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, 2020

☐ **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.)**
21 Erie Street Cambridge, MA	**02139**
(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. ☐

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 $695.1 million (based on the closing price of the registrant's common stock on June 30, 2020 of $24.51 per share).

As of March 1, 2021, the registrant had 30,457,250 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, 2020. 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 current and future preclinical studies and 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;
- the timing of and our ability to submit applications for, 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 establish collaborations or obtain additional funding; and
- the impacts of the COVID-19 pandemic.

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 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.

- We are a clinical-stage biopharmaceutical company, have no history of generating commercial revenue, have a history of operating losses, and we 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 one of which is currently being tested in a clinical trial, 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.
- The outbreak of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19, could adversely impact our business, including our clinical trials and preclinical studies.
- We plan 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. Our collaboration agreements with Merck and LG Chem contain exclusivity provisions that restrict our research and development activities.
- 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 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.
- 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 obtain regulatory approval for or commercialize our 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 is 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.
- We will be subject to stringent domestic and foreign regulation in respect of any potential products. The regulatory approval processes of the FDA and other comparable regulatory authorities outside the United States are lengthy, time-consuming and inherently unpredictable. Any unfavorable regulatory action may materially and adversely affect our future financial condition and business operations.
- Even if a potential therapeutic is ultimately approved by the various regulatory authorities, it may be approved only for narrow indications which may render it commercially less viable.
- Even if we receive regulatory approval of our drug product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drug product candidates.

PART I

Item 1. Business

Overview

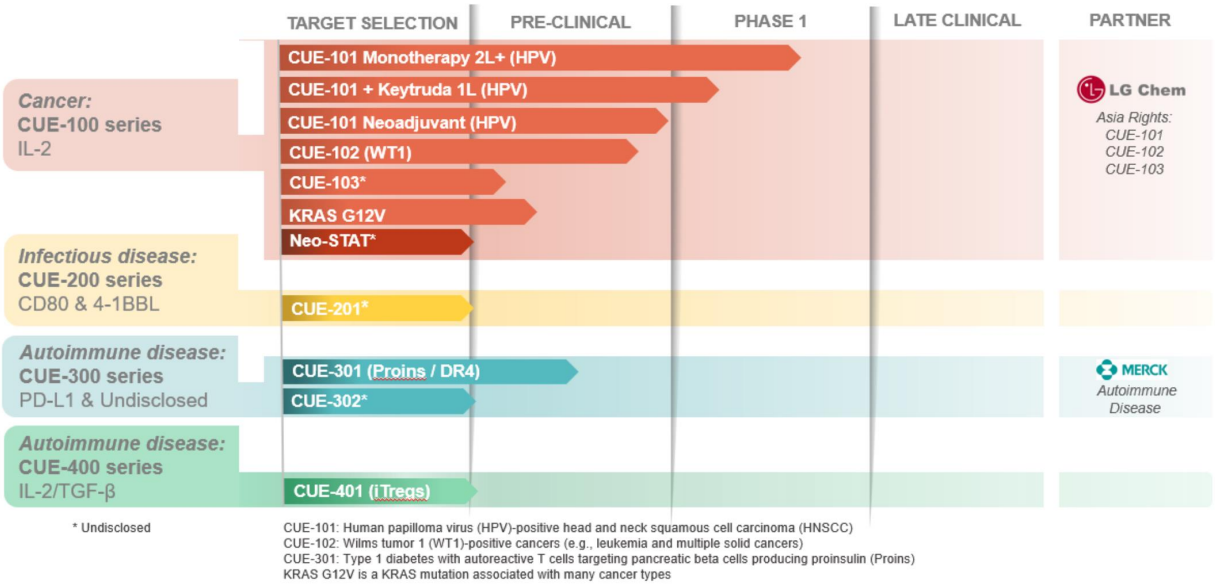
We are a clinical-stage biopharmaceutical company engineering a novel class of injectable biologics to selectively engage and modulate targeted T cells directly within the patient's body. We believe our proprietary Immuno-STAT™ (*Selective Targeting and Alteration of T Cells*) platform, as described below, will allow us to harness the fullest potential of an individual's intrinsic immune repertoire for restoring health while avoiding the deleterious side effects of broad immune activation (for immuno-oncology or infectious immunity) or broad immune suppression (for autoimmunity and inflammation). In addition to the selective modulation of T cell activity, we believe Immuno-STATs offer several key points of potential differentiation over competing approaches, including modularity and versatility providing broad disease coverage, manufacturability, and convenient administration.

Through rational protein engineering, we leverage the modular and versatile nature of the Immuno-STAT platform to design drug product candidates for selective immune modulation in cancer, chronic infectious disease, and autoimmune disease. To address the needs of these clinical indications, we have developed four biologic series within the Immuno-STAT platform: CUE-100, CUE-200, CUE-300, and CUE-400, each specifically designed through rational engineering to possess distinct signaling modules for desired biological mechanisms that may be applied across many diseases. The CUE-100 series exploits rationally engineered IL-2 in context of the core Immuno-STAT framework for selective activation of targeted tumor-specific T cells, while the CUE-200 series is focused on cell surface receptors including CD80 and/or 4-1BBL to address T cell exhaustion associated with chronic infections. The CUE-300 series, being developed for autoimmune diseases, incorporates the inhibitory PD-L1 co-modulator for selective inhibition of the autoreactive T cell repertoire. This approach is pertinent for autoimmune diseases with known, well characterized, limited or few autoantigens, such as type 1 diabetes. The CUE-400 series, for autoimmune diseases with diverse or unknown autoantigens, represents a novel class of bispecific molecules that can selectively and effectively expand induced regulatory T cells, or iTregs. We categorize these molecules as "pathway-specific modulators" or PSM. The first candidate, CUE-401, incorporates the two key biological signals that are necessary for generation of iTregs, namely IL-2 and TGF-beta. Based on structure-based rational protein engineering, both IL-2 and TGF-beta have been affinity tuned (i.e. the binding strength has been optimized) to maintain on-target engagement while minimizing systemic toxicities.

Our drug product candidates are in various stages of clinical and preclinical development, and while we believe that these candidates hold potential value, our activities are 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 additional capital to fund our growth and ongoing business operations.

Our Immuno-STAT Platform Pipeline

The pipeline below details our current portfolio assets and their stages of development. CUE-101 is our most advanced clinical stage asset, currently being dosed in a Phase1 monotherapy trial for human papilloma virus (HPV)-driven recurrent/metastatic (R/M) head and neck cancer, as well as in a first line Phase 1 combination trial with KEYTRUDA® (pembrolizumab) in the same indication. CUE-102 focuses on Wilm's tumor-1 (WT1) as the tumor antigen.



