem Collaboration Agreement. On December 7, 2020, we earned a $1.25 million milestone payment on the selection of a preclinical candidate pursuant to the LG Chem Collaboration Agreement. On November 23, 2021, we earned a $3.0 million milestone payment for the selection of a Drug Product Candidate. In addition, the LG Chem Collaboration Agreement also provides that LG Chem will pay us tiered single-digit royalties on net sales of commercialized Drug Product Candidates, or Collaboration Products, in the LG Chem Territory on a product-by-product and country-by-country basis, until the later of expiration of patent rights in a country, the expiration of regulatory exclusivity in such country, or ten years after the first commercial sale of a Collaboration Product in such country, subject to certain royalty step-down provisions set forth in the LG Chem Collaboration Agreement.

Pursuant to the LG Chem Collaboration Agreement, the parties will share research costs related to Collaboration Products, and LG Chem will provide CMC process development for selected Drug Product Candidates and potentially additional downstream manufacturing capabilities, including clinical and commercial supply for Collaboration Products. In return for performing CMC process development, LG Chem is eligible to receive low-single digit percentage royalty payments on the sales of Collaboration Products sold in all countries outside the LG Chem Territory. For the years ended December 31, 2024 and 2023, we recognized revenue of less than $0.1 million and $0.3 million, respectively, related to the LG Chem

Collaboration Agreement. As of December 31, 2024, we had recorded $20.0 million in collaboration revenue related to this agreement since the agreement was entered into. The majority of the research phase of the LG Chem Collaboration Agreement was substantially completed by March 31, 2022.

On March 11, 2025 we and LG Chem entered into the Ninth Amendment to the LG Chem Collaboration Agreement. As of the date of the amendment, we regained our rights to the CUE-101 program which were licensed to LG Chem, and LG Chem terminated all of its rights to the same program. Pursuant to the Ninth Amendment, we agreed to make future payments to LG Chem, if and when, one or more potential scenarios related to the CUE-101 program occur up to a predetermined aggregate amount. LG Chem continues to maintain its interest and rights in the CUE-102 program, targeting WT1 expressing cancers, pursuant to the LG Chem Collaboration Agreement.

The LG Chem Collaboration Agreement includes various representations, warranties, covenants, indemnities and other customary provisions. LG Chem may terminate the LG Chem Collaboration Agreement for convenience or change of control of us on a program-by-program, product-by-product or country-by-country basis, or in its entirety, at any time following the notice period set forth in the LG Chem Collaboration Agreement. Either party may terminate the LG Chem Collaboration Agreement, in its entirety or on a program-by-program, product-by-product or country-by-country basis, in the event of an uncured material breach. The LG Chem Collaboration Agreement is also terminable by either party (i) upon the bankruptcy, insolvency or liquidation of the other party or (ii) for certain activities involving the challenge of certain patents controlled by the other party. Unless earlier terminated, the LG Chem Collaboration Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the applicable royalty term.

Collaboration and Option Agreement with Ono

On February 22, 2023, we entered into a strategic collaboration agreement, or the Ono Collaboration and Option Agreement, with Ono Pharmaceutical Co., Ltd., or Ono, to further develop CUE-401 and provide dedicated resources and capabilities to help advance CUE-401 toward the clinic. Under the terms of the Ono Collaboration and Option Agreement, Ono paid us an upfront payment and agreed to fully fund all research activities related to CUE-401 through a specified option period. During this option period, we were responsible for the research and development of CUE-401. Upon Ono's exercise of its option to license CUE-401, we would have received an option exercise payment and been eligible for development and commercial milestone payments up to an aggregate of $220.0 million, as well as tiered royalties on sales. Upon any such exercise, Ono would have received worldwide rights to develop and commercialize CUE-401, with us retaining a 50% co-development and co-commercialization right in the United States. Our decision to elect the co-development and co-commercialization option could have been made within 30 days of Ono's option exercise to license CUE-401.

Under the terms of the Ono Collaboration and Option Agreement, we performed research activities related to CUE-401 through a specified option period of 24 months, or the Research Term. During this Research Term, we were responsible for the execution of scientific investigation, nonclinical, preclinical, and clinical drug research and development activities designed to progress CUE-401 toward a potential IND and regulatory approval, collectively referred to as R&D. Ono was responsible for the funding of R&D activities performed by us. Per the Ono Collaboration and Option Agreement, as consideration for the R&D activities performed by us, Ono (i) has made a one-time, non-refundable, non-creditable upfront payment of $3.0 million to us in March 2023, and (ii) agreed to reimburse us for all costs incurred in conducting research, including (a) pass through costs from third party contractors and (b) full time employee salaries capped at $2.1 million in the first 18 months of the Research Term. Subsequently, we and Ono agreed to increase this cap for full time employee salaries to $3.1 million.

On March 11, 2025, we and Ono agreed to terminate the Ono Collaboration and Option Agreement, effective as of March 6, 2025. Effective upon termination, we regained worldwide development and commercialization rights for CUE-401 from Ono. At such time, the agreement had no further force or effect with the exception of certain customary provisions which are intended to survive termination and expiration of the agreement. .

As of the date of this Annual Report on Form 10-K, both Ono and the Company have satisfied all of their performance obligations and made all outstanding payments required under the agreement. Aside from the $3.0 million upfront payment and funding related to pass through costs, we do not believe that any variable consideration should be included in the transaction price as of December 31, 2024. Such assessment considered the application of the constraint to ensure that estimates of variable consideration would be included in the transaction price only to the extent we have a high degree of confidence that revenue would not be reversed in a subsequent reporting period. We will re-evaluate the transaction price, including the estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as other changes in circumstances occur. As of December 31, 2024 and 2023, we recognized revenue of

$9.2 million and $5.2 million, respectively, related to the Ono Collaboration and Option Agreement and recorded deferred revenue of $0.1 million and $2.1 million, respectively, on our consolidated balance sheets.

See "Our Collaboration and Option Agreement with Ono" under Part I, Item 1 of this Annual Report on Form 10-K for additional discussion of the Ono Collaboration and Option Agreement.

Components of Results of Operations

Collaboration Revenue

We have not yet generated commercial revenue from product sales. To date, we have generated revenue from collaboration agreements with Merck Sharp & Dohme Corp. (which terminated in December 2022), LG Chem, and Ono. Collaboration revenue may vary from period to period depending on the progress of our work in connection with our collaboration agreements.

Operating Expenses

We generally recognize operating expenses as they are incurred in two general categories, general and administrative expenses and research and development expenses. Our operating expenses also include non-cash components related to depreciation and amortization of property and equipment and stock-based compensation, which are allocated, as appropriate, to general and administrative expenses and research and development expenses.

General and administrative expenses consist of salaries and related expenses for executive, legal, finance, human resources, information technology and administrative personnel, as well as professional fees, insurance costs, and other general corporate expenses. We expect general and administrative expenses to remain consistent in future periods as we continue to incur expenses related to our operation as a public company, which requires our ongoing compliance with certain laws and regulations.

Research and development expenses consist primarily of compensation expenses, fees paid to consultants, outside service providers and organizations (including research institutes at universities), facility expenses, and development and clinical trial expenses with respect to our drug product candidates. We charge research and development expenses to operations as they are incurred. We expect that our research and development expenses may increase in future periods based on our strategic re-prioritization of our autoimmune programs.

Interest Income

We earn interest income from cash invested in money market funds.

Results of Operations

Years Ended December 31, 2024 and 2023

Our consolidated statements of operations for the years ended December 31, 2024 and 2023, as discussed herein are presented below.

	2024	2023
Collaboration revenue	$ 9,287	$ 5,490
Operating expenses (income):		
General and administrative	14,585	16,680
Research and development	36,295	40,802
(Gain) loss on fixed asset disposal	(93)	157
Total operating expenses	50,787	57,639
Loss from operations	(41,500)	(52,149)
Other income (expense):		
Interest income	1,622	2,661
Interest expense	(796)	(1,245)
Total other income, net	826	1,416
Net loss	$ (40,674)	$ (50,733)

Collaboration Revenue

Collaboration revenue increased by $3.8 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. The increase was due to revenue recognized from the Ono Collaboration and Option Agreement executed in February 2023.

General and Administrative

General and administrative expenses decreased by $2.1 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. This was due to a decrease in employee compensation, which includes stock-based compensation, of $1.5 million, and a decrease in professional fees of $0.6 million.

Research and Development

Research and development expenses decreased by $4.5 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. This was due to a decrease in clinical trial costs of $2.5 million, a decrease in employee compensation, which includes stock-based compensation, of $1.3 million, and a decrease in manufacturing and lab costs of $0.7 million.

(Gain) Loss on Fixed Asset Disposal

Gain on fixed asset disposal was $0.1 million for the year ended December 31, 2024 compared to a loss on fixed asset disposal of $0.2 million for the year ended December 31, 2023. These gains and losses were recognized from the sale of laboratory equipment.

Interest Income

Interest income decreased by $1.0 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. The decrease was due to less interest earned on cash and cash equivalents balances.

Interest Expense

Interest expense decreased by $0.4 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. The decrease was due to less interest incurred from our Loan and Security Agreement, as amended, or the Loan Agreement, with Silicon Valley Bank, or SVB, a division of First Citizens Bank & Trust Company, or First Citizens Bank, as the loan principal balance decreased year over year.

Net Loss

As a result of the foregoing, our net loss decreased by $10.1 million for the year ended December 31, 2024 compared to the year ended December 31, 2023.

Liquidity and Capital Resources

We have financed our working capital requirements primarily through private and public offerings of equity securities, cash received from Merck Sharp & Dohme Corp., LG Chem, and Ono under the respective collaboration agreements and borrowings under the Loan Agreement. At December 31, 2024 and December 31, 2023, we had cash and cash equivalents totaling $22.5 million and $48.5 million, respectively, available to fund our ongoing business activities. Additional information concerning our financial condition and results of operations is provided in the financial statements included in this Annual Report on Form 10-K.

The amounts that we actually spend for any specific purpose may vary significantly and will depend on a number of factors, including, but not limited to, our research and development activities and programs, clinical testing, regulatory approval, market conditions, and changes in or revisions to our business strategy and technology development plans.

On May 9, 2023, we filed a registration statement on Form S-3, which was declared effective on May 26, 2023 (File No. 333-271786), to register for sale from time to time up to $300.0 million of our common stock, preferred stock, debt securities, warrants, subscription rights and/or units in one or more offerings.

In October 2021, we entered into an open market sale agreement, or the ATM Sales Agreement, with Jefferies LLC, or Jefferies, to sell shares of our common stock for aggregate gross proceeds of up to $80.0 million, from time to time, through an "at-the-market" equity offering program under which Jefferies acts as sales agent. The ATM Sales Agreement will terminate

upon the earliest of (a) the sale of $80.0 million of shares of our common stock pursuant to the ATM Sales Agreement or (b) the termination of the ATM Sales Agreement by us or Jefferies. During the years ended December 31, 2024 and 2023, we sold 1,471,858 and 4,006,966 shares, respectively, of common stock under the ATM Sales Agreement for proceeds of $3.4 million and $13.4 million, respectively, net of commission paid, but excluding transaction expenses. As of December 31, 2024, we had sold an aggregate of 9,072,231 shares of common stock under the ATM Sales Agreement for proceeds of $40.4 million, net of commission paid, but excluding transaction expenses.

On February 15, 2022, we entered into the Loan Agreement, pursuant to which we have borrowed $10.0 million. The Loan Agreement was amended in April 2023 and October 2024. The term loans under the Loan Agreement, or the Term Loans, bear interest at a floating rate per annum equal to the greater of (A) the prime rate (as published in the money rates section of The Wall Street Journal) plus 2.25% and (B) 5.50%. On the first calendar day of each month, we will be required to make monthly interest payments and commencing on June 30, 2023, we began repayment of the Term Loans in (i) 30 consecutive installments of principal plus monthly payments of accrued interest if the additional term loans are not advanced and (ii) 24 months if the additional term loans are advanced. All outstanding principal and accrued and unpaid interest under the Term Loans and all other outstanding obligations with respect to the Term Loans are due and payable in full on December 1, 2025.

The Loan Agreement permits voluntary prepayment of all, but not less than all, of the Term Loans, subject to a prepayment premium except if the facility is refinanced with another First Citizens Bank facility. Such prepayment premium would be 1.00% of the principal amount of the Term Loans. Upon prepayment or repayment in full of the Term Loans, we will be required to pay a one-time final payment fee equal to 5.00% of the original principal amount of any funded Term Loans being repaid. The Loan Agreement, as amended, also requires us to have at all times on deposit in our accounts maintained with SVB, unrestricted and unencumbered cash in an amount equal to the lesser of (i) 100% of the dollar value of our consolidated cash, in the aggregate, at all financial institutions, and (ii) $20,000,000.

On March 10, 2023, SVB was closed and the Federal Deposit Insurance Company, or FDIC, was appointed receiver for the bank. The FDIC created a successor bridge bank, and all deposits of SVB were transferred to the bridge bank under a systemic risk exception approved by the U.S. Department of the Treasury, the Federal Reserve and the FDIC. On March 27, 2023, First Citizens Bank assumed all of SVB's deposits and certain other liabilities and acquired substantially all of SVB's loans and certain other assets from the FDIC. First Citizens Bank continues to hold our Term Loans under the same existing terms and covenants which were in place with SVB.

On November 14, 2022, we entered into securities purchase agreements with accredited investors pursuant to which, on November 16, 2022, we issued and sold to such investors in a private placement an aggregate of 7,656,966 shares of common stock and, in lieu of shares of common stock to certain investors, pre-funded warrants, or the 2022 Pre-Funded Warrants, to purchase an aggregate of 1,531,440 shares of common stock, and, in each case, accompanying warrants, or the 2022 Common Stock Warrants, to purchase an aggregate of up to 9,188,406 additional shares of common stock (or 2022 Pre-Funded Warrants in lieu thereof) at a price of $3.265 per share and accompanying 2022 Common Stock Warrant (or $3.2649 per 2022 Pre-Funded Warrant and accompanying 2022 Common Stock Warrant), or the PIPE Financing. The exercise price of the 2022 Common Stock Warrants is $3.93 per share, or if exercised for a 2022 Pre-Funded Warrant in lieu thereof, $3.9299 per 2022 Pre-Funded Warrant. The 2022 Common Stock Warrants are exercisable at any time after they are issued and ending on the fifth anniversary of the closing. The 2022 Pre-Funded Warrants are exercisable at any time after they are issued and will not expire. We received aggregate gross proceeds from the PIPE Financing of $30 million, before deducting placement agent fees and offering expenses of $2.6 million. Piper Sandler & Co. acted as lead placement agent and Public Ventures LLC acted as co-placement agent for the PIPE Financing.