We have made significant progress advancing the IL-2-based CUE-100 series for oncology. We dosed the first patient in September 2019 in a monotherapy Phase 1 dose escalation clinical trial of CUE-101 for the treatment of HPV16-driven recurrent/metastatic, or R/M, head and neck squamous cell carcinoma, or HNSCC, in late-stage treatment-refractory patients with R/M HNSCC who have received and failed several prior lines of systemic therapy including checkpoint inhibitors such as KEYTRUDA, already approved for first-line, or 1L, HPV+R/M HNSCC. To date CUE-101 has demonstrated a favorable tolerability profile in the monotherapy trial and continues to generate encouraging emerging data pertaining to its pharmacokinetic, or PK, and pharmacodynamic, or PD, profile, as well as anti-tumor clinical activity.

During the fourth quarter of 2020 we initiated a Phase 1 clinical trial into the first-line R/M HNSCC setting to evaluate the combination of CUE-101 with Merck Sharp & Dohme Corp., or Merck's, anti-PD-1 therapy KEYTRUDA®. The first patient in this combination study was dosed in the first quarter of 2021. The potential synergy with KEYTRUDA is due to CUE-101's design and protein engineering to selectively activate and expand tumor-targeted T cells directly in the patient's body. We believe the potential of CUE-101 to synergize with and enhance the clinical activity of KEYTRUDA is mechanistically attractive since the presence of expanded tumor-specific T cells are a pre-requisite for and an obligatory target of anti-PD-1. In preclinical studies, we have observed activation and expansion of the targeted T cells circulating in the peripheral blood, as well as a significant expansion of tumor infiltrating lymphocytes. In addition to the Phase 1 monotherapy and combination trial with KEYTRUDA, we also intend to initiate a neoadjuvant study in locally advanced HPV+ HNSCC patients in the second half of 2021, which is expected to provide further mechanistic evidence and insights into the activation and effector function of T cells resident in tumor tissue and their impact on tumor viability.

CUE-101 is the most advanced candidate from our IL-2 based CUE-100 series and is exemplary of the union of the rational protein engineering underscoring the Immuno-STAT platform and key immunological targets, or activity nodes, to selectively enhance anti-tumor immunity. Data relating to this work were recently published in a peer-reviewed journal (Quayle et al., Clinical Cancer Research 2020, https://clincancerres.aacrjournals.org/content/early/2020/01/15/1078-0432.CCR-19-3354). Importantly, we believe that the totality of clinical data with CUE-101, effectively reduces the risk profile of the IL-2 based CUE-100 series due to the fact that the core framework of the CUE-100 series remains essentially the same for each drug candidate, except for the targeting peptide epitope within the major histocompatibility complex, or MHC, pocket or the human leukocyte antigen, or HLA, in humans. Therefore, with the exception of some protein engineering modifications to ensure stability and manufacturability the core IL-2 scaffold is a shared molecular feature of all molecules generated within this series (including CUE-102, and the next-gen platform, Neo-STAT™, as described below).

We are also advancing a pipeline of additional promising preclinical candidates that we believe hold the potential to treat multiple cancers. Data from our second candidate of the CUE-100 series, CUE-102 (WT1) were recently presented at the New York Academy of Science, or NYAS, Frontiers in Cancer Immunotherapy meeting and at the Society for Immunotherapy of Cancer, or SITC, meeting in November 2020. These data support early evidence of selective T cell expansion, along with polyfunctional effector function including killing of target cells. We are continuing to develop CUE-102 toward an investigational new drug application, or IND, through enabling studies, and we anticipate filing an investigational new drug application, or IND, for this candidate in the first half of 2022. We have also generated foundational data with Immuno-STATs targeting the mutated G12V KRAS T cell epitope including demonstration of activation and expansion of T cells expressing G12V-specific T cell receptors, or TCRs. These data were presented at the SITC meeting in November 2020 and more recently at the Immuno-Oncology conference, IO-360, in February 2021.

Importantly, through rational protein engineering, we have expanded the reach of the Immuno-STAT platform to potentially address the heterogeneity and diversity of many cancers by developing a derivative scaffold from the CUE-100 series that contains stable “peptide-less” or “empty” MHC pocket or human leukocyte antigen, or HLA, molecules, to which peptides of interest may be covalently attached. We refer to this derivative scaffold as Neo-STAT™. Neo-STAT is designed to provide greater flexibility for targeting multiple tumor epitopes, enhance production efficiencies, decrease time and cost to manufacture and potentially lend itself to personalized neo-antigen strategies in cancer immunotherapy as an off-the-shelf approach.

In addition to oncology, we have made recent advances in autoimmune diseases where our core strategy has centered on two major themes: (i) modulating antigen-specific T cells with Immuno-STATs in diseases with restricted or known autoantigens (e.g., type 1 diabetes), and (ii) exploiting a pathway-specific approach via modalities focused on regulatory T cells and other mechanisms that could be broadly applied to autoimmune diseases with unknown or diverse autoantigens. In the first instance we have made significant advances with the CUE-300 series for targeting antigen-specific T cells in autoimmune disorders, including progress made in our collaboration with Merck which was recently extended and further supported through 2021. To date, we have generated proof of concept data demonstrating the potential for targeting autoreactive T cells in type 1 diabetes; https://www.cuebiopharma.com/wp-content/uploads/2020/03/CUE-Merck-Autoimmune-Data.pdf. Based upon the promising progress we have made through our Merck collaboration to date, we expect to further develop a growing pipeline of autoimmune candidates throughout 2021.

Additionally, we have expanded our reach into chronic autoimmune diseases with diverse and/or uncharacterized antigens by focusing on activating and increasing regulatory T cells for re-setting immune balance. Our first candidate from this effort, CUE-401, incorporates two key signals, namely IL-2 and TGF-beta, for differentiation and expansion of iTregs.

Furthermore, we are assessing the potential of developing programs from the Immuno-STAT platform for treating infectious diseases with the CUE-200 series through research being conducted by Dr. Steven Almo, a co-founder of the company and Chair of Biochemistry at The Albert Einstein College of Medicine. Data supporting these applications were recently presented at the SITC meeting in November 2020; https://www.cuebiopharma.com/wp-content/uploads/2020/11/Immuno-STAT-SITC-2020-Poster.pdf.

Our Business Strategy

Our primary objective is to become a leading biopharmaceutical company developing breakthrough, highly selective and differentiated biologics for safe and effective therapeutic immune modulation directly in patients having high unmet medical need. In order to achieve this objective, we are focused on the following strategies:

Advance and establish our IL-2-based CUE-100 series, as demonstrated by our lead Immuno-STAT program, CUE-101

- Through CUE-101 we intend to demonstrate that IL-2 can be selectively and tolerably delivered to the specific cellular immune compartment that is relevant for anti-tumor immunity. This is in contrast to other approaches that are focused on systemic delivery of IL-2 variants with little specificity for the anti-tumor T cell repertoire.