On September 26, 2024, we entered into an underwriting agreement, or the Underwriting Agreement, with Oppenheimer & Co. Inc., as representative of the several underwriters named therein, or, collectively, the Underwriters, relating to an underwritten public offering of (i) 11,564,401 shares, or the Shares, of our common stock, $0.001 par value per share, and accompanying common stock warrants, or the 2024 Common Stock Warrants, to purchase 2,891,100 shares of our common stock, and (ii) to certain investors in lieu of common stock, pre-funded warrants, or the 2024 Pre-Funded Warrants, to purchase 12,435,599 shares of our common stock and accompanying 2024 Common Stock Warrants to purchase 3,108,900 shares of common stock. All of the Shares, the 2024 Pre-Funded Warrants and the 2024 Common Stock Warrants were sold by us. Each Share was offered and sold together with an accompanying 2024 Common Stock Warrant at a combined offering price of $0.50, and each 2024 Pre-Funded Warrant was offered and sold together with an accompanying 2024 Common Stock Warrant at a combined offering price of $0.499, which is equal to the combined offering price per share of common stock and accompanying 2024 Common Stock Warrant less the $0.001 exercise price of each 2024 Pre-Funded Warrant. We received net proceeds from the offering of $10.8 million, after deducting underwriting discounts and commissions and offering expenses of

$1.2 million, and excluding any proceeds that may be received from exercise of the 2024 Common Stock Warrants and the 2024 Pre-Funded Warrants.

If we issue additional equity securities to raise funds, the ownership percentage of our existing stockholders would be reduced. New investors may demand rights, preferences or privileges senior to those of existing holders of our common stock. If we issue debt securities, we may be required to grant security interests in our assets, could have substantial debt service obligations, and lenders may have a senior position (compared to stockholders) in any potential future bankruptcy or liquidation. Additionally, corporate collaboration and licensing arrangements may require us to incur non-recurring and other charges, give up certain rights relating to our intellectual property and research and development activities, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, issue debt which may require liens on our assets and which will increase our monthly expense obligations, or disrupt our management and business.

Cash Flows

Based on our current plans and forecasted expenses, we believe that our existing cash and cash equivalents, as of December 31, 2024, will enable us to fund our operations into the fourth quarter of 2025. However, we will need to raise additional capital to fund our future operations and remain as a going concern. We expect to finance our future cash needs through a combination of equity offerings, collaborations, and other strategic alliances. Volatility in capital markets and general economic conditions in the United States may be a significant obstacle to raising the required funds and, as a result, we may be unable to secure the necessary funding on acceptable terms. This raises substantial doubt about our ability to continue as a going concern.

The following table summarizes our changes in cash, cash equivalents, and restricted cash for the year ended December 31, 2024 and 2023:

	December 31,	
	2024	2023
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (36,329)	$ (39,961)
Investing activities	32	25,002
Financing activities	10,243	11,860
Net decrease in cash, cash equivalents, and restricted cash	$ (26,054)	$ (3,099)

Operating Activities

Net cash used in operating activities decreased by $3.6 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. This was primarily attributable to a lower net loss recognized during the year ended December 31, 2024, as well as decreases in research and development contract liabilities, accrued expenses, and stock based compensation, partially offset by an increase in accounts receivable.

Investing Activities

Net cash provided by investing activities decreased by $25.0 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. This was due to redemptions of marketable securities during the year ended December 31, 2023.

Financing Activities

Net cash provided by financing activities decreased by $1.6 million for the year ended December 31, 2024 compared to the year ended December 31, 2023. This was primarily due to a decrease in proceeds received from sales pursuant to our ATM Sales Agreement in 2024 compared to 2023, partially offset by net proceeds received from our underwritten public offering in September 2024.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of our Immuno-STAT platform and continue ongoing and initiate new clinical trials of and seek marketing approval for our drug product candidates. In addition, we expect to incur additional costs associated with operating as a public company. Our expenses will also increase if, and as, we:

- continue to assess maturing clinical data of our CUE-100 series, including CUE-101 and CUE-102, which we have deprioritized;
- continue the preclinical development of CUE-401 and CUE-501;
- leverage our programs, including our autoimmune programs, to advance our other drug product candidates into preclinical and clinical development;
- seek regulatory approvals for any drug product candidates for which we successfully complete clinical trials;
- seek to discover and develop additional drug product candidates;
- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any drug product candidates for which we may obtain marketing approval and intend to commercialize on our own or jointly;
- expand our manufacturing, quality, operational, financial and management systems, including personnel to support these functions;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license other drug product candidates and technologies; and
- incur additional legal, accounting and other expenses in operating as a public company.

In July 2024, we determined to strategically prioritize our autoimmune programs, including CUE-401 and CUE-501, and completed an organizational restructuring to strengthen operational efficiencies, including an approximate 25% reduction in our workforce.

Under Accounting Standards Update, or ASU, 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40), or, ASC 205-40, we have the responsibility to evaluate whether conditions or events raise substantial doubt about our ability to meet our future financial obligations as they become due within one year after the date the financial statements are issued. Under ASC 205-40, this evaluation initially cannot take into consideration the potential mitigating effects of plans that have not been fully implemented as of the date the financial statements are issued. Since we currently believe that our existing cash and cash equivalents, as of December 31, 2024, and our current operating plan will enable us to fund our operations into the fourth quarter of 2025, we have determined that this cash runway of less than 12 months from the date of issuance of our financial statements included in this Annual Report on Form 10-K, along with our accumulated deficit, history of losses, and future expected losses meet the ASC 205-40 standard for raising substantial doubt about our ability to continue as a going concern within one year of the issuance date of our financial statements included in this Annual Report on Form 10-K. While we have plans in place to mitigate this risk, which primarily consist of raising additional capital through a combination of equity offerings, collaborations, and other strategic alliances, and, depending on the availability and level of additional financings, and cash expenditure reduction, there is no guarantee that we will be successful in these mitigation efforts.

We will need to raise additional capital or incur additional indebtedness to continue to fund our operations in the near term. Our ability to raise additional funds will depend on financial, economic and market conditions, many of which are outside of our control, and we may be unable to raise financing when needed, or on terms favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market drug product candidates that we would otherwise prefer to develop and market ourselves, which could adversely affect our business prospects, and we may be unable to continue our operations. Because of numerous risks and uncertainties associated with the research, development and commercialization of our drug product candidates, we are unable to estimate the exact amount of our working capital requirements. Factors that may affect our planned future capital requirements and accelerate our need for additional working capital include the following:

- the progress, timing, scope and costs of our clinical trials, including the ability to timely enroll patients in our ongoing, planned and any future clinical trials;
- our ability to secure third party support through partnerships and collaborations to further develop the CUE-100 series programs, including CUE-101 and CUE-102, as well as CUE-501;
- the outcome, timing and cost of regulatory approvals by the FDA and other comparable regulatory authorities, including the potential that the FDA or other comparable regulatory authorities may require that we perform more studies than those that we currently expect;
- the number and characteristics of drug product candidates that we may in-license and develop;
- our ability to successfully commercialize our drug product candidates, if approved;
- the amount of sales and other revenues from drug product candidates that we may commercialize, if any, including the selling prices for such potential products and the availability of adequate third-party reimbursement;
- selling and marketing costs associated with our potential products, including the cost and timing of expanding our marketing and sales capabilities;
- the terms and timing of any potential future collaborations, licensing or other arrangements that we may establish;
- cash requirements of any future acquisitions and/or the development of other drug product candidates;
- the costs of operating as a public company;
- the cost and timing of completion of commercial-scale, outsourced manufacturing activities;
- the time and cost necessary to respond to technological and market developments;
- any disputes which may occur between us and our employees, collaborators, including Einstein, LG Chem and Ono, or other prospective business partners; and
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these or other variables with respect to the development of any of our drug product candidates could significantly change the costs and timing associated with the development of that drug product candidate. Further, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties and grants from organizations and foundations. If we raise additional funds by selling shares of our common stock or other equity-linked securities, the ownership interest of our current stockholders will be diluted. We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or drug product candidates or to grant licenses on terms that may not be acceptable to us. If we raise additional funds through debt financing, we may have to grant a security interest on our assets to the future lenders, our debt service costs may be substantial, and the lenders may have a preferential position in connection with any future bankruptcy or liquidation.

If we are unable to raise additional capital when needed, we may be required to curtail the development of our technology or materially curtail or reduce our operations. We could be forced to sell or dispose of our rights or assets. Any inability to raise adequate funds on commercially reasonable terms could have a material adverse effect on our business, results of operation and financial condition, including the possibility that a lack of funds could cause our business to fail, dissolve and liquidate with little or no return to investors.

Principal Commitments

Leased Facilities

On March 28, 2022, we entered into a License Agreement, or the License, with MIL 40G, LLC, or the Licensor, pursuant to which we lease approximately 13,000 square feet of office, research and development and laboratory space located at 40 Guest Street, Boston, Massachusetts 02135, or the Premises. We relocated our corporate headquarters to the Premises in April 2022. On March 28, 2022, we terminated our operating lease agreement for laboratory and office space in Cambridge, Massachusetts at 21 Erie Street, or the Laboratory and Office Lease, with an effective termination date of April 30, 2022.

We recognized a right of use asset of $9.1 million and an operating lease liability of $9.1 million which were recorded as of the Term Commencement Date (as defined below) related to the License.

The term of the License commenced on April 15, 2022, or the Term Commencement Date, and expires on April 14, 2026, or the Term. The License has a monthly rental rate of $200,700 for the first year of the Term, $208,728 for the second year of the Term, $217,077 for the third year of the Term and $225,760 for the remainder of the Term. Pursuant to the License, we prepaid two months of rent and a security deposit. The Licensor is obligated under the License to provide certain services to us, including providing certain gases, chemicals and equipment to the Premises' laboratory space, IT support, security, office support and health and safety training. The Licensor has the right to terminate the License for Cause (as defined in the License).

On May 3, 2022, we entered into the First Amendment to the License, or the First Amendment, with the Licensor, pursuant to which the License was expanded to include an additional room effective July 15, 2022. In consideration of the First Amendment, the security deposit was increased from $225,760 to $235,884 effective July 15, 2022. Upon execution of the First Amendment, we prepaid three months of rent, two of which will be held in escrow and credited against future rent payments and the other of which was applied to the first month's rent. Effective July 15, 2022, the monthly rental rate under the First Amendment increased to $209,700 from $200,700. During the year ended December 31, 2022, we recognized a right of use asset of $0.4 million and short and long term operating lease liabilities of $0.1 million and $0.3 million, respectively, using a discount rate of 8%, which were recorded as of the Term Commencement Date related to the License.

On May 31, 2022, we entered into an operating lease for additional laboratory space at 40 Guest Street, Boston, Massachusetts for the period from December 1, 2022, through December 1, 2024, or the 40G Additional Laboratory Lease. The 40G Additional Laboratory Lease contains escalating payments during the lease period. The monthly rental rate under the 40G Additional Laboratory Lease was $59,153 for the first 12 months and $61,519 for the remainder of the initial term. Under the terms of the 40G Additional Laboratory Lease, we prepaid three months of rent, two of which are held in escrow and credited against future rent payments and the other of which was applied to the first month's rent. On November 20, 2024, we extended the lease through July 14, 2026. The monthly rental rate is $61,519 through November 30, 2025 and $63,979 for the remainder of the term until July 14, 2026. During the year ended December 31, 2024, we recognized a right of use asset of $1.1 million and a short and long term operating lease liability of $0.7 million, and $0.4 million, respectively, using a discount rate of 10%, which were recorded as of the Term Commencement Date related to the 40G Additional Laboratory Lease, as amended.

For the year ended December 31, 2024, we recorded $0.3 million in interest expense to the lease liability.

At December 31, 2024, we recorded an operating lease right-of-use asset of $4.4 million, as well as corresponding short-term and long-term operating lease liabilities of $3.5 million and $1.0 million, respectively. At December 31, 2023, we recorded an operating lease right-of-use asset of $6.3 million, as well as corresponding short-term and long-term operating lease liabilities of $3.4 million and $3.2 million, respectively. As of December 31, 2024 and 2023, a security deposit of $0.5 million was included in deposits on our consolidated balance sheet related our leases.

Manufacturing Agreement with Catalent

We have entered into agreements with Catalent Pharma Solutions, LLC or Catalent, for Catalent to provide us with contracted manufacturing services related to the manufacture of CUE-401 materials and CUE-101 late stage process optimization. Work related to these services began in 2023, and at December 31, 2024, work totaling $8.4 million is still to be performed.

Einstein License Agreement

Our commitments with respect to the Einstein License are summarized above at "Significant Contracts and Agreements Related to Research and Development Activities."

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

As a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act, we are not required to provide the information under this item.

Item 8. Financial Statements and Supplementary Data.

Our financial statements and the related notes, together with the Report of Independent Registered Public Accounting Firm thereon, are set forth 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

As of the end of the period covered by this report, management performed, with the participation of our principal executive and principal financial officers, an evaluation of the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act 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, to allow timely decisions regarding required disclosures. Based on the evaluation, our principal executive and principal financial officers concluded that, as of December 31, 2024, our disclosure controls and procedures were effective.

Inherent Limitations on Effectiveness of Controls

Our management, including our principal executive officer and our principal financial officer, do not expect that our disclosure controls or our internal control over financial reporting will prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. The design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Further, because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of a simple error or mistake. Controls can also be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the controls. The design of any system of controls is based in part on 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. Projections of any evaluation of control effectiveness to future periods are subject to risks. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rule 13a-15(f) of the Exchange Act. Management evaluated the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control Integrated Framework (the 2013 Framework). Based on this assessment, our management concluded that, as of December 31, 2024, our internal control over financial reporting was effective based on those criteria. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. There were no changes in our internal control over financial reporting during the fiscal quarter ended December 31, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

As a non-accelerated filer and a "smaller reporting company", as defined in Rule 12b-2 under the Exchange Act, our independent registered public accounting firm is not required to issue an attestation report on the internal control over financial reporting.

Item 9B. Other Information.

(b) Director and Officer Trading Arrangements

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during the three months ended December 31, 2024.

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

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 is incorporated by reference to our Definitive Proxy Statement on Schedule 14A relating to our 2025 annual meeting of stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 11. Executive Compensation

The information required by this Item 11 (other than the information required by Item 402(v) of Regulation S-K) is incorporated by reference to our Proxy Statement on Schedule 14A relating to our 2025 annual meeting of stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by this Item 12 is incorporated by reference to our Proxy Statement on Schedule 14A relating to our 2025 annual meeting of stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by this Item 13 is incorporated by reference to our Proxy Statement on Schedule 14A relating to our 2025 annual meeting of stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 is incorporated by reference to our Proxy Statement on Schedule 14A relating to our 2025 annual meeting of stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Cue Biopharma, Inc.

Opinion on the Financial Statements
We have audited the accompanying consolidated balance sheets of Cue Biopharma, Inc. and its subsidiary (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for the years then ended, and the related notes to the consolidated financial statements (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 accounting principles generally accepted in the United States of America.

The Company's Ability to Continue as a Going Concern
The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and used cash in operations in each of the two years ended December 31, 2024 and 2023. This raises substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters also are described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion
These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with 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.

Critical Audit Matter
The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Research and Development Costs of Clinical Trials
As discussed in Note 2 to the financial statements, the Company accounts for the research and development costs relating to clinical trials based on estimates of costs incurred through the balance sheet date. This process involves estimating the associated costs incurred and recording accruals or prepayments as appropriate. The Company's accrual for contract services costs relating to its clinical trials totaled $0.8 million at December 31, 2024, as disclosed in Note 6.

We identified the accounting for research and development costs of clinical trials to be a critical audit matter because auditing the Company's analysis of costs incurred is complex as the information necessary to make an estimate is accumulated from multiple sources and there may be delays in invoicing from clinical study sites and other vendors, or payments may depend on

factors such as the achievement of clinical trial milestones. Additionally, in certain circumstances, it requires judgment, as the timing and pattern of vendor invoicing may not correspond to the level of services provided.

Our audit procedures related to clinical trials expense included, among others:

- Tested the accuracy and completeness of the underlying data used in the estimates and evaluated the reasonableness of assumptions used by management.
- Inspected certain contracts with third parties and related information received by the Company to test proper recording of costs incurred to date, contract service periods, and services and/or deliverables to be provided within each contract.
- Corroborated the progress of research and development activities through discussion with the Company's research and development personnel, specifically those who oversee the projects, and confirmations with certain third parties.
- Tested subsequent invoices received from third parties and cash disbursements to assess completeness of recorded accruals or prepaids, as appropriate.

/s/ RSM US LLP

We have served as the Company's auditor since 2018.

Boston, Massachusetts
March 31, 2025

CUE BIOPHARMA, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except shares and per share amounts)

	December 31,	
	2024	**2023**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 22,459	$ 48,514
Accounts receivable	945	1,698
Deposits, current portion	929	287
Prepaid expenses and other current assets	805	955
Total current assets	25,138	51,454
Property and equipment, net	471	795
Operating lease right-of-use asset	4,370	6,323
Deposits, net of current portion	1,955	2,690
Restricted cash	152	151
Other long term assets	105	117
Total assets	$ 32,191	$ 61,530
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,823	$ 3,501
Accrued expenses	2,908	4,137
Research and development contract liability	85	2,112
Operating lease liabilities, current portion	3,540	3,368
Current portion of long-term debt, net	4,333	3,963
Total current liabilities	13,689	17,081
Operating lease liabilities, net of current portion	1,003	3,162
Long-term debt, net	—	4,202
Total liabilities	$ 14,692	$ 24,445
Commitments and contingencies (Note 14)		
Stockholders' equity:		
Preferred stock, $0.001 par value, authorized – 10,000,000 shares; issued and outstanding – none	—	—
Common stock, $0.001 par value; 200,000,000 and 100,000,000 shares authorized at December 31, 2024 and December 31, 2023, respectively; 61,819,101 shares and 47,215,116 shares issued and outstanding at December 31, 2024 and 2023, respectively	62	47
Additional paid-in capital	359,301	338,228
Accumulated deficit	(341,864)	(301,190)
Total stockholders' equity	17,499	37,085
Total liabilities and stockholders' equity	$ 32,191	$ 61,530

The accompanying notes are an integral part of these consolidated financial statements.

CUE BIOPHARMA, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except shares and per share amounts)

	Years Ended December 31,	
	2024	**2023**
Collaboration revenue	$ 9,287	$ 5,490
Operating expenses (income):		
General and administrative	14,585	16,680
Research and development	36,295	40,802
(Gain) loss on fixed asset disposal	(93)	157
Total operating expenses	50,787	57,639
Loss from operations	(41,500)	(52,149)
Other income (expense):		
Interest income	1,622	2,661
Interest expense	(796)	(1,245)
Total other income, net	826	1,416
Net loss	$ (40,674)	$ (50,733)
Unrealized gain from available-for-sale securities	—	96
Comprehensive loss	$ (40,674)	$ (50,637)
Net loss per common share – basic and diluted	$ (0.72)	$ (1.11)
Weighted average common shares outstanding – basic and diluted	56,328,348	45,754,794

The accompanying notes are an integral part of these consolidated financial statements.

CUE BIOPHARMA, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except shares and per share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Par Value				
Balance, December 31, 2022	43,042,548	$ 43	$ 316,192	(96)	$ (250,457)	$ 65,682
Issuance of common stock from ATM offering, net of sales agent commission and fees	4,006,966	4	13,383	—	—	13,387
Stock-based compensation	—	—	8,180	—	—	8,180
Exercise of stock options	165,602	—	473	—	—	473
Unrealized gain from available-for-sale securities	—	—	—	96	—	96
Net loss	—	—	—	—	(50,733)	(50,733)
Balance, December 31, 2023	47,215,116	$ 47	$ 338,228	$ —	$ (301,190)	$ 37,085
Issuance of common stock from ATM offering, net of sales agent commission and fees	1,471,858	1	3,410	—	—	3,411
Issuance of common stock, warrants and pre-funded warrants, net of issuance costs	11,564,401	12	10,801	—	—	10,813
Stock-based compensation	—	—	6,846	—	—	6,846
Issuance of common stock upon exercise of warrants and pre-funded warrants, net	1,567,726	2	16	—	—	18
Net loss	—	—	—	—	(40,674)	(40,674)
Balance, December 31, 2024	61,819,101	$ 62	$ 359,301	$ —	$ (341,864)	$ 17,499

The accompanying notes are an integral part of these consolidated financial statements.

CUE BIOPHARMA, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,	
	2024	**2023**
Cash flows from operating activities:		
Net loss	$ (40,674)	$ (50,733)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	397	556
Stock-based compensation	6,846	8,180
Decrease in the carrying amount of right-of-use assets	1,953	2,880
Amortization of premium/discount on purchased securities	—	(234)
(Gain) loss on fixed asset disposal	(93)	157
Amortization of debt issuance costs	37	37
Accretion of final payment of term loan	130	130
Changes in operating assets and liabilities:		
Account receivable	753	(1,641)
Prepaid expenses and other current assets	150	(401)
Deposits	93	426
Accounts payable	(678)	770
Accrued expenses	(1,229)	588
Research and development contract liability	(2,027)	2,112
Operating lease liability	(1,987)	(2,788)
Net cash used in operating activities	(36,329)	(39,961)
Cash flows from investing activities:		
Purchases of property and equipment	(66)	—
Cash received from sale of fixed asset	98	2
Redemption of marketable securities	—	25,000
Net cash provided by investing activities	32	25,002
Cash flows from financing activities:		
Proceeds from ATM offering, net of sales agent commission and fees	3,411	13,387
Proceeds from issuance of common stock, warrants and pre-funded warrants, net of transaction costs	10,813	—
Repayment of term loans	(3,999)	(2,000)
Proceeds from the exercise of stock options	—	473
Issuance of common stock upon exercise of warrants and pre-funded warrants, net	18	—
Net cash provided by financing activities	10,243	11,860
Net decrease in cash, cash equivalents, and restricted cash	(26,054)	(3,099)
Cash, cash equivalents, and restricted cash at beginning of year	48,665	51,764
Cash, cash equivalents, and restricted cash at end of year	$ 22,611	$ 48,665
Supplemental disclosures of cash flow information:		
Cash paid for interest	$ 669	$ 1,003
Right-of-use asset and lease liability (new lease)	$ 1,119	$ —

The accompanying notes are an integral part of these consolidated financial statements.

CUE BIOPHARMA, INC.
NOTES TO FINANCIAL STATEMENTS
Years Ended December 31, 2024 and 2023

1. Organization and Basis of Presentation

Cue Biopharma, Inc. (the "Company") is a clinical-stage biopharmaceutical company developing a novel class of therapeutic biologics to selectively modulate disease-specific T cells directly within the patient's body. The Company's vision is to translate nature's signals, or "cues", into protein therapeutics by generating a new class of T cell engagers for selective modulation of disease specific T cells. The Company's corporate office and research facilities are located in Boston, Massachusetts.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities and commitments in the normal course of business. The Company is in the development stage and has incurred recurring losses and negative cash flows from operations since inception. As of December 31, 2024, the Company had cash and cash equivalents of $22.5 million. The future viability of the Company is dependent on its ability to raise additional capital to finance its operations and to fund research and development costs in order to seek approval for commercialization of its drug product candidates. While the Company is exploring raising additional capital through a combination of equity offerings, collaborations, and other strategic alliances, and, depending on the availability and level of additional financings, and cash expenditure reduction, there is no guarantee that the Company will be successful in these mitigation efforts. The Company's failure to raise capital as and when needed would have a negative impact on its financial condition and its ability to pursue its business strategies as this capital is necessary for the Company to perform the research and development activities required to develop and commercialize the Company's drug product candidates in order to generate future revenue streams. Therefore, management has determined that the Company's accumulated deficit, history of losses, negative cash flows from operations and future expected losses raise substantial doubt about the Company's ability to continue as a going concern within one year of the issuance date of these financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements for the years ended December 31, 2024 and 2023, have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (the "SEC") and generally accepted accounting principles in the United States ("U.S. GAAP") for financial information, which prescribes elimination of all significant intercompany accounts and transactions in the accounts of the Company and its wholly owned subsidiary, Cue Biopharma Securities Corp., which was incorporated in the Commonwealth of Massachusetts in December 2018. In the opinion of management, these financial statements reflect all adjustments which are necessary for a fair statement of the Company's financial position and results of its operations, as of and for the periods presented.

Public Offerings and Private Placement

In October 2021, the Company entered into an open market sale agreement (the "ATM Sales Agreement") with Jefferies LLC ("Jefferies"), as agent, to sell shares of the Company's common stock for aggregate gross proceeds of up to $80 million, from time to time, through an at-the-market equity offering program. The ATM Sales Agreement will terminate upon the earliest of (a) the sale of $80 million of shares of the Company's common stock pursuant to the ATM Sales Agreement or (b) the termination of the ATM Sales Agreement by the Company or Jefferies. During the year ended December 31, 2024, the Company sold 1,471,858 shares of common stock under the ATM Sales Agreement for proceeds of $3.4 million, net of commissions paid, but excluding transaction expenses. As of December 31, 2024, the Company had sold an aggregate of 9,072,231 shares of common stock under the ATM Sales Agreement for proceeds of $40.4 million, net of commissions paid, but excluding transaction expenses, since its inception.

On November 14, 2022, the Company entered into securities purchase agreements with accredited investors pursuant to which, on November 16, 2022, the Company issued and sold to such investors in a private placement an aggregate of 7,656,966 shares of common stock and, in lieu of shares of common stock to certain investors, pre-funded warrants (the "2022 Pre-Funded Warrants") to purchase an aggregate of 1,531,440 shares of common stock, and, in each case, accompanying warrants (the "2022 Common Stock Warrants," and together with the 2022 Pre-Funded Warrants, the "2022 Warrants") to purchase an aggregate of up to 9,188,406 additional shares of common stock (or 2022 Pre-Funded Warrants in lieu thereof) at a price of $3.265 per share and accompanying 2022 Common Stock Warrant (or $3.2649 per 2022 Pre-Funded Warrant and accompanying 2022 Common Stock Warrant), (such financing, the "PIPE Financing"). The exercise price of the 2022 Common Stock Warrants is $3.93 per share, or if exercised for a 2022 Pre-Funded Warrant in lieu thereof, $3.9299 per 2022 Pre-Funded Warrant. The exercise price of the 2022 Pre-Funded Warrants is $0.0001 per share. The 2022 Common Stock

Warrants are exercisable at any time after they are issued and ending on the fifth anniversary of the closing. The 2022 Pre-Funded Warrants are exercisable at any time after they are issued and will not expire. The Company received aggregate gross proceeds from the PIPE Financing of $30 million, before deducting placement agent fees and offering expenses of $2.6 million. Piper Sandler & Co. acted as lead placement agent and Public Ventures LLC acted as co-placement agent for the PIPE Financing. At December 31, 2024, the weighted average exercise price of the 2022 Warrants is $3.93 and the weighted average contractual life is 2.87 years.