- We plan to execute clinical trials that are designed with a translational approach to demonstrate CUE-101’s ability to selectively activate and expand patients’ own endogenous HPV16-specific T cell repertoire to target, attack and kill tumor cells.

- We plan to expand patient access and potentially enhance clinical outcomes by addressing the significant unmet patient need first by establishing foundational mechanistic evidence in the second line and beyond monotherapy Phase 1 clinical trial for HPV16-driven R/M HNSCC, then in first line therapy in combination with anti-PD1 therapy, where it is our intention to generate evidence of synergy with a checkpoint blockade. We also plan to further expand into newly diagnosed HPV16-driven R/M HNSCC with a Phase 1 neoadjuvant trial designed to study surgically excised tumors after the patients have received two to three dose regimens of CUE-101, potentially allowing us to gather further data that may demonstrate mechanistic evidence of selective T cell activation, proliferation and infiltration of tumor tissue resulting in tumor cell killing.

- We are working to build a clinical data set that demonstrates the PK/PD, tolerability and anti-tumor effect of CUE-101 as a monotherapy and in combination with anti-PD-1 therapy in patients with HPV16-driven HNSCC.

Leverage our modular and versatile Immuno-STAT platform to generate and advance a pipeline of Immuno-STATs and Neo-STATs with strategic partnering to enable global patient reach

- Within the CUE-100 series, we are expanding our clinical reach through a collaboration and strategic territory partnership with LG Chem, Ltd., or LG Chem, for CUE-101, CUE-102 and CUE-103 for Asian markets. Through this collaboration and partnership, we are able to reach patients within the Asian territory.

- Beyond the IL-2-based CUE-100 series for addressing a broad range of cancers, we have a growing pipeline of therapeutic frameworks and programs designed to address the significant, unmet medical need for treating serious, life threatening indications, such as autoimmune disease and infectious disease.

- The recent extension of our collaboration with Merck, encompassing two defined autoimmune indications, including type I diabetes, or T1D, allows us to further progress the CUE-300 series, which is focused on targeting antigen-specific T cells in autoimmune disease.

- We continue to evaluate the mechanisms within the CUE-200 series via research being conducted at the Albert Einstein College of Medicine to demonstrate the ability to enhance T cell activation and/ or reverse T cell exhaustion, an area of critical need for infectious disease. Mechanistic data demonstrating proof-of-concept were recently disclosed at the SITC meeting in November 2020.

- We will continue to selectively explore other opportunities to create value from the protein engineering platform and may further develop these programs with or without partners.

Expand and enhance our core capabilities and Immuno-STAT platform

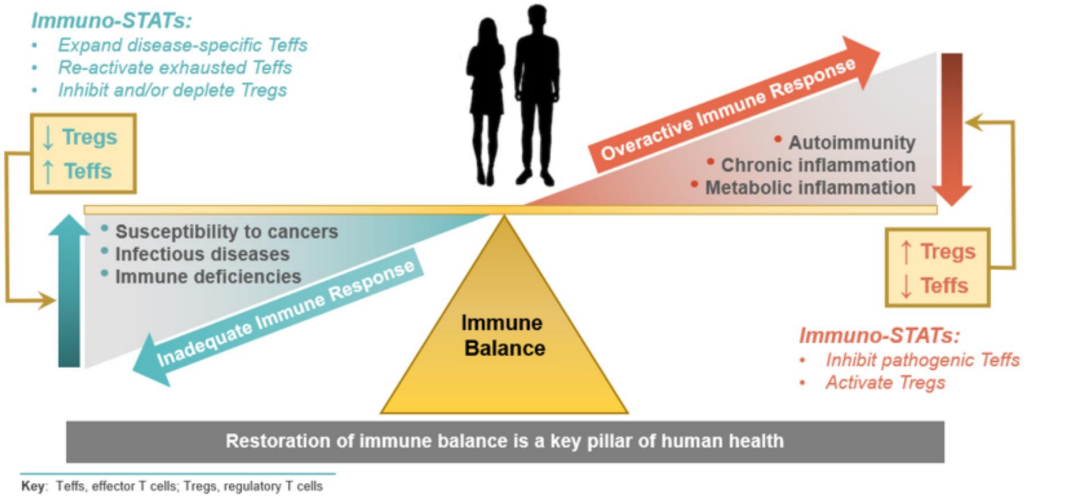
- We view protein engineering and translational immunology as our core competencies, and to expand our competitive advantages, we plan to continue to invest in these areas to further optimize the platform for rapid and cost-effective drug development. We may also in-license, acquire, or invest in complementary businesses, technologies, products or assets.

Our Approach

The Immune System and T Cell Immunity

As highlighted in the figure below, we believe a critical component of human health is achieving and maintaining a state of immune balance. Imbalance of the immune system underscores many diseased states: susceptibility to cancers and infectious disease can be attributed to inadequate or compromised/attenuated immune responses, while autoimmune diseases result from an overactive immune response reacting against the host.

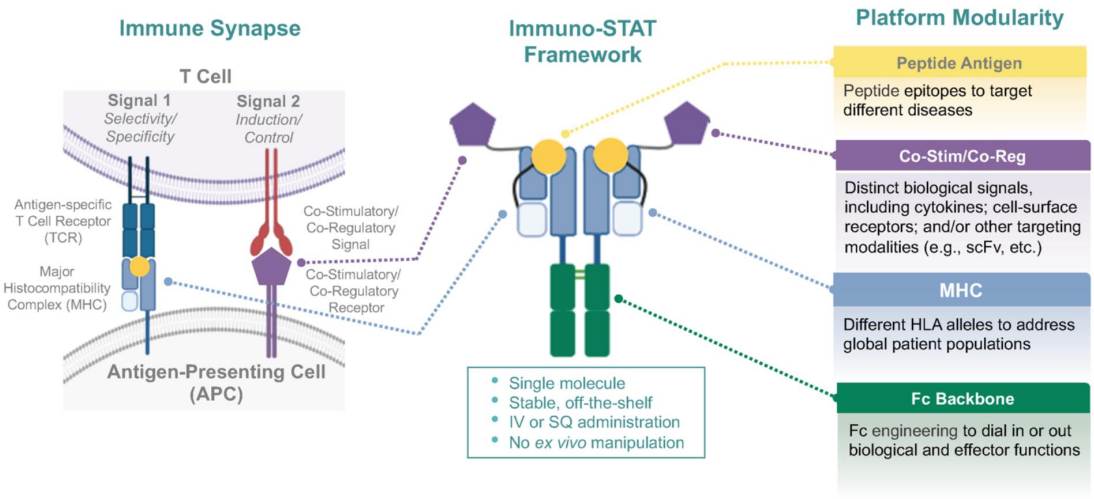
Restoring Immune Balance



The human immune system comprises a number of specialized cell types that collectively function to identify and defend the body against foreign threats. One such specialized cell type, the human T cell, is a subtype of a white blood cell that plays a central role in the immune system. During an immune response, T cells are activated via close encounters with a specialized cell type known as the antigen presenting cell, or APC. Prominent APC types include dendritic cells, macrophages, and B cells. The primary function of an APC is to uptake antigens, primarily proteins, catabolize, (i.e., break them down into peptides) and display them on their cell-surface in complex with specialized molecules known as the major histocompatibility complex molecules or human leukocyte antigen, or MHC (HLA in humans). This critical function of an APC, also referred to as “antigen processing and presentation”, ultimately results in generation of the key molecular substrate – the peptide MHC complex (pMHC will also be used to designate pHLA in humans) – that is recognized by the T cell via its T cell receptor, or TCR.

The source of the antigen for the APC is vast and expansive: antigens from pathogens such as viruses, bacteria and others activate T cells for protective immunity; antigens from tumor cells are key for robust anti-tumor T cell responses; and antigens from self-tissue are aberrantly recognized by autoreactive T cells that ultimately induce damage to the host. Hence, the nature of the pMHC complex on the APC sets the specificity of the T cell response. The intimate interactions between the T cells and APCs occur within a molecular interface known as the immunological or immune synapse (as shown in the figure below) wherein the TCR-pMHC engagement as well as additional accessary signals are sensed by T cells resulting in T cell activation or regulation. In essence, the immune synapse allows controlled engagement and selective activation of T cells through the presentation of two distinct signals: Signal 1, TCR engagement of the pMHC; and Signal 2, activating co-stimulatory (or co-inhibitory signals). The core protein framework for the Immuno-STAT platform builds upon our ability to combine the key signals for T cell modulation (i.e., Signal 1 and Signal 2) into a singular molecular scaffold, as shown below.

Immuno-STAT Platform Framework



Signal 1*: A stabilized peptide-major histocompatibility complex (pMHC), Class I or II, to selectively engage disease-relevant T cells by incorporating diverse antigenic peptides of interest and choosing different MHC (or HLA) alleles to provide broad coverage for global patient populations.*

Signal 2: *Distinct co-stimulatory or co-regulatory signals, including cytokines, cell-surface receptors, and other targeting modalities, to control the activity of disease-relevant T cells.*

Fc Backbone: *Well-characterized protein construct from human antibodies to provide stability and ease of manufacturability that can be engineered to dial in or out biological and effector functions.*

While the elegant and dynamic nature of T cell-APC interactions is an essential component of immunity or tolerance (i.e., not reactive to self), it is often encumbered by many considerations including: (i) antigen availability and release for presentation by APCs; (ii) antigen uptake and processing efficiencies of an APC that generate the appropriate pMHC complex for the T cell; (iii) stability, amount and turnover of pMHC complexes displayed on the cell surface of an APC; (iv) the "right" kind of the APC phenotype for the desired biological outcome (e.g. activating versus tolerogenic); (v) effects of the local tissue/tumor microenvironment on the APC (e.g., immunosuppressive tumor microenvironments directly impede local APC function in the tumor lesion); and (vi) the absolute dependency on localization and encounter of the right T cell with the right APC in the individual.

These challenges could be potentially circumvented if the essential components for T cell activation (i.e., pMHC complex and appropriate co-stimulatory signals) are provided to the T cells directly with no dependency on the APCs. This is the core focus of the Immuno-STAT platform.

The Immuno-STAT: "***Immune Responses, on Cue"***

Through rational protein engineering, we are developing a proprietary class of Immuno-STAT drug product candidates to selectively modulate the activity of antigen-specific T cells directly in a patient's body. Our Immuno-STATs modulate T cell activity via two distinct signals, emulating or "mimicking" the signals presented naturally within the immune synapse when the body is mounting an immune response. We accomplish this signaling through the fusion of a TCR targeting pMHC complex (i.e., Signal 1) with co-stimulatory signaling molecules (i.e., Signal 2). This co-engagement of signals through the TCR and co-stimulatory receptor mimics and recapitulates the signals encountered in nature by T cells upon successful interactions with APCs. Hence, the Immuno-STATs harness "nature's cues" for antigen specificity, along with appropriate secondary activating or inhibitory signals, resulting in targeted T cell modulation.

During the last decade, there has been substantial progress in therapeutically modifying the function of immune cells, such as T cells, to either enhance tumor killing in the context of oncology, or protect tissue in the context of autoimmune disease. Much of the focus has centered on approaches that result in broad and non-specific/non-selective immune modulation (e.g., cytokines, cytokine inhibitors, checkpoint inhibitors, and bi-specifics) with significant challenges remaining to be addressed regarding specificity, efficacy and patient safety.

More recently in oncology, adoptive cell therapies (e.g., CAR-Ts, TCR-Ts or ACTs) have shown promise in a process requiring the extraction and modification of T cells from patients, activating, stimulating, and expanding them outside the body (i.e., ex vivo) and then infusing large numbers of cells back into the patients for potential therapeutic benefit. While these approaches have demonstrated some encouraging and impressive clinical responses in several hematologic malignancies, and some solid cancers, they are also associated with significant toxicities, including life threatening cytokine release syndrome and induction of self-reactivity. Moreover, labor-intensive technical requirements and expense associated with individualized T cell extraction, ex vivo amplification /modification, and patient re-infusion represent significant scaling and cost challenges. This is in addition to the rigorous procedures required to condition the patient prior to re-infusion might limit broad usage and eventual successful commercialization of this therapeutic modality.

We believe that our Immuno-STAT and other protein engineering drug product candidates may offer important key features of potential clinical differentiation and advantages over competing immunotherapy approaches, including:

- "Off-the-Shelf" and ready to use biologics that specifically target and selectively modulate disease relevant T cells;
- Administration directly into the patient's body without involving ex-vivo manipulation of T cells (e.g., cell therapy) or rigorous pre- and post- therapy conditioning of the patient;
- Freedom from the barriers of natural antigen presentation via antigen presenting cells, APCs, or the phenotype of APC; and
- Ability to target disease specific T cells with specificity, and selectively control the quantity and quality of a modulator/co-stimulator signal in contrast to global activation through systemic, non-selective signaling (e.g., rIL-2, bi-specifics, etc.).