On September 26, 2024, the Company entered into an underwriting agreement (the "Underwriting Agreement") with Oppenheimer & Co. Inc., as representative of the several underwriters named therein (collectively, the "Underwriters"), relating to an underwritten public offering of (i) 11,564,401 shares (the "Shares") of the Company's common stock, $0.001 par value per share, and accompanying common stock warrants (the "2024 Common Stock Warrants") to purchase 2,891,100 shares of the Company's common stock, and (ii) to certain investors in lieu of common stock, pre-funded warrants (the "2024 Pre-Funded Warrants," and together with the 2024 Common Stock Warrants, the "2024 Warrants") to purchase 12,435,599 shares of the Company's common stock and accompanying 2024 Common Stock Warrants to purchase 3,108,900 shares of the Company's common stock. All of the Shares and the 2024 Warrants were sold by the Company. Each Share was offered and sold together with an accompanying 2024 Common Stock Warrant at a combined offering price of $0.50, and each 2024 Pre-Funded Warrant was offered and sold together with an accompanying 2024 Common Stock Warrant at a combined offering price of $0.499, which is equal to the combined offering price per share of common stock and accompanying 2024 Common Stock Warrant less the $0.001 exercise price of each 2024 Pre-Funded Warrant. The Company received net proceeds from the offering of $10.8 million, after deducting underwriting discounts and commissions and offering expenses of $1.2 million, and excluding any proceeds that may be received from exercise of the 2024 Warrants. At December 31, 2024, the weighted average exercise price of the 2024 Warrants is $0.50 and the weighted average contractual life is 4.75 years.

The 2022 Warrants and 2024 Warrants are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the 2022 Pre-Funded Warrants and 2024 Pre-Funded Warrants do not provide any guarantee of value or return, and do not have an expiration date. The 2022 Warrants and 2024 Warrants met the permanent equity criteria classification, and have been classified as a component of permanent equity in the Company's consolidated financial statements.

Consolidation

The accompanying consolidated financial statements include the Company and its wholly owned subsidiary, Cue Biopharma Securities Corp. The Company has eliminated all intercompany transactions.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Significant estimates include estimates related to collaboration revenue, the accounting for potential liabilities and accrued expenses, the assumptions utilized in valuing stock-based compensation issued for services, the realization of deferred tax assets, and the useful life with respect to long-lived assets and intangibles. Actual results could differ from those estimates.

Cash Concentrations

The Company maintains its cash balances with financial institutions in federally insured accounts and may periodically have cash balances in excess of insurance limits. The Company maintains its accounts with financial institutions with a high credit rating. The Company has not experienced any losses to date from the Company's deposits with these financial institutions and believes that it is not exposed to any significant credit risk on cash.

Cash and Cash Equivalents

The Company considers all highly liquid investments with a maturity of three months or less at the date of purchase to be cash equivalents. The Company invests available cash in money market funds.

Marketable Securities

Marketable securities consist of investments with original maturities greater than ninety days and less than one year from the date of the Company's consolidated balance sheets. The Company classifies all of its investments as available-for-sale securities. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains and losses are recognized and determined on a specific identification basis and are included in comprehensive loss. Realized gains and losses are determined on a specific identification basis and are included in other income on the consolidated statements of operations and comprehensive loss. Amortization and accretion of discounts and premiums is recorded in interest income. The Company did not invest in any marketable securities as of December 31, 2024 and 2023.

Restricted Cash

The Company had $0.2 million in restricted cash deposited with a separate commercial bank to collateralize Company credit cards as of December 31, 2024 and 2023.

Property and Equipment

Property and equipment is recorded at cost. Major improvements are capitalized, while maintenance and repairs are charged to expense as incurred. Gains and losses from dispositions of property and equipment are included in income and expense when realized. Amortization of leasehold improvements is provided using the straight-line method over the shorter of the lease term or the useful life of the underlying assets. Depreciation of property and equipment is provided using the straight-line method over the following estimated useful lives:

Laboratory equipment	5 years
Computer equipment	3 years
Furniture and fixtures	3-8 years

The Company recognizes depreciation and amortization expense in general and administrative expenses and in research and development expenses in the Company's consolidated statements of operations and comprehensive loss, depending on how each category of property and equipment is utilized in the Company's business activities.

Trademark

Trademark consists of the Company's right, title and interest to the CUE BIOLOGICS Mark, and any derivative mark incorporating CUE, throughout the world, together with all associated goodwill and common law rights appurtenant thereto, including, but not limited to, any right, title and interest in any corporate name, company name, business, name, trade name, dba, domain name, or other source identifier incorporating CUE.

The Company has classified the trademark as a component of other long-term assets, having a useful life of 15 years. The Company evaluates the status of this intangible asset for amortization and impairment at each quarter end and year end reporting date. The Company recorded $11,000 of amortization expense related to the trademark for the years ended December 31, 2024 and 2023.

Debt Issuance Costs

Debt issuance costs are deferred and presented as a reduction to long-term debt. Debt issuance costs are amortized using the effective interest rate method over the term of the loan. Amortization of deferred debt issuance costs are included in interest expense in the consolidated statements of operations and comprehensive loss.

Revenue Recognition

The Company recognizes collaboration revenue under certain of the Company's license and collaboration agreements that are within the scope of Accounting Standards Codification ("ASC"), Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). The Company's contracts with customers typically include promises related to licenses to intellectual property and research and development services. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the

combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. Accordingly, the transaction price is generally comprised of a fixed fee due at contract inception and variable consideration in the form of milestone payments due upon the achievement of specified events and tiered royalties earned when customers recognize net sales of licensed products. The Company measures the transaction price based on the amount of consideration to which it expects to be entitled in exchange for transferring the promised goods and/or services to the customer. The Company utilizes the "expected value method" method to estimate the amount of variable consideration, to predict the amount of consideration to which it will be entitled for its one open contract. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. At the inception of each arrangement that includes development and regulatory milestone payments, the Company evaluates whether the associated event is considered probable of achievement and estimates the amount to be included in the transaction price using the expected value method.

Research and Development Expenses

Research and development expenses consist primarily of compensation costs, fees paid to consultants, outside service providers and organizations (including research institutes at universities), facility costs, and development and clinical trial costs with respect to the Company's drug product candidates.

Research and development expenses incurred under contracts are expensed ratably over the life of the underlying contracts, unless the achievement of milestones, the completion of contracted work, or other information indicates that a different pattern of performance is more appropriate. Other research and development expenses are charged to operations as incurred.

Nonrefundable advance payments are recognized as an expense as the related services are performed. The Company evaluates whether it expects the services to be rendered at each quarter end and year end reporting date. If the Company does not expect the services to be rendered, the advance payment is charged to expense. Nonrefundable advance payments for research and development services are included in prepaid and other current assets on the Company's consolidated balance sheets. To the extent that a nonrefundable advance payment is for contracted services to be performed within 12 months from the reporting date, such advance is included in current assets; otherwise, such advance is included in non-current assets.

The Company evaluates the status of its research and development agreements and contracts, and the carrying amount of the related assets and liabilities, at each quarter end and year end reporting date, and adjusts the carrying amounts and their classification on the Company's consolidated balance sheets as appropriate.

Patent Expenses

The Company is the exclusive worldwide licensee of, and has patent applications pending for, numerous domestic and foreign patents. Due to the significant uncertainty associated with the successful development of one or more commercially viable drug product candidates based on the Company's research efforts and any related patent applications, all patent costs, including patent-related legal fees, filing fees and other costs are charged to general and administrative expense as incurred. For the years ended December 31, 2024 and 2023, patent expenses were $2.2 million and $2.5 million, respectively.

Licensing Fees and Costs

Licensing fees and costs consist primarily of costs relating to the acquisition of the Company's license agreement with the Albert Einstein College of Medicine, including related royalties, maintenance fees, milestone payments and product development costs. Licensing fees and costs are charged to research and development expense as incurred.

Long-Lived Assets

The Company reviews long-lived assets, consisting of property and equipment, for impairment when events or changes in circumstances indicate the carrying value of these assets may exceed their current fair values. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized for the amount by which the carrying amount of the asset exceeds the fair value of the assets. Assets to be disposed of are separately presented in the Company's consolidated balance sheets and reported at the lower of the carrying amount or fair value less costs to sell and are no longer depreciated. The Company has not historically recorded any impairment to its long-lived assets. In the future, if events or market conditions affect the estimated fair value to the extent that

a long-lived asset is impaired, the Company will adjust the carrying value of these long-lived assets in the period in which the impairment occurs.

Leases

The Company accounts for leases under ASC 842, Leases, which requires a lessee to record a right-of-use asset and a corresponding lease liability for most lease arrangements on the Company's consolidated balance sheets. Under the standard, disclosure of key information about leasing arrangements to assist users of the financial statements with assessing the amount, timing and uncertainty of cash flows arising from leases are required.

Stock-Based Compensation

The Company periodically issues stock-based awards to officers, directors, employees, Scientific and Clinical Advisory Board members and consultants for services rendered. Such issuances vest and expire according to terms established at the issuance date.

Stock-based payments to officers, directors, employees, Scientific and Clinical Advisory Board members and consultants, including grants of employee stock options, are recognized in the financial statements based on their grant date fair values. Stock option grants, which are generally time-vested, are measured at the grant date fair value and charged to operations on a straight-line basis over the service period, which generally approximates the vesting term. The Company also grants performance-based awards periodically to officers of the Company. The Company recognizes compensation costs related to performance awards over the requisite service period if and when the Company concludes that it is probable that the performance condition will be achieved.

The fair value of stock options and restricted stock units is determined utilizing the Black-Scholes valuation model. This valuation model takes into account the exercise price of the award, as well as a variety of significant assumptions. The assumptions used to estimate the fair value of stock options include the expected term, the expected volatility of the Company's stock over the expected term, the risk-free interest rate over the expected term, and the Company's expected annual dividend yield. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant. The expected dividend yield is based on the current yield at the grant date; the Company has never declared or paid dividends and has no plans to do so for the foreseeable future. As permitted by Staff Accounting Bulletin No. 107, due to the Company's limited trading history and option activity, management utilizes the simplified method to estimate the expected term of options at the date of grant. The exercise price is determined based on the fair value of the Company's common stock at the date of grant. The Company accounts for forfeitures as they occur.

The Company recognizes the fair value of stock-based compensation in general and administrative expenses and in research and development expenses in the Company's consolidated statements of operations and comprehensive loss, depending on the type of services provided by the recipient of the equity award.

Income Taxes

The Company accounts for income taxes under an asset and liability approach for financial accounting and reporting for income taxes. Accordingly, the Company recognizes deferred tax assets and liabilities for the expected impact of differences between the financial statements and the tax basis of assets and liabilities.

The Company accounts for uncertainties in income tax law under a comprehensive model for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns as prescribed by U.S. GAAP. The tax effects of a position are recognized only if it is "more-likely-than-not" to be sustained by the taxing authority as of the reporting date. If the tax position is not considered "more-likely-than-not" to be sustained, then no benefits of the position are recognized.

The Company records a valuation allowance to reduce its deferred tax assets to the amount that is more likely than not to be realized. In the event the Company was to determine that it would be able to realize its deferred tax assets in the future in excess of its recorded amount, an adjustment to the deferred tax assets would be credited to operations in the period such determination was made. Likewise, should the Company determine that it would not be able to realize all or part of its deferred tax assets in the future, an adjustment to the deferred tax assets would be charged to operations in the period such determination was made.

The Company is subject to U.S. federal and Massachusetts state income taxes. As the Company's net operating losses have yet to be utilized, all previous tax years remain open to examination by federal and state taxing authorities in which the Company currently operates.

For the years ended December 31, 2024 and 2023, there is no provision for income taxes in the U.S. because the Company has historically incurred net operating losses and maintains a full valuation allowance against its net deferred assets. The reported amount of income tax expense for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of changes in valuation allowance.

The Company recognizes interest accrued relative to unrecognized tax benefits in interest expense and penalties in operating expense. During the years ended December 31, 2024 and 2023, the Company did not recognize any income tax related interest and penalties. The Company did not have any accruals for income tax related interest and penalties at December 31, 2024 and 2023.

Comprehensive Income (Loss)

Components of comprehensive income or loss, including net income or loss, are reported in the financial statements in the period in which they are recognized. Other comprehensive income or loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Net income (loss) and other comprehensive income (loss) are reported net of any related tax effect to arrive at comprehensive income (loss). Comprehensive income (loss) includes net income (loss) as well as changes in stockholders' equity that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive income (loss) in periods presented was unrealized gain or loss on available-for-sale securities.

Earnings (Loss) Per Share

The Company's computation of earnings (loss) per share ("EPS") for the respective periods includes basic and diluted EPS. Basic EPS is measured as the income (loss) attributable to common stockholders divided by the weighted average number of common shares outstanding for the period. Diluted EPS is similar to basic EPS but presents the dilutive effect on a per share basis of potential common shares that would result from the exercise of outstanding stock options and warrants as if they had been exercised at the beginning of the periods presented, or issuance date, if later. Potential common shares that have an anti-dilutive effect (i.e., those that increase income per share or decrease loss per share) are excluded from the calculation of diluted EPS. Basic and diluted loss per common share is the same for all periods presented because all outstanding stock options and warrants are anti-dilutive.

Per ASC 260-10-45-13, shares issuable for little to no consideration should be included in the number of outstanding shares used for basic EPS. The Financial Accounting Standards Board ("FASB") proposed that warrants or options exercisable for little to no cost (sometimes referred to as "penny warrants") be included in the denominator of basic EPS (and therefore diluted EPS) once there were no further vesting conditions or contingencies associated with them. The Company included 12,435,599 and 1,531,440 pre-funded warrants in the denominator of basic EPS at December 31, 2024 and 2023, respectively.

At December 31, 2024 and 2023, the Company excluded the securities summarized below, which entitled the holders thereof to acquire shares of common stock, from its calculation of EPS, as their effect would have been anti-dilutive.

	December 31,	
	2024	**2023**
Common stock warrants	15,151,906	9,188,406
Common stock options	10,836,838	10,800,379
Total	25,988,744	19,988,785

Fair Value of Financial Instruments

The authoritative guidance with respect to fair value established a fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value into three levels and requires that assets and liabilities carried at fair value be classified and disclosed in one of three categories, as presented below.

Level 1. Observable inputs such as quoted prices in active markets for an identical asset or liability that the Company has the ability to access as of the measurement date. Financial assets and liabilities utilizing Level 1 inputs include active exchange-traded securities and exchange-based derivatives.