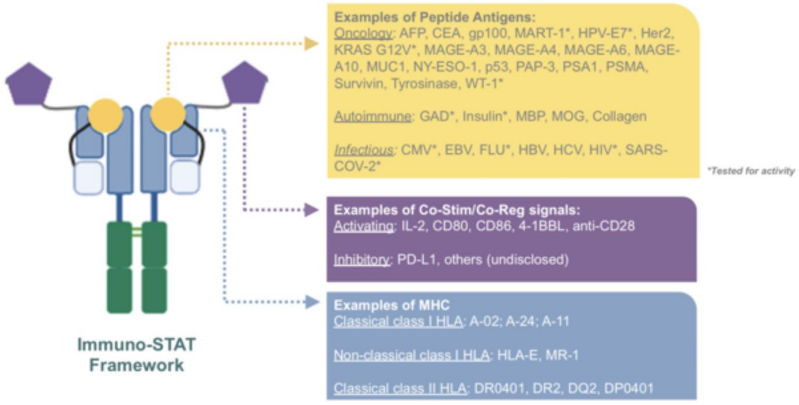
Therapeutic Applications

An insufficient T cell response may result in susceptibility to cancers or chronic infectious diseases. Conversely, an aberrant overactive T cell response against self-tissue results in autoimmune disease. In each of the above diseased states, the desired therapeutic approach should specifically target the dysregulated immune axis thereby providing the maximal potential for patient benefit.

- In the context of cancer and chronic infectious disease, Immuno-STATs are designed to selectively activate disease-specific T cells.
- For the treatment of autoimmune disease, Immuno-STATs are designed to selectively inhibit pathogenic autoreactive T cells. In those autoimmune diseases where the antigen(s) remain unknown, or entail multiple antigens, we have developed a biologic that has demonstrated in early studies to provide a potent signal 2, IL2-TGFβ, to Tregs where active autoimmune disease involves the endogenous presence of "Signal 1".

We plan to leverage the platform's modularity and versatility to design Immuno-STATs addressing the particular therapeutic objectives of T cell modulation. We achieve this through the flexibility of designing the various components of Immuno-STATs, including different co-stimulatory/co-inhibitory signals across disease areas (e.g., cancer vs. autoimmune) and different specific targeting peptides associated with various indications (e.g., head and neck cancer vs. breast cancer); and different global patient populations via targeting distinct HLA alleles. The modularity of this unique platform, as highlighted in the above figure, provides us the opportunity to generate therapeutic molecules across many different indications to serve distinct patient populations and allows the design of novel constructs incorporating structures having desired combined properties, e.g., IL2-TGF-β for Treg modulation. The figure below exemplifies the platform modularity to accommodate diverse T cell epitopes for different disease indications, distinct activating or inhibitory secondary signals, and the incorporation of diverse HLA molecules.

Immuno-STAT Platform Flexibility and Modularity Accommodates T cell Antigens and Immuno-modulatory Signals



Potential Commercialization Advantages

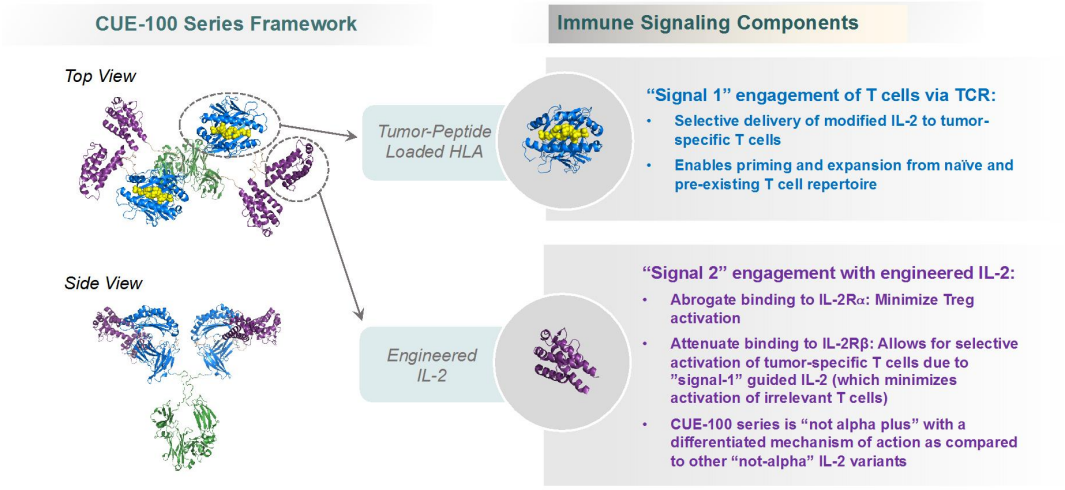
In addition to the selective control of T cell activity, we believe our Immuno-STAT platform provides us with several key points of potential superiority and differentiation over competing approaches:

- Access to a broad set of disease targets (extracellular and intracellular antigens) and patient populations (diverse HLA types) providing access to broad patient reach with the ability to address diverse disease conditions;
- Utilization of industry standard development and production process to support a cost-of-goods and supply chain similar to monoclonal antibodies providing for timely and efficient drug supply; and
- Standard delivery format (IV, SubQ) with a convenient dosing schedule (weekly, monthly) for the patient that can be administered by specialists and community-based physicians.

Immuno-Oncology

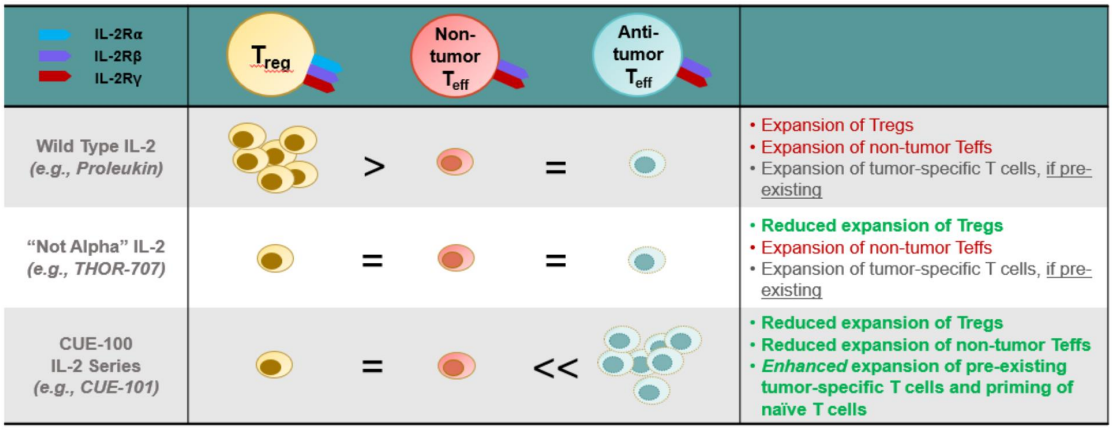
CUE-100 Series

Drug product candidates developed within our CUE-100 framework selectively stimulate the IL-2 receptor, a potent activator of the pathway critical to the growth, expansion and survival of T cells. We have engineered the CUE-100 framework to activate specific T cell populations through pMHC targeting of TCRs and selective deployment of the IL-2 signal. The IL-2 component of the framework has been modified to minimize engagement of the high affinity IL-2 receptor alpha chain (CD25) and reduce the affinity on the beta chain (CD122). This enables our Immuno-STATs to harness the cooperative nature of T cell signaling via preferentially activating tumor specific T-cells via the pMHC-TCR binding/targeting without systemically activating other T cell populations, thereby potentially mitigating the dose-limiting toxicities associated with current IL-2-based therapies. This effect is supported by our emerging CUE-101 monotherapy clinical data, where we have successfully dosed this molecule up to 8 mg/kg in second line and beyond R/M HNSCC patients. In contrast, other IL-2 variants, such as the variants of the so-called "not-alpha" IL-2 modalities, have remained in the low µg/kg dosing concentrations.



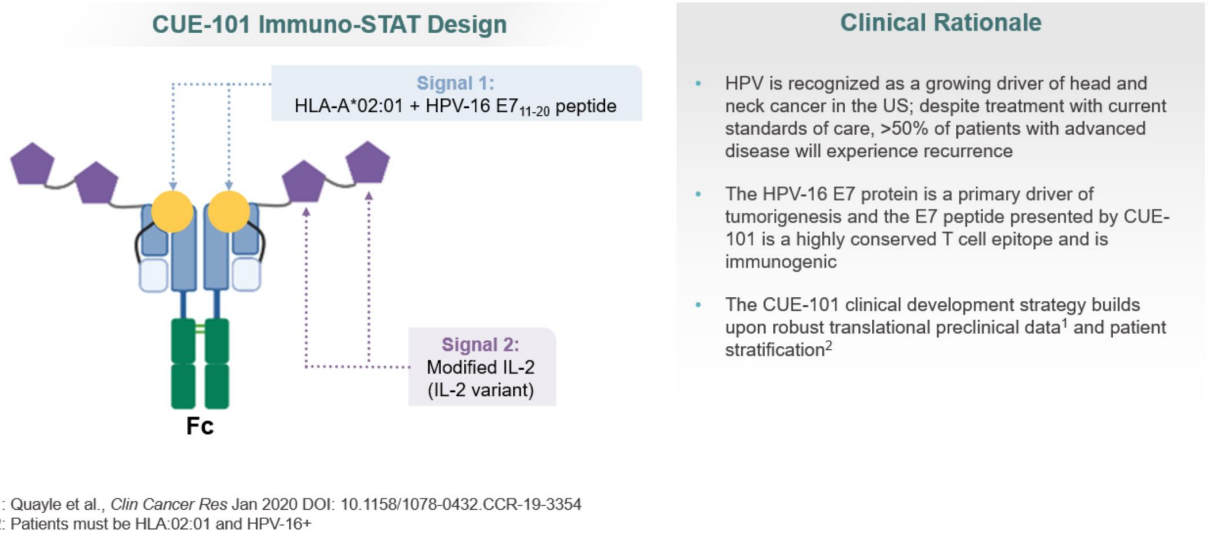
We believe the selective deployment of our rationally designed and engineered IL-2 molecules in context of the Immuno-STAT framework may provide superior differentiation over competing approaches focused on IL-2, including the "not-alpha" IL-2 variants wherein the modified IL-2 possesses no bias towards tumor-specific T cells. The graphic below summarizes some of the key biological factors and considerations of the different approaches.

CUE-100 Series: Differentiation Over Existing Modalities Targeting IL-2



CUE-101

Our lead product candidate from the CUE-100 framework, CUE-101, contains IL-2 and a pMHC composed of HLA-A*02:01 complexed with a dominant peptide derived from the human papilloma virus E7 protein (HPV-E7), as shown in the figure below. It is a fusion protein biologic designed to target and activate antigen-specific T cells to fight HPV-driven cancers.



1: Quayle et al., *Clin Cancer Res* Jan 2020 DOI: 10.1158/1078-0432.CCR-19-3354
2: Patients must be HLA:02:01 and HPV-16+

We have performed extensive in vitro and in vivo pre-clinical studies with CUE-101, which have been published in *Clinical Cancer Research (Quayle et. al. CUE-101, a Novel HPV16 E7-pHLA-IL-2-Fc Fusion Protein, Enhances Tumor Antigen Specific T Cell Activation for the Treatment of HPV16-Driven Malignancies https://clincancerres.aacrjournals.org/content/early/2020/01/15/1078-0432.CCR-19-3354)*

CUE-101 Clinical Development Plan

In September 2019, we dosed the first patient in a Phase 1 dose escalation clinical trial of CUE-101 for the treatment of HPV16-driven R/M HNSCC. This program is representative of the IL-2 based CUE-100 series for which we have generated a robust preclinical data package, including activation of human HPV specific T cells from human blood, as noted above. Our initial CUE-101 Phase 1 monotherapy trial focuses on R/M HNSCC, where patients will likely have received several lines of systemic therapy including checkpoint inhibition. In the fourth quarter of 2020, we extended this Phase 1 clinical trial into the front-line R/M HNSCC setting to evaluate the combination of CUE-101 with Merck's anti-PD-1 therapy KEYTRUDA. This combination study will offer the opportunity to assess relevant biomarkers of CUE-101 activity in peripheral blood when administered as a first line therapy. To date, we have generated promising early data sets from our Phase 1 monotherapy trial demonstrating dose dependent peripheral expansion of E7- specific CD8+ T cells as well as dose proportional pharmacokinetics. To date, CUE-101 has been well tolerated, demonstrating early signs of clinical activity, including signs of anti-tumor effect. A synopsis of data observed were recently presented at the SITC meeting in November 2020; https://www.cuebiopharma.com/wp-content/uploads/2020/11/Pai_CUE-101-01_SITC-2020-Abstract-354.pdf. During the first half of 2021, we plan to expand patient enrollment in selected cohorts to generate additional data that will inform our selection of the recommended Phase 2 dose.

We view R/M HNSCC as an important first market opportunity for CUE-101 with the potential for accelerated approval. Head and neck cancer was the seventh most common cancer worldwide in 2018 (650,000 new cases and 330,000 deaths), accounting for 3% of all cancers (51,540 new cases) and just over 1.5% of all cancer deaths (10,030 deaths) in the United States alone and more than 20,000 deaths each year in the US and Europe combined. A majority of these cancers are driven by HPV-16, which carries the E7 antigen targeted by CUE-101. Despite treatment with current standards of care, approximately 50% of patients with advanced disease will experience recurrence and significant quality of life impact. Patients with HPV-driven head and neck, cervical and genitoanal cancers represent an important unmet clinical need and underscore the opportunity for promising new therapeutics.