Level 2. Inputs, other than quoted prices included within Level 1, which are directly observable for the asset or liability or indirectly observable through corroboration with observable market data. Financial assets and liabilities utilizing Level 2 inputs include fixed income securities, non-exchange-based derivatives, mutual funds, and fair-value hedges.

Level 3. Unobservable inputs in which there is little or no market data for the asset or liability which requires the reporting entity to develop its own assumptions. Financial assets and liabilities utilizing Level 3 inputs include infrequently traded non-exchange-based derivatives and commingled investment funds and are measured using present value pricing models.

The Company determines the level in the fair value hierarchy within which each fair value measurement falls in its entirety, based on the lowest level input that is significant to the fair value measurement in its entirety. In determining the appropriate levels, the Company performs an analysis of the assets and liabilities at each reporting period end.

The Company had $21.8 million in cash equivalents that were measured and recorded at fair value on the Company's consolidated balance sheets at December 31, 2024. The Company had $39.1 million in cash equivalents that were measured and recorded at fair value on the Company's consolidated balance sheets at December 31, 2023.

The carrying value of financial instruments (consisting of cash, a certificate of deposit, debt, accounts payable, accrued compensation and accrued expenses) is considered to be representative of their respective fair values due to the short-term nature of those instruments.

Recent Accounting Pronouncements

ASU 2023-07 - Segment Reporting

In November 2023, the FASB issued ASU 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures ("ASU 2023-07"). ASU 2023-07 requires disclosure of incremental segment information on an annual and interim basis. The amendments also require companies with a single reportable segment to provide all disclosures required by this amendment and all existing segment disclosures in ASC 280, Segment Reporting. The amendments are effective for fiscal years beginning after December 15, 2023, and interim periods beginning after December 15, 2024. The Company adopted ASU 2023-07 effective December 31, 2024.

Operating segments are defined as components of an entity for which separate financial information is available and that is regularly reviewed by the Chief Operating Decision Maker (the "CODM") in deciding how to allocate resources to an individual segment and in assessing performance. The Company's CODM is the chief executive officer.

The Company is in the development stage, has not yet earned revenue from product sales, and has incurred recurring losses and negative cash flows from operations since inception. The Company operates as a single reporting segment, focused on developing a novel class of therapeutic biologics to selectively modulate disease-specific T cells directly within the patient's body. The CODM manages and allocates resources to the operations of the Company on a total company basis and therefore does not measure separate segment profit or loss. Managing and allocating resources on a total company basis enables the CODM to assess the overall level of resources available and how to best deploy these resources across functions and research and development programs that are in line with the Company's long-term strategic corporate goals. Consistent with this decision-making process, the CODM uses consolidated financial information for purposes of evaluating performance, forecasting future period financial results, allocating resources and setting incentive targets. Operating expenses are used to monitor budget versus actual results. All the Company's long-lived assets are held in the United States and all the Company's revenues since inception have been earned from collaboration agreements as none of the company's drug product candidates have yet been approved for commercial sale. The resources utilized for any specific purpose may vary significantly and will depend on a number of factors, including, but not limited to, the Company's research and development activities and programs, clinical testing, regulatory approval, market conditions, and changes in or revisions to the Company's business strategy and technology development plans.

ASU 2023-09 - Income Taxes

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes* (Topic 740): *Improvements to Income Tax Disclosures* ("ASU 2023-09"). The guidance in ASU 2023-09 improves the transparency of income tax disclosures by greater disaggregation of information in the rate reconciliation and income taxes paid disaggregated by jurisdiction. The standard is effective for public companies for fiscal years beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the impact that the adoption of ASU 2023-09 may have on its consolidated financial statements.

Management does not believe that any other recently issued, but not yet effective, authoritative guidance, if currently adopted, would have a material impact on the Company's financial statement presentation or disclosures.

3. Fair Value

The Company accounts for its financial assets and liabilities using fair value measurements. The authoritative accounting guidance defines fair value, establishes a framework for measuring fair value under U.S. GAAP and enhances disclosures about fair value measurements. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

The following table presents information about the Company's assets that are measured at fair value on a recurring basis as of December 31, 2024 and 2023 and indicate the level of the fair value hierarchy utilized to determine such fair value:

	Fair Value Measurements as of December 31, 2024			
(In thousands)	**Level 1**	**Level 2**	**Level 3**	**Fair Value**
Cash equivalents	$ 21,813	$ —	$ —	$ 21,813
Marketable securities	—	—	—	—
Total	$ 21,813	$ —	$ —	$ 21,813

	Fair Value Measurements as of December 31, 2023			
(In thousands)	**Level 1**	**Level 2**	**Level 3**	**Fair Value**
Cash equivalents	$ 39,148	$ —	$ —	$ 39,148
Marketable securities	—	—	—	—
Total	$ 39,148	$ —	$ —	$ 39,148

As of December 31, 2024 and 2023, the Company invested $21.8 million and $39.1 million, respectively in money market funds, which were classified as cash equivalents on the Company's consolidated balance sheets. The Company measured its cash equivalents using Level 1 inputs for identical securities. During the years ended December 31, 2024 and 2023, there were no transfers between Level 2 and Level 3.

4. Property and Equipment, Net

Property and equipment, net as of December 31, 2024 and 2023 consisted of the following:

	December 31,	
	2024	**2023**
	(in thousands)	
Laboratory equipment	$ 3,785	$ 4,069
Furniture and fixtures	68	81
Computer equipment	180	143
Leasehold improvements	118	118
Total property and equipment	4,151	4,411
Less accumulated depreciation	(3,680)	(3,616)
Property and equipment, net	$ 471	$ 795

Depreciation expense for the years ended December 31, 2024 and 2023 was included in the consolidated statements of operations and comprehensive loss as follows:

	Years Ended December 31,	
	2024	2023
	(in thousands)	
General and administrative	$ 17	$ 19
Research and development	368	526
Depreciation total	$ 385	$ 545

The depreciation reported above excludes $11,000 of trademark amortization recorded in the year ended December 31, 2024, and $11,000 of trademark amortization and $80,000 of capitalized license amortization recorded during the year ended December 31, 2023.

During the year ended December 31, 2024, the Company disposed of lab equipment and furniture and fixtures of $0.3 million and recorded a gain of $0.1 million for cash collected for the sale of lab equipment, which is included in the consolidated statements of operations and comprehensive loss.

During the year ended December 31, 2023, the Company sold fully depreciated lab equipment with an acquisition cost of $41,000 and collected cash of $2,000, and disposed of gross assets of $1.3 million. The Company recorded a loss on the sale of fixed assets of $0.2 million, which is presented in operating expenses on the consolidated statements of operations and comprehensive loss.

5. Loan with First Citizens Bank (formerly with Silicon Valley Bank)

On February 15, 2022 (the “Closing Date”), the Company entered into a Loan and Security Agreement (the “Loan Agreement”), with Silicon Valley Bank, as lender (“SVB”). The Company drew $10,000,000 in term loans under the Loan Agreement (the "Term Loans") on the Closing Date. The Loan Agreement was amended in April 2023 and October 2024.

The Term Loans bear interest at a floating rate per annum equal to the greater of (A) the prime rate (as published in the money rates section of The Wall Street Journal) plus 2.25% and (B) 5.50%. The Term Loans were interest only from the Closing Date through June 30, 2023, after which the Company is required to pay 30 equal monthly installments of principal. At December 31, 2024, the interest rate was 10.00% which is based on the prime rate plus 2.25%.

The Term Loans may be prepaid in full with payment of a 1.00% prepayment premium. Upon prepayment or repayment in full of the Term Loans, the Company will be required to pay a one-time final payment fee equal to 5.00% of the original principal amount of any funded Term Loans being repaid. This one-time final payment fee is recorded to interest expense using the effective interest method over the period of the Term Loans in the consolidated statements of operations and comprehensive loss.

The Term Loans and related obligations under the Loan Agreement are secured by substantially all of the Company’s properties, rights and assets, except for its intellectual property which is subject to a negative pledge under the Loan Agreement.

The Loan Agreement, as amended, contains customary representations, warranties, events of default and covenants. In addition to the foregoing, the Company is required to have at all times on deposit in accounts of the Company maintained with SVB, unrestricted and unencumbered cash in an amount equal to the lesser of (i) 100% of the dollar value of the Company’s consolidated cash, in the aggregate, at all financial institutions and (ii) $20,000,000. On March 10, 2023, SVB was closed and the Federal Deposit Insurance Corporation (the “FDIC”) was appointed receiver for the bank. The FDIC created a successor bridge bank, and all deposits and loans of SVB were transferred to the bridge bank under a systemic risk exception approved by the United States Department of the Treasury, the Federal Reserve and the FDIC. On March 27, 2023, First Citizens Bank & Trust Company (“First Citizens Bank”), assumed all of SVB’s deposits and certain other liabilities and acquired substantially all of SVB’s loans and certain other assets from the FDIC. First Citizens Bank continues to hold the Company’s Term Loans under the same existing terms and covenants which were in place with SVB.

During the years ended December 31, 2024 and 2023, the Company recognized interest expense related to the Term Loans of $0.6 million and $1.0 million, respectively. For both the years ended December 31, 2024 and 2023, the Company

recognized interest expense related to accretion of the final repayment of $0.1 million. As of December 31, 2024 the Company has recorded a short term liability for the net remaining balance due on the loans of $4.0 million. The loans are due to be paid in full by December 1, 2025.

Debt Issuance Costs

The Company incurred a total of $142,000 in debt issuance costs upon entering into the Loan Agreement. Debt issuance costs are deferred, presented as a reduction of debt, and are amortized using the effective interest rate method over the term of the loan. For both the years ended December 31, 2024 and 2023, the Company recorded approximately $37,000 in amortization of debt issuance costs to interest expense in the consolidated statements of operations and comprehensive loss. At December 31, 2024, the Company recorded the $37,000 of debt issuance costs to short term contra-liabilities.

As of December 31, 2024 the Company recorded a $4.3 million short term liability consisting of the net remaining balance due on the loans of $4.0 million, plus $370,000 of accretion of the final payment, less $37,000 of unamortized issuance costs. The loans are due to be paid in full by December 1, 2025.

6. Accrued Expenses

Accrued expenses as of December 31, 2024 and 2023 are summarized as follows:

	December 31,	
(In thousands)	**2024**	**2023**
Employee and board compensation	$ 1,812	$ 2,219
Contract research services	773	1,411
Professional services	314	344
Contract manufacturing services	9	163
Total	$ 2,908	$ 4,137

7. Einstein License Agreement

On January 14, 2015, the Company entered into a license agreement, as amended and restated on July 31, 2017 and as further amended on October 30, 2018 and January 13, 2024 (the "Einstein License"), with Albert Einstein College of Medicine ("Einstein") for certain patent rights relating to the Company's core technology platform for the engineering of biologics to control T cell activity, precision, immune-modulatory drug product candidates, and two supporting technologies that enable the discovery of costimulatory signaling molecules (ligands) and T cell targeting peptides.

Under the Einstein License, the Company holds an exclusive worldwide license, with the right to sublicense, import, make, have made, use, provide, offer to sell, and sell all products, processes and services that use the patents covered by the Einstein License, including certain technology received from Einstein relating thereto (the "Licensed Products"). Under the Einstein License, the Company is required to:

- Pay royalties and amounts based on a certain percentage of proceeds, as defined in the Einstein License, from sales of Licensed Products and sublicense agreements.
- Pay escalating annual maintenance fees, which are nonrefundable, but are creditable against the amount due to Einstein for royalties.
- Make significant payments based upon the achievement of certain milestones, as defined in the Einstein License. Payments made upon achievement of milestones are nonrefundable and are not creditable against any other payment due to Einstein. At December 31, 2024, the Company has made aggregate payments totaling $1.2 million since inception with respect to achievement of these milestones.
- Incur minimum product development costs until the first commercial sale of the first licensed product.

The Company was in compliance with its obligations under the Einstein License at December 31, 2024 and 2023.

The Einstein License expires upon the expiration of the Company's last obligation to make royalty payments to Einstein which may be due with respect to certain Licensed Products, unless terminated earlier under the provisions thereof. The Einstein License includes certain termination provisions if the Company fails to meet its obligations thereunder.

Pursuant to the Einstein License, the Company issued to Einstein 671,572 shares of the Company's common stock in connection with the consummation of the initial public offering of its common stock on December 27, 2017.

The Company accounts for license fees incurred in connection with the Einstein License in accordance with ASC 730, Research and Development. Please refer to Note 10 Collaboration Revenue.

8. Stock-Based Compensation

Effective March 23, 2016, the Company adopted the 2016 Omnibus Incentive Plan (the "Omnibus Plan") and the 2016 Non-Employee Equity Incentive Plan (the "Non-Employee Plan"), which are intended to allow the Company to compensate and retain the services of key employees, non-employees, Scientific and Clinical Advisory Board members, and outside advisors and consultants. The plans are under the administration of the Company's Board of Directors. Under the plans, the Company, at its discretion, may grant stock option awards to certain employees and non-employees through March 23, 2026. The Omnibus Plan and the Non-Employee Plan initially provided for the grant of a total of 2,000,000 shares of common stock and 500,000 shares of common stock, respectively.

On August 13, 2017, the Company's Board of Directors approved an amendment and restatement of the Company's Omnibus Plan to increase the number of shares authorized for issuance under such plan by 800,000 shares, from 2,000,000 shares to 2,800,000 shares, subject to stockholder approval of such amendment within 12 months following board approval thereof. The Company's stockholders approved the plan in December 2017. Additionally, on May 17, 2019, the Company's Board of Directors approved Amendment No. 1 to the Omnibus Plan to increase the number of shares that may be issued as incentive stock options under the plan, which the Company's stockholders approved on August 6, 2019. The Omnibus Plan, as amended and restated, provides that on the first day of each fiscal year of the Company during the period beginning in fiscal year ended December 31, 2018 and ending on the second day of fiscal year ending December 31, 2027, the number of shares of common stock authorized to be issued under such plan shall be increased by an amount equal to the lesser of (i) the number of shares necessary such that the aggregate number of shares available to be issued under the plan equals 20% of the number of fully diluted outstanding shares on such date (assuming the conversion of all outstanding shares of preferred stock and other outstanding convertible securities and exercise of all outstanding options and warrants to purchase shares) and (ii) an amount to be determined by the Company's Board of Directors.

Pursuant to the plans, during the year ended December 31, 2024, the Company granted stock options to purchase 4,383,300 shares of the Company's common stock, no options to purchase shares of common stock were exercised, and 1,404,493 shares of common stock were cancelled. At December 31, 2024, stock options for 15,307,821 shares of common stock and 320,000 restricted stock units had been granted and 365,114 shares of common stock were reserved for future grants under the Omnibus Plan, and stock options for 494,600 shares of common stock had been granted and no shares of common stock were reserved for future grants under the Non-Employee Plan. In the aggregate, at December 31, 2024, stock options for a total of 15,802,421 shares of common stock and 320,000 restricted stock units had been granted and 365,114 shares of common stock were reserved for future grants. Such grants are accounted for as stock-based compensation in accordance with ASC 718, *Compensation - Stock Compensation*, and ASC 505-50, *Equity-Based Payments to Non-Employees*.

Stock Option Valuation

For stock options requiring an assessment of value during the years ended December 31, 2024 and 2023, the fair value of each stock option award was estimated using the Black-Scholes option-pricing model utilizing the following assumptions:

	December 31,	
	2024	**2023**
Risk-free interest rate	3.95 to 4.43%	3.40 to 4.21%
Expected dividend yield	0%	0%
Expected volatility	75.73-86.52%	97.0-114.21%
Expected life	5.5 to 6.25 years	5.5 to 6.25 years

The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant for periods corresponding with the expected term of the stock option award; as permitted by Staff Accounting Bulletin 107, due to insufficient history of stock option activity, management has utilized the simplified approach to estimate the expected term of the stock options, which represents the period of time that stock options granted are expected to be outstanding; the expected volatility is based upon historical volatility of the Company's stock; and the expected dividend yield based upon the Company's current dividend rate and future expectations.

A summary of stock option activity for the years ended December 31, 2024 and 2023 is as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in Years)
Stock options outstanding at December 31, 2022	6,173,867	$ 9.60	5.05
Granted	2,591,900	3.64	
Exercised	(165,602)	2.86	
Cancelled	(1,107,248)	4.76	
Stock options outstanding at December 31, 2023	7,492,917	8.41	6.12
Granted	4,383,300	1.41	
Exercised	—	—	
Cancelled	(1,404,493)	7.39	
Stock options outstanding at December 31, 2024	10,471,724	5.61	7.27
Stock options exercisable at December 31, 2024	5,147,383	$ 9.12	5.46

The Company recognized $6.8 million and $8.2 million, in stock-based compensation expense during the years ended December 31, 2024 and 2023, respectively. At December 31, 2024, total unrecognized stock-based compensation was $6.0 million, which is expected to be recognized as an operating expense in the Company's consolidated statements of operations and comprehensive loss through June 2028. The weighted average remaining recognition period of unrecognized stock-based compensation was 1.79 years at December 31, 2024.

The aggregate intrinsic value of exercisable but unexercised in-the-money stock options at December 31, 2024 was zero based on a weighted average exercise price of $9.12 per share. The aggregate intrinsic value of options is calculated as the difference of the market close price of $1.09 on December 31, 2024, and the weighted average exercise price of $9.12, with a weighted average remaining contractual term of 5.46.

The aggregate intrinsic value of exercisable but unexercised in-the-money stock options of 4,597,265 at December 31, 2023 was $594 based on a weighted average exercise price of $10.18 per share. The aggregate intrinsic value of options is calculated as the difference of the market close price of $2.64 on December 31, 2023, and the weighted average exercise price of $10.18, with a weighted average remaining contractual term of 4.50 years.

Stock-based Compensation

Stock-based compensation for the years ended December 31, 2024 and 2023 was included in the consolidated statements of operations and comprehensive loss as follows:

	December 31,	
(In thousands)	2024	2023
General and administrative	$ 3,464	$ 3,687
Research and development	3,382	4,493
Total	$ 6,846	$ 8,180

9. Warrants

On September 26, 2024, the Company entered into the Underwriting Agreement with Oppenheimer & Co. Inc., as representative of the Underwriters, relating to an underwritten public offering of (i) 11,564,401 shares of the Company's

common stock, $0.001 par value per share, and accompanying common stock warrants to purchase 2,891,100 shares of common stock, and (ii) to certain investors in lieu of common stock, pre-funded warrants to purchase 12,435,599 shares of common stock and accompanying common stock warrants to purchase 3,108,900 shares of common stock. All of the Shares and the 2024 Warrants were sold by the Company. Each Share was offered and sold together with an accompanying 2024 Common Stock Warrant at a combined offering price of $0.50, and each 2024 Pre-Funded Warrant was offered and sold together with an accompanying 2024 Common Stock Warrant at a combined offering price of $0.499, which is equal to the combined offering price per share of common stock and accompanying 2024 Common Stock Warrant less the $0.001 exercise price of each 2024 Pre-Funded Warrant. The Company received net proceeds from the offering of $10.8 million, after deducting underwriting discounts and commissions and offering expenses of $1.2 million, and excluding any proceeds that may be received from exercise of the 2024 Warrants. At December 31, 2024 5,963,500 of the 2024 Common Stock Warrants and 12,435,599 of the 2024 Pre-Funded Warrants remain outstanding.

On November 16, 2022 the Company issued 9,188,406 warrants with an exercise price of $3.93 and a 5-year term and 1,531,440 pre-funded warrants at a nominal exercise price of $0.0001 per share. The Company recorded cash received from 7,656,966 shares of common stock, 9,188,406 2022 Common Stock Warrants and 1,531,440 2022 Pre-Funded Warrants to additional paid in capital in the amount of $27.4 million, net of placement fees of $2.6 million during the year ended December 31, 2022. At December 31, 2024, 9,188,406 of the 2022 Common Stock Warrants and zero of the 2022 Pre-Funded Warrants remained outstanding. At December 31, 2023 9,188,406 of the 2022 Common Stock Warrants and 1,531,440 of the 2022 Pre-Funded Warrants remained outstanding.

Each tranche of warrants was evaluated under ASC 480, Distinguishing Liabilities from Equity, and ASC 815, *Derivatives and Hedging*, and the Company determined that equity classification was appropriate. The Company determined equity classification for both warrants and pre-funded warrants as they do not embody an obligation for the Company to repurchase its shares and permit the holders to receive a fixed number of shares of common stock upon exercise. Per ASC 815-40-25, the Company accounts for the warrants and pre-funded warrants as equity, as the Company does not provide the holder a fixed or guaranteed return.

10. Collaboration Revenue

The Company recognizes collaboration revenue under certain of the Company's license or collaboration agreements that are within the scope of ASC 606. The Company's contracts with customers typically include promises related to licenses to intellectual property and research and development services. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and if, over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company's contracts may include options to acquire additional goods and/or services.

The terms of the Company's arrangements with customers typically include the payment of one or more of the following: (i) non-refundable, up-front payment, and pass through costs related to research activities, (ii) development, regulatory and commercial milestone payments, (iii) future options and (iv) royalties on net sales of licensed products. Accordingly, the transaction price is generally comprised of a fixed fee due at contract inception and variable consideration in the form of pass through costs and milestone payments due upon the achievement of specified events and tiered royalties earned when customers recognize net sales of licensed products. The Company measures the transaction price based on the amount of consideration to which it expects to be entitled in exchange for transferring the promised goods and/or services to the customer. The Company utilizes the "expected value method" method to estimate the amount of variable consideration, to predict the amount of consideration to which it will be entitled for its one open contract. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. Milestone payments that are not within the control of the Company or the licensee, such as those dependent upon receipt of regulatory approval, are not considered to be probable of achievement until the triggering event occurs. At the end of each reporting period, the Company reevaluates the probability of achievement of each milestone and any related constraint, and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment.

For arrangements that include sales-based royalties, including milestone payments based upon the achievement of a certain level of product sales, the Company recognizes revenue upon the later of: (i) when the related sales occur or (ii) when the performance obligation to which some or all of the payment has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any development, regulatory or commercial milestones or royalty revenue resulting from

any of its collaboration arrangements. Consideration that would be received for optional goods and/or services is excluded from the transaction price at contract inception.

The Company allocates the transaction price to each performance obligation identified in the contract on a relative standalone selling price basis, when applicable. However, certain components of variable consideration are allocated specifically to one or more particular performance obligations in a contract to the extent both of the following criteria are met: (i) the terms of the payment relate specifically to the efforts to satisfy the performance obligation or transfer the distinct good or service and (ii) allocating the variable amount of consideration entirely to the performance obligation or the distinct good or service is consistent with the allocation objective of the standard whereby the amount allocated depicts the amount of consideration to which the entity expects to be entitled in exchange for transferring the promised goods or services. The Company develops assumptions that require judgment to determine the standalone selling price for each performance obligation identified in each contract. The key assumptions utilized in determining the standalone selling price for each performance obligation may include forecasted revenues, development timelines, estimated research and development costs, discount rates, likelihood of exercise and probabilities of technical and regulatory success.

Revenue is recognized based on the amount of the transaction price that is allocated to each respective performance obligation when or as the performance obligation is satisfied by transferring a promised good and/or service to the customer. For performance obligations that are satisfied over time, the Company recognizes revenue by measuring the progress toward complete satisfaction of the performance obligation using a single method of measuring progress which depicts the performance in transferring control of the associated goods and/or services to the customer. The Company uses input methods to measure progress toward the complete satisfaction of performance obligations satisfied over time. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment. The Company measures progress toward satisfaction of the performance obligation over time as effort is expended.

Collaboration Agreement with LG Chem

On November 6, 2018, the Company entered into a collaboration agreement (the “LG Chem Collaboration Agreement”) with LG Chem Ltd. (“LG Chem”) related to the development of the Company’s CUE-101 and CUE-102 Immuno-STATs focused in the field of oncology. Pursuant to the LG Chem Collaboration Agreement, the Company granted LG Chem an exclusive license to develop, manufacture and commercialize CUE-101, as well as Immuno-STATs that target T cells against two additional cancer antigens, in Australia and certain Asian countries (collectively, the “LG Chem Territory”). On April 30, 2021, LG Chem’s option pursuant to the Global License and Collaboration Agreement entered into between the Company and LG Chem on December 18, 2019 and as amended on November 5, 2020 (the "Global License and Collaboration Agreement"), expired, and accordingly the Company no longer has any material obligations under the Global License and Collaboration Agreement. In June 2021, after ongoing discussions regarding the selection of the second of the two additional cancer antigens, LG Chem and the Company agreed to let the selection period expire without a second antigen being selected. The Company retains rights to develop and commercialize all assets included in the LG Chem Collaboration Agreement in the United States and in global markets outside of the LG Chem Territory. In exchange for the licenses and other rights granted to LG Chem under the LG Chem Collaboration Agreement, LG Chem made a $5.0 million equity investment in common stock of the Company and a $5.0 million nonrefundable up-front cash payment. The Company is also eligible to receive up to an additional $400.0 million in research, development, regulatory and sales milestones. In addition, the LG Chem Collaboration Agreement also provides that LG Chem will pay the Company tiered single-digit percentage royalties on net sales of commercialized drug product candidates in the LG Chem Territory.

On May 16, 2019, LG Chem paid the Company a $2.5 million milestone payment for the U.S. Food and Drug Administration’s (“FDA”) acceptance of the investigational new drug application (“IND”) for the Company’s lead drug product candidate, CUE-101, pursuant to the LG Chem Collaboration Agreement. The $2.5 million milestone payment was recorded as a contract liability upon receipt of payment as it requires deferral of revenue recognition to a future period until the Company performs its obligations under the arrangement. Of the $2.5 million milestone payment, $0.4 million was recognized as tax withholding, shown as income tax expense on the consolidated statements of operations and comprehensive loss.

On December 7, 2020, the Company earned a $1.3 million milestone payment on the selection of a preclinical candidate pursuant to the LG Chem Collaboration Agreement. The $1.3 million milestone payment was recorded as a contract liability upon receipt. Revenue related to this milestone payment was recognized by the Company pursuant to the Company’s revenue recognition policy in relation to the performance of its obligations related to the development of this preclinical candidate. Of the $1.25 million milestone payment, $0.2 million was withheld as payment of foreign tax withholding and shown as income tax expense on the consolidated statements of operations and comprehensive loss.

On November 23, 2021, the Company earned a $3.0 million milestone payment for the selection of a clinical product candidate in partnership with LG Chem. The $3.0 million milestone payment was recorded as a contract liability upon receipt. Revenue related to this milestone payment was recognized by the Company pursuant to the Company's revenue recognition policy in relation to the performance of its obligations related to the development of this preclinical candidate. Of the $3.0 million milestone payment, $0.5 million was withheld as payment of foreign tax withholding and shown as income tax expense on the consolidated statements of operations and comprehensive loss. Cash was collected in relation to this milestone payment in February 2022.

On March 11, 2025 the Company and LG Chem entered into the Ninth Amendment to the LG Chem Collaboration Agreement. As of the date of the amendment, the Company regained its rights to the CUE-101 program which had been licensed to LG Chem, and LG Chem terminated all of its rights to the same program. Pursuant to the Ninth Amendment, the Company agreed to make future payments to LG Chem, if and when, one or more potential scenarios related to the CUE-101 program occur up to a predetermined aggregate amount. LG Chem continues to maintain its interest and rights in the CUE-102 program, targeting WT1 expressing cancers, pursuant to the LG Chem Collaboration Agreement.

Aside from the $6.8 million in milestone payments earned to date, the Company does not believe that any variable consideration should be included in the transaction price as of December 31, 2024. Such assessment considered the application of the constraint to ensure that estimates of variable consideration would be included in the transaction price only to the extent the Company had a high degree of confidence that revenue would not be reversed in a subsequent reporting period. The Company will re-evaluate the transaction price, including the estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as other changes in circumstances occur. For the years ended December 31, 2024 and 2023, the Company recognized revenue of less than $0.1 million and $0.3 million, respectively, related to the LG Chem Collaboration Agreement. The Company did not record short or long-term research and development liabilities on its consolidated balance sheets dated December 31, 2024 and December 31, 2023, as the performance obligation was met and completed. Research and development cost sharing provisions under the agreement expired on March 31, 2022, and thereafter, the Company recognized revenue on intellectual patent filing passthrough costs in the LG Chem Territory.