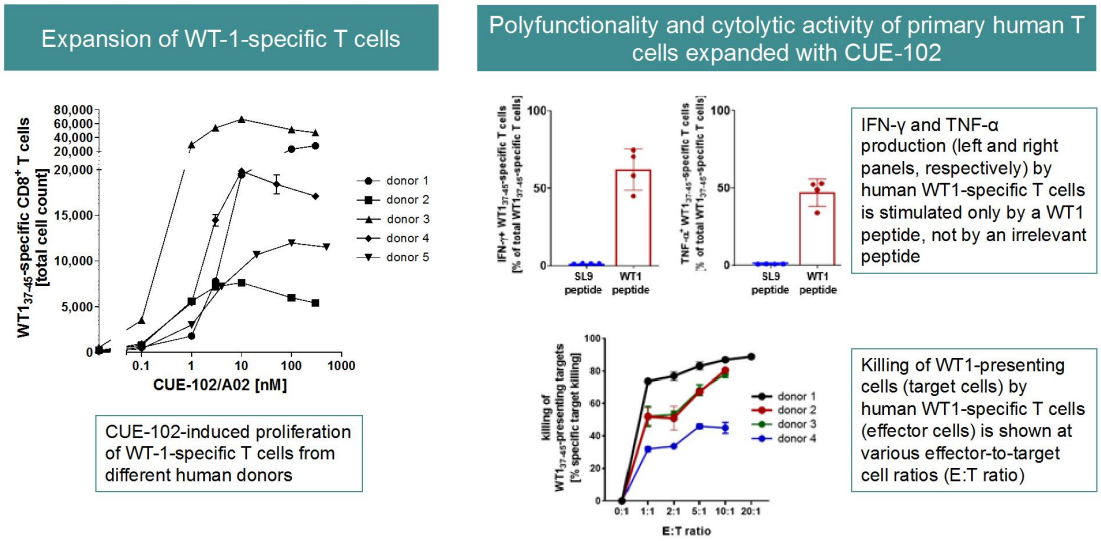
Cases of HPV-associated oropharyngeal cancer, induced primarily by HPV type 16, are increasing, in North America and western Europe. The fraction of head and neck cancers diagnosed as HPV-positive oropharyngeal cancers in the United States rose from just 16% in the 1980s to more than 70% in the 2000s. In addition to HNSCC, we also intend to pursue expansion studies for cervical cancers which we view as an attractive opportunity with significant unmet need and potentially other HPV-driven cancers (e.g., anal, vulvar, etc.). Outside of the US and EU, we will work with our partner LG Chem to commercialize CUE-101 in Asia, if approved.

CUE-102

CUE-102 leverages the same CUE-100 framework with a pMHC derived from the Wilms' Tumor protein, or WT1, an oncofetal antigen known to be over-expressed in a number of cancers, including solid tumors and hematologic malignancies. We have generated a comprehensive pre-clinical data set with CUE-102 to support our planned IND filing in the first half of 2022, highlights of which are shown in the figure below. We have observed ex-vivo expansion of WT1-specific T cells from primary human donors, and in vivo expansion of T cells in HLA-A02 transgenic mice treated with CUE-102. Importantly, we observed T cells expanded with CUE-102 activating polyfunctionality and cytotoxic killing of target cells, both of which are key attributes of a desirable anti-tumor T cell response. These data were also presented at the SITC meeting in November 2020. In 2021, we plan to continue to progress with our IND enabling studies for this program in collaboration with our partner LG Chem. Similar to CUE-101, CUE-102 is a fusion protein biologic built on the IL-2 based CUE-100 series designed to target and activate antigen-specific T cells to fight cancers—in the case of CUE-102, those overexpressing WT1.

WT1 is known to be expressed in more than 20 different cancers, including both solid tumors (e.g., ovarian, pancreatic, lung) and hematologic malignancies (e.g., acute myeloid leukemia, multiple myeloma, myelodysplastic syndromes). Patients with WT1 associated cancers represent an important unmet clinical need and underscore the opportunity for promising new therapeutics.

CUE-102: Expansion and Polyfunctionality of WT1-Specific T Cells



CUE-103

CUE-103 will also leverage the IL-2 based CUE-100 framework and target an antigen to be selected in collaboration with LG Chem. We are currently in active discussions with LG Chem regarding the evaluation of several candidate tumor antigens to be selected for the CUE-103 drug product candidate.

KRAS G12V

We are also developing a CUE-100 series Immuno-STAT for targeting the KRAS G12V mutation, which generates a T cell epitope in the context of HLA-A11. This mutation is associated with many solid tumors including colorectal carcinoma, or CRC, lung cancer and pancreatic cancer. We believe the KRAS G12V T cell epitope provides a novel opportunity for therapeutic intervention of a primary tumor driver like KRAS. Data suggesting the feasibility of production of HLA-A11 Immuno-STATs and their functional activity on cells expressing T cell receptors specific for G12V were recently disclosed at the SITC meeting in November 2020 (https://www.cuebiopharma.com/wp-content/uploads/2020/11/Cemerski_CUE-100_series_SITC_poster_553_FINAL.pdf). These data further underscore the modularity of the Immuno-STAT platform by extending the application to include additional HLA alleles, in this case HLA-A11.