Collaboration and Option Agreement with Ono

On February 22, 2023, the Company entered into a strategic collaboration agreement (the "Ono Collaboration and Option Agreement") with Ono Pharmaceutical Co., Ltd. ("Ono") to further develop CUE-401 and provide dedicated resources and capabilities to help advance CUE-401 toward the clinic. Under the terms of the Ono Collaboration and Option Agreement, Ono paid the Company an upfront payment and agreed to fully fund all research activities related to CUE-401 through a specified option period. During this option period, the Company was responsible for the research and development of CUE-401. Upon Ono's exercise of its option to license CUE-401, the Company would have received an option exercise payment and been eligible for development and commercial milestone payments up to an aggregate of $220.0 million, as well as tiered royalties on sales. Upon any such exercise, Ono would have received worldwide rights to develop and commercialize CUE-401, with the Company retaining a 50% co-development and co-commercialization right in the United States. The Company's decision to elect the co-development and co-commercialization option could have be made within 30 days of Ono's option exercise to license CUE-401.

Under the terms of the Ono Collaboration and Option Agreement, the Company will perform research activities related to CUE-401 through a specified option period of 24 months (the "Research Term"). During this Research Term, the Company will be responsible for the execution of scientific investigation, nonclinical, preclinical, and clinical drug research and development activities designed to progress CUE-401 toward a potential IND and regulatory approval (such activities, collectively referred to as "R&D"). Ono was responsible for the funding of R&D activities performed by the Company. Per the agreement, as consideration for the R&D activities performed by the Company, Ono (i) made a one-time, non-refundable, non-creditable upfront payment of $3.0 million to the Company in March 2023 and (ii) agreed to reimburse the Company for all costs incurred in conducting research, including (a) pass through costs from third party contractors and (b) full time employee salaries capped at $2.1 million in the first 18 months of the Research Term. Subsequently, the Company and Ono agreed to increase this cap for full time employee salaries to $3.1 million.

On March 11, 2025, the Company received written notice from Ono that they have terminated the Collaboration and Option Agreement (the "Agreement), dated February 22, 2023, by and between Ono and the Company. Ono and the Company have acknowledged and agreed that the Agreement terminated in its entirety effective as of March 6, 2025 (the "Termination Date"). At such time, the Agreement had no further force or effect with the exception of certain customary provisions which are intended to survive termination and expiration of the Agreement. The Company retained all rights to CUE-401.

As of the date of this Annual Report on Form 10-K, both Ono and the Company have satisfied all of their performance obligations and made all outstanding payments required under the agreement. Aside from the $3.0 million upfront payment and funding related to pass through costs, the Company did not include any variable consideration in the transaction price as of December 31, 2024. For the years ended December 31, 2024 and 2023, the Company recognized revenue of $9.2 million and $5.2 million, respectively, related to the Ono Collaboration and Option Agreement.

For the years ended December 31, 2024 and 2023, the Company recorded short-term research and development liabilities on its consolidated balance sheets of $0.1 million and $2.1 million, respectively.

11. Stockholders' Equity

Preferred Stock

The Company has authorized a total of 10,000,000 shares of preferred stock, par value $0.001 per share, none of which were outstanding at December 31, 2024 and 2023. The Company's Board of Directors has the authority to issue preferred stock and to determine the rights, preferences, privileges, and restrictions, including voting rights.

Common Stock

The Company has authorized a total of 200,000,000 shares of common stock, par value $0.001 per share as of December 31, 2024, of which 61,819,101 shares were issued and outstanding. At December 31, 2023 100,000,000 shares were authorized and a total of 47,215,116 were issued and outstanding.

Warrants

Information with respect to warrants and pre-funded warrants issued is described in Note 9.

12. Related Party Transactions

Information with respect to payments under the Einstein License is described in Note 7.

13. Income Taxes

The Company accounts for income taxes under the provision of ASC 740, Income Taxes. The Company did not report a tax provision for the years ended December 31, 2024 and 2023 due to historically incurred net operating losses.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets as of December 31, 2024 and 2023 are as follows:

	December 31,	
(In thousands)	**2024**	**2023**
Deferred tax assets:		
Net operating loss carryforwards	$ 58,121	$ 53,376
Research and other credits	8,272	7,482
R&D capitalization	20,764	16,181
Stock-based compensation	6,096	6,207
Reserves and accruals	1,681	2,312
Other	244	270
Total gross deferred tax assets	95,178	85,828
Less valuation allowance	(93,965)	(84,039)
Total deferred tax assets	1,213	1,789
Deferred tax liability:		
Depreciation	(1,213)	(1,789)
Other	—	—
Net deferred tax assets	$ —	$ —

In assessing the potential realization of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will be realized. The ultimate realization of deferred tax assets is dependent upon

the Company attaining future taxable income during the periods in which those temporary differences become deductible. As of December 31, 2024, and 2023, management was unable to determine if it is more likely than not that the Company's deferred tax assets will be realized and has therefore recorded a 100% valuation allowance against deferred tax assets at such dates.

No Federal tax provision has been provided for the years ended December 31, 2024 and 2023 due to the losses incurred during such periods. A reconciliation of the difference between the income tax rate computed by applying the U.S. Federal statutory rate and the effective tax rate for the years ended December 31, 2024 and 2023 is as follows:

	December 31,	
	2024	2023
U. S. federal statutory tax rate	(21)%	(21)%
State taxes	(5)%	(6)%
Change in valuation allowance	24%	28%
Tax credits	(2)%	(3)%
Stock-based compensation	4%	2%
Foreign withholding taxes	0%	0%
Other	0%	0%
Effective tax rate	0%	0%

On October 4, 2023, Massachusetts enacted tax law changes which included the adoption of a single sales apportionment factor effective on January 1, 2025. As required under ASC 740, the Company has accounted for the deferred tax impacts of this tax law change in the period the tax law was enacted, which resulted in an insignificant increase in state deferred tax assets and offset with a valuation allowance.

The Company has applied the provisions of ASC 740, which clarifies the accounting for uncertainty in tax positions and requires the recognition of the impact of a tax position in the financial statements if that position is more likely than not of being sustained on a tax return, based on the technical merits of the position, upon examination by the relevant taxing authority. At December 31, 2024 and 2023, the Company had unrecognized tax benefits related to Federal and state research tax credits of $3.1 million and $2.9 million, respectively. The Company is subject to Federal and state income tax examinations by tax authorities for all years since its incorporation in 2014 to the extent tax attributes from those years are utilized. The Company is currently not under examination by any tax authority.

At December 31, 2024, the Company has available net operating loss carryforwards for Federal and state income tax purposes of $213.4 million and $211.3 million, respectively, which, if not utilized earlier, will begin to expire in 2035. $184.9 million of the federal net operating losses have an indefinite carryforward. The Company has Federal research credits of $9.3 million, which, if not utilized earlier, will begin to expire in 2035, and state research credits of $2.5 million, which, if not utilized earlier, will begin to expire in 2033. State research credits of $0.2 million have an indefinite carryforward.

Ownership changes, as defined in the Internal Revenue Code, including those resulting from the issuance of common stock in connection with the Company's public offerings, may limit the amount of net operating loss and tax credit carryforwards that can be utilized to offset future taxable income or tax liability. The amount of the limitation is determined in accordance with Section 382 of the Internal Revenue Code. The Company has performed an analysis of ownership changes through September 30, 2024. Based on this analysis, the Company does not believe that any of the Company's tax attributes will expire unutilized due to Section 382 limitations.

The following is a reconciliation of the Company's gross uncertain tax position at December 31, 2024 and 2023:

	December 31,	
(In thousands)	2024	2023
Balance at the beginning of year	$ 2,927	$ 2,491
Additions for current year tax provisions	278	424
Additions for prior year tax provisions	—	14
Reductions of prior year tax provisions	(67)	(2)
Balance as of end of year	$ 3,138	$ 2,927

14. Commitments and Contingencies

Einstein License Agreement

In 2015, the Company entered into the Einstein License with Einstein for certain patent rights relating to the Company's core technology platform for the engineering of biologics to control T cell activity, precision, immune-modulatory drug product candidates, and two supporting technologies that enable the discovery of costimulatory signaling molecules (ligands) and T cell targeting peptides. The Company entered into an amended and restated license agreement on July 31, 2017, as amended on October 2018, which modified certain obligations of the parties under the Einstein License. The Einstein License was further amended on January 13, 2024. For the years ended December 31, 2024 and 2023, the Company incurred $0.1 million and $7,000, respectively, in fees payable to Einstein in relation to this license.

The Company's remaining commitments with respect to the Einstein License are based on the attainment of future milestones. The aggregate amount of milestone payments made under the Einstein License may equal up to $1.85 million for each Licensed Product, and up to $1.85 million for each new indication of a Licensed Product. Additionally, the aggregate amount of one-time milestone payments based on cumulative sales of all Licensed Products may equal up to $5.75 million. The Company is also party to a service agreement with Einstein to support the Company's ongoing research and development activities.

Collaboration Agreement with LG Chem

See discussion of the LG Chem Collaboration Agreement in Note 10.

Collaboration and Option Agreement with Ono

See discussion of the Ono Collaboration and Option Agreement in Note 10.

Contingencies

The Company accrues contingent liabilities to the extent that the liability is probable and estimable. There are no accruals for contingent liabilities in these consolidated financial statements.

The Company may be subject to various legal proceedings from time to time as part of its business. As of December 31, 2024, the Company was not a party to any legal proceedings or threatened legal proceedings, the adverse outcome of which, individually or in the aggregate, would have a material adverse effect on its business, financial condition or results of operations.

15. Leases

On March 28, 2022, the Company entered into a License Agreement (the "License") with MIL 40G, LLC (the "Licensor"), pursuant to which the Company leases approximately 13,000 square feet of office, research and development and laboratory space located at 40 Guest Street, Boston, Massachusetts 02135 (the "Premises"). The Company relocated its corporate headquarters to the Premises in April 2022. On March 28, 2022, the Company terminated its office and lab space lease in Cambridge Massachusetts (the "Laboratory and Office Lease") effective April 30, 2022. The Company performed an analysis of the accounting implications of this termination based on ASC 360 Impairments and Abandonments guidance. For the year ended December 31, 2022, the Company recorded an adjustment to decrease the right-of-use asset and lease liability of $8.1 million and $8.4 million, respectively, and recorded a gain on right-of-use asset included in the consolidated statements of operations and comprehensive loss of $0.3 million.

The Company recognized a right of use asset of $9.1 million and an operating lease liability of $9.1 million which were recorded as of the Term Commencement Date (as defined below) related to the License.

The term of the License commenced on April 15, 2022 (the "Term Commencement Date") and expires on April 14, 2026 (the "Term"). The License has a monthly rental rate of $200,700 for the first year of the Term, $208,728 for the second year of the Term, $217,077 for the third year of the Term and $225,760 for the remainder of the Term. Pursuant to the License, the Company prepaid two months of rent and a security deposit. The Licensor is obligated under the License to provide certain services to the Company, including providing certain gases, chemicals and equipment to the Premises' laboratory space, IT support, security, office support and health and safety training. The Licensor has the right to terminate the License for Cause (as defined in the License).

On May 3, 2022, the Company entered into the First Amendment to the License ("First Amendment") with the Licensor, pursuant to which the License was expanded to include an additional room effective July 15, 2022. In consideration of the First Amendment, the security deposit was increased from $225,760 to $235,884 effective July 15, 2022. Upon execution of the First Amendment, the Company prepaid three months of rent, two of which will be held in escrow and credited against future rent payments and the other of which was applied to the first month's rent. Effective July 15, 2022, the monthly rental rate under the First Amendment increased to $209,700 from $200,700. During the year ended December 31, 2022, the Company recognized a right of use asset of $369,000 and a short and long term operating lease liability of $100,300 and $260,600, respectively, using a discount rate of 8%, which were recorded as of the Term Commencement Date related to the License.

On May 31, 2022, the Company entered into an operating lease for additional laboratory space at 40 Guest Street, Boston, Massachusetts for the period from December 1, 2022, through December 1, 2024 (the "40G Additional Laboratory Lease"). During the year ended December 31, 2022, the Company recognized a right of use asset of $1.3 million and short term and long term operating lease liabilities of $0.7 million, and $0.5 million, respectively, using a discount rate of 10%, which were recorded as of the Term Commencement Date related to the 40G Additional Laboratory Lease.

On November 20, 2024, the Company extended the term of the 40G Additional Laboratory Lease through July 14, 2026. The monthly rental rate is $61,519 through November 30, 2025 and $63,979 for the remainder of the term until July 14, 2026. During the year ended December 31, 2024, the Company recognized a right of use asset of $1.1 million and short term and long term operating lease liabilities of $0.7 million, and $0.4 million, respectively, using a discount rate of 10%, which were recorded as of the Term Commencement Date related to the 40G Additional Laboratory Lease.

For the year ended December 31, 2024, the Company recorded $0.3 million in interest expense to the lease liability.

At December 31, 2024, the Company recorded $4.4 million to operating lease right-of-use asset, and $3.5 million and $1.0 million to the short-term and long-term operating lease liability, respectively. At December 31, 2023, the Company recorded $6.3 million to operating lease right-of-use asset, and $3.4 million and $3.2 million to the short-term and long-term operating lease liability, respectively.

Future minimum lease payments under these leases at December 31, 2024 are as follows:

Year	*(in thousands)*
2025	3,540
2026	1,234
2027	—
Total lease payments	4,774
Less: present value discount	(231)
Present value of lease payments	$ 4,543

For both the years ended December 31, 2024 and 2023, total rent expense of $3.4 million was included in the consolidated statements of operations and comprehensive loss.

The weighted average remaining lease term and discount rate related to the Company's leases were as follows:

	December 31,	
	2024	**2023**
Weighted average remaining lease term (years)	1.35	2.16
Weighted average discount rate	6.85%	6.25%

16. Cue Biopharma 401(k) Plan

Effective as of January 1, 2017, the Company adopted the Cue Biopharma 401(k) Plan (the "Plan") for all employees of the Company. Employees may participate in the Plan upon complying with the Plan's eligibility requirements, subject to limitations imposed by the Internal Revenue Service. Under the Plan, the Company may match employee contributions at its discretion. The Company made contributions of $0.3 million to the Plan for both the years ended December 31, 2024 and 2023.

17. Subsequent Events

Ono Collaboration and Option Agreement

On March 11, 2025, the Company and Ono agreed to terminate the Ono Collaboration and Option Agreement, effective as of March 6, 2025. At such time, the agreement had no further force or effect with the exception of certain customary provisions which are intended to survive termination and expiration of the agreement. As a result, the Company regained all rights to CUE-401.

LG Chem Collaboration Agreement

On March 11, 2025, the Company and LG Chem entered into the Ninth Amendment to the LG Chem Collaboration Agreement. As of the date of the amendment, the Company regained its rights to the CUE-101 program which had been licensed to LG Chem, and LG Chem terminated all of its rights to the same program. Pursuant to the Ninth Amendment, the Company agreed to make future payments to LG Chem, if and when, one or more potential scenarios related to the CUE-101 program occur up to a predetermined aggregate amount. LG Chem continues to maintain its interest and rights in the CUE-102 program, targeting WT1 expressing cancers, pursuant to the LG Chem Collaboration Agreement.

PART IV

Item 15. Exhibit and Financial Statement Schedules

(a) List of documents filed as part of this report:

1. Financial Statements (see "Financial Statements and Supplementary Data" at Item 8 and incorporated herein by reference).

2. Financial Statement Schedules (Schedules to the Financial Statements have been omitted because the information required to be set forth therein is not applicable or is shown in the accompanying Financial Statements or notes thereto)

3. Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K:

		Incorporated by Reference				
Exhibit Number	Exhibit Description	Filed Herewith	Form	Exhibit	Filing Date	Registration /File No.
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended		10-Q	3.1	11/14/2024	001-38327
3.2	Amended and Restated Bylaws of the Registrant		S-1	3.5	12/05/2017	333-220550
4.1	Specimen Certificate representing shares of common stock of the Registrant		S-1	4.1	12/05/2017	333-220550
4.2	Description of Common Stock of the Registrant Registered Pursuant to Section 12 of the Securities Exchange Act of 1934	X				
4.3	Form of Pre-Funded Warrant to Purchase Common Stock		8-K	4.1	9/27/2024	001-38327
4.4	Form of Warrant to Purchase Common Stock		8-K	4.2	9/27/2024	001-38327
4.5	Form of Pre-Funded Warrant to Purchase Common Stock		8-K	4.1	11/15/2022	001-38327
4.6	Form of Warrant to Purchase Common Stock or Pre-Funded Warrant		8-K	4.2	11/15/2022	001-38327
10.1	Form of Registration Rights Agreement between the Registrant and investors for an offering completed on June 15, 2015		S-1	10.4	09/21/2017	333-220550
10.2	Form of Joinder and Amendment to Registration Rights Agreement between the Registrant and investors for an offering completed on December 22, 2016		S-1	10.6	09/21/2017	333-220550
10.3#	First Amendment to Collaboration, License and Option Agreement, dated March 15, 2019, between the Registrant and LG CHEM LTD.		10-K	10.3	03/09/2021	001-38327
10.4#	Second Amendment to Collaboration, License and Option Agreement, dated August 5, 2019, between the Registrant and LG CHEM LTD.		10-K	10.4	03/09/2021	001-38327
10.5#	Third Amendment to Collaboration, License and Option Agreement, dated October 29, 2019, between the Registrant and LG CHEM LTD.		10-K	10.5	03/09/2021	001-38327

10.6#	Fourth Amendment to Collaboration, License and Option Agreement, dated December 18, 2019, between the Registrant and LG CHEM LTD.		10-K	10.6	03/09/2021	001-38327
10.7#	Fifth Amendment to Collaboration, License and Option Agreement, dated January 10, 2020, between the Registrant and LG CHEM LTD.		10-K	10.7	03/09/2021	001-38327
10.8#	Sixth Amendment to Collaboration, License and Option Agreement, dated February 14, 2020, between the Registrant and LG CHEM LTD.		10-K	10.8	03/09/2021	001-38327
10.9#	Seventh Amendment to Collaboration, License and Option Agreement, dated May 14, 2020, between the Registrant and LG CHEM LTD.		10-K	10.9	03/09/2021	001-38327
10.10#	Eighth Amendment to Collaboration, License and Option Agreement, dated December 7, 2020, between the Registrant and LG CHEM LTD.		10-K	10.10	03/09/2021	001-38327
10.11#	Ninth Amendment to Collaboration, License and Option Agreement, dated March 6, 2025, between the Registrant and LG CHEM LTD.	X				
10.12	Form of Indemnification Agreement between the Registrant and its directors and officers	X				
10.13†	Amended and Restated License Agreement by and between the Registrant and Albert Einstein College of Medicine dated July 31, 2017		S-1	10.11	12/13/2017	333-220550
10.14*	Cue Biopharma, Inc. 2016 Omnibus Incentive Plan, as amended and restated		S-1	10.13	09/21/2017	333-220550
10.15*	Form of stock option award under 2016 Omnibus Incentive Plan		10-Q	10.1	08/14/2024	001-38327
10.16*	Cue Biopharma, Inc. 2016 Non-Employee Equity Incentive Plan		S-1	10.15	09/21/2017	333-220550
10.17*	Form of stock option award under 2016 Non-Employee Equity Incentive Plan		10-Q	10.2	08/14/2024	001-38327
10.18*	Director Compensation Policy effective June 5, 2024		10-Q	10.2	11/14/2024	001-38327
10.19*	Executive Employment Agreement between the Registrant and Colin G. Sandercock dated as of November 15, 2017		S-1	10.22	12/04/2017	333-220550
10.20†	Collaboration, License and Option Agreement between the Registrant and LG Chem, Ltd. dated November 6, 2018		8-K	10.1	12/26/2018	001-38327
10.21*	Amendment No. 1 to Cue Biopharma, Inc. 2016 Omnibus Incentive Plan		10-K	10.16	03/12/2020	001-38327
10.22*	Amended and Restated Executive Employment Agreement between the Registrant and Anish Suri dated October 3, 2019		8-K	10.1	10/07/2019	001-38327
10.23	Third Amended and Restated Executive Employment Agreement dated March 4, 2021 between the Company and Daniel Passeri		10-K	10.26	03/09/2021	001-38327
10.24	Executive Employment Agreement dated August 21, 2020 between Registrant and Kerri-Ann Millar		8-K	10.1	08/24/2020	001-38327

10.25	First Amendment to the Amended and Restated License Agreement with Albert Einstein College of Medicine dated October 30, 2018		10-K	10.30	03/09/2021	001-38327
10.26	Open Market Sale Agreement[SM], dated October 1, 2021, by and between Cue Biopharma, Inc. and Jefferies LLC		10-Q	10.1	11/09/2021	001-38327
10.27#	Loan and Security Agreement, dated February 15, 2022, by and between Cue Biopharma, Inc. and Silicon Valley Bank		10-K	10.34	03/16/2022	001-38327
10.28	License Agreement, dated March 28, 2022, between Cue Biopharma, Inc. and MIL 40G, LLC		8-K	10.1	03/30/2022	001-38327
10.29	First Amendment to the License Agreement, dated May 3, 2022, between Cue Biopharma, Inc. and MIL 40G, LLC		10-Q	10.1	08/04/2022	001-38327
10.30	Rider to License Agreement, dated as of July 7, 2022, between Cue Biopharma, Inc. and MIL 40G, LLC		10-Q	10.2	08/04/2022	001-38327
10.31	First Amendment to Rider to License Agreement, dated May 3, 2024, between Cue Biopharma, Inc. and MIL 40G, LLC	X				
10.32	Second Amendment to Rider to License Agreement, dated November 20, 2024, between Cue Biopharma, Inc. and MIL 40G, LLC	X				
10.33	Termination of License Agreement, dated September 9, 2022, between Cue Biopharma, Inc. and MIL 21E, LLC		10-Q	10.1	11/14/2022	001-38327
10.34	Form of Securities Purchase Agreement, dated November 14, 2022, by and among the Company and the other parties thereto		8-K	10.1	11/15/2022	001-38327
10.35	Registration Rights Agreement, dated November 14, 2022, by and among the Company and the other parties thereto		8-K	10.2	11/15/2022	001-38327
10.36	Waiver and First Amendment to Loan and Security Agreement, dated April 10, 2023, by and between Cue Biopharma, Inc. and Silicon Valley Bridge Bank, N.A., as successor in interest to Silicon Valley Bank		10-Q	10.2	05/09/2023	001-38327
10.37	Second Amendment to Loan and Security Agreement, dated October 2, 2024, by and between Silicon Valley Bank, a division of First-Citizens Bank & Trust Company, and Cue Biopharma, Inc.		8-K	10.1	10/4/2024	001-38327
10.38*	Amendment No. 2 to Cue Biopharma, Inc. 2016 Omnibus Incentive Plan		10-Q	10.1	08/08/2023	001-38327
10.39*	Amendment No. 1 to Cue Biopharma, Inc. 2016 Non-Employee Equity Incentive Plan		10-Q	10.2	08/08/2023	001-38327
10.40*	Consulting Agreement effective June 7, 2023 entered into between Cue Biopharma, Inc. and Peter A Kiener, D.Phil		10-Q	10.3	08/08/2023	001-38327

10.41*	Amendment No. 1 to Consulting Agreement between Cue Biopharma, Inc. and Peter A. Kiener, dated September 1, 2023		10-Q	10.1	11/03/2023	001-38327
10.42#	Second Amendment to the Amended and Restated License Agreement with Albert Einstein College of Medicine dated January 13, 2024		10-K	10.38	03/28/2024	001-38327
10.43*	Form of inducement stock option award	X				
19.1	Amended and Restated Insider Trading Policy effective March 21, 2025	X				
21.1	List of Subsidiaries	X				
23.1	Consent of RSM US LLP, Independent Registered Public Accounting Firm	X				
24.1	Power of Attorney (included on signature page)	X				
31.1	Certification Pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934	X				
31.2	Certification Pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934	X				
32.1	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X				
97.1*	Compensation Recovery Policy		10-K	97.1	03/28/2024	001-38327
101.INS	Inline eXtensible Business Reporting Language (XBRL) Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document	X				
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X				
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101)	X				

***** Indicates management compensatory plan, contract or arrangement.
† Confidential treatment has been granted as to portions of this exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.
# Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

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

Cue Biopharma, Inc.

Dated: March 31, 2025

By: /s/ Daniel R. Passeri
Daniel R. Passeri
Chief Executive Officer and Director
(Principal Executive Officer)

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Cue Biopharma, Inc., hereby severally constitute and appoint Daniel R. Passeri and Kerri-Ann Millar our true and lawful attorney, with full power to him or her to sign for us and in our names in the capacities indicated below, any amendments to this Annual Report on Form 10-K, and generally to do all things in our names and on our behalf in such capacities to enable Cue Biopharma, Inc. to comply with the provisions of the Securities Exchange Act of 1934, as amended, and all the requirements of the Securities Exchange Commission.

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

Signatures	Title	Date
/s/ Daniel R. Passeri Daniel R. Passeri	Chief Executive Officer and Director (Principal Executive Officer)	March 31, 2025
/s/ Kerri-Ann Millar Kerri-Ann Millar	Chief Financial Officer (Principal Financial and Accounting Officer)	March 31, 2025
/s/ Peter A. Kiener Peter A. Kiener	Director	March 31, 2025
/s/ Frederick Driscoll Frederick Driscoll	Director	March 31, 2025
/s/ Pamela Garzone Pamela Garzone	Director	March 31, 2025
/s/ Patrick Verheyen Patrick Verheyen	Director	March 31, 2025
/s/ Frank Morich Frank Morich	Director	March 31, 2025
/s/ Pasha Sarraf Pasha Sarraf	Director	March 31, 2025

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Cautionary Note Regarding Forward-Looking Statements

This Annual Report, including the CEO's Letter to Cue Biopharma Shareholders, contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, including without limitation any statements with respect to Cue Biopharma's plans, strategies, objectives, prospects, results, or financial condition; statements of belief and expectation concerning research and development, including development plans with respect to the CUE-100, CUE-400 and CUE-500 series, timelines, anticipated results, partnering opportunities and the therapeutic potential of drug product candidates; statements of assumptions underlying any of the foregoing and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "goal," "project," "future," "predict," "potential," "will, "would," "could," "should," "continue," "seek," "strategy," and similar expressions. All statements, other than statements of historical fact, contained in this Annual Report, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. These forward-looking statements are not guarantees of future performance and involve risks, uncertainties, assumptions and other important factors that may cause actual results to be materially different from those indicated by such forward-looking statements. Factors that may cause or contribute to actual results being materially different from those indicated by forward-looking statements including the factors set forth under the captions "Risk Factor Summary" and "Risk Factors" in the accompanying Annual Report on Form 10-K for the fiscal year ended December 31, 2024 and any subsequent reports filed by Cue Biopharma with the Securities and Exchange Commission. In addition, any forward-looking statements in this Annual Report, including the CEO's Letter to Cue Biopharma Shareholders, represent the views of Cue Biopharma only as of the date of this Annual Report and should not be relied upon as representing Cue Biopharma's views as of any subsequent date. Cue Biopharma disclaims any intention or obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law.

CUE® BIOPHARMA

Corporate Headquarters
40 Guest Street
Boston, Massachusetts 02135

Transfer Agent
Computershare
Canton, Massachusetts

Legal Counsel
WillmerHale LLP
Boston, Massachusetts

Independent Auditors
RSM US LLP
Boston, Massachusetts

Stock Information
The company's common stock is traded on the Nasdaq Capital Market under the symbol CUE.

Mobilizing the Patient's Immune System to Treat Serious Diseases

ANNUAL REPORT 2024

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