CUE-200 Framework

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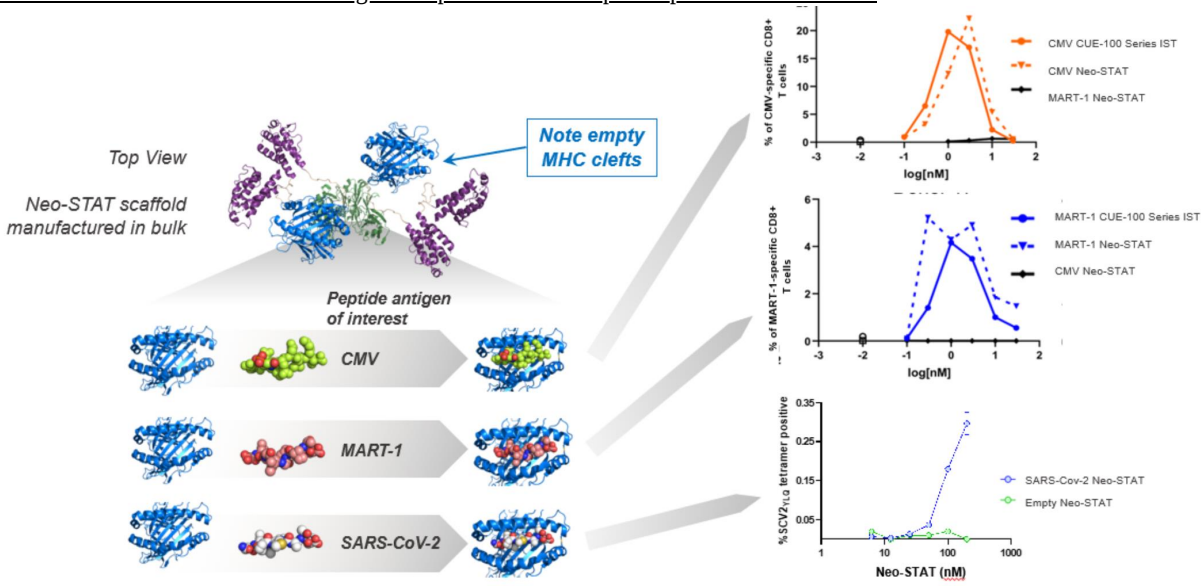
The CUE-200 framework utilizes co-stimulatory cell surface receptors, including CD80 and/or 4-1BBL, to reactivate exhausted T cells and is designed to promote enhanced antigen-specific T cell activation and function for the treatment of chronic infectious diseases. Both CD80/CD28 and 4-1BBL/4-1BB pathways have been implicated in enhancing anti-tumor T cell responses, including re-invigorating exhausted T cells. We see this as a unique opportunity to potentially harness and deploy these co-stimulatory signaling molecules to selectively modulate anti-tumor T cells. We continue to evaluate these mechanisms within the CUE-200 series via research at the Albert Einstein College of Medicine. Early data supporting these potential applications were disclosed at the SITC meeting in November 2020; https://www.cuebiopharma.com/wp-content/uploads/2020/11/Immuno-STAT-SITC-2020-Poster.pdf.

Neo-STAT Platform

In addition to the Immuno-STAT biologics described above, engineered as fusion protein biologics requiring dedicated stable cell lines for production of good manufacturing practice, or GMP, material, we are also developing a next generation derivative approach, referred to as Neo-STAT™, that we expect could significantly enhance productivity and increase our flexibility, including targeting multiple tumor antigens, neo-antigens and post-translationally modified epitopes. A key focus of the Neo-STAT platform is to generate a “peptide-less” or “empty” MHC pocket within the Immuno-STAT scaffold of the CUE-100 series. We then deploy peptide-conjugation chemistry to covalently attach peptides to the Neo-STAT scaffold. To that end, Neo-STAT has the potential to provide enhanced productivities and greater flexibility enabling the ability to generate therapeutic molecules targeting multiple tumor antigens, including post-translationally modified antigens (e.g., targeting of phospho-peptides from tumor cells), and to develop future strategies to deploy the Neo-STAT platform for personalized tumor neo-antigens. Importantly, the Neo-STAT framework should enable us to maximize our efficiencies – both from a cost- and timing-perspective.

We have made significant promising progress with our Neo-STAT platform, including proof of concept, or PoC, experiments demonstrating expansion and activation of primary human T cells with HLA-A02 Neo-STAT molecules deploying different T cell epitopes including tumor antigens (MART-1) or infectious antigens (CMV, SARS-Cov-2), as examples. We presented a detailed description on the protein engineering of the Neo-STAT platform at the Protein Engineering and Cell Therapy Summit, or PEGS, meeting in August 2020; https://www.cuebiopharma.com/wp-content/themes/cuebio/images/2020-PEGS-Poster.mp4. In 2021, we plan to continue to progress the Neo-STAT platform with specific efforts focused on generation of HLA-A02-based stable cell line to support our future GMP material and on peptide-conjugation process development to support the generation of our clinical grade material for future applications.

Neo-STATs and Immuno-STATs with the Same Antigenic Peptide Activate Peptide Specific CD8+ T Cells



Leveraging Immuno-STATs to address tumor resistance mechanisms through antigen presentation defects and HLA loss.

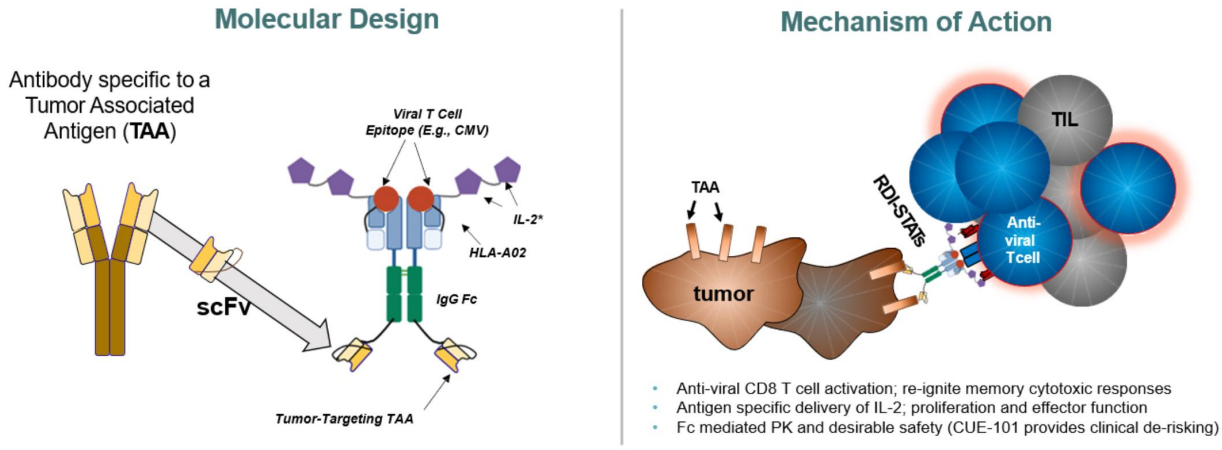
A significant and ongoing challenge in tumor immunotherapy pertains to tumor resistance or escape mechanisms whereby a subset of tumors are able to evade T cell detection, by suppressing or downregulating the production of proteins involved in antigen processing and presentation of tumor antigens/epitopes to the adaptive immune system, including T cells. Among the escape mechanisms are changes or mutations of the antigen processing compartment (e.g., TAP transporters) or antigen presentation molecules (such as HLA or ß2-microglobulin), which make the tumor invisible to the anti-tumor T cells. The loss of immunogenicity of the tumor is an adaptive evolution of the cancer to avoid immune detection – a stage defined as the escape phase of cancer immuno-editing. It is estimated that upwards of 20%-30% of patients may have tumor cells utilizing this escape mechanism.

Our approach to addressing this escape mechanism takes advantage of related observations from detailed cellular analysis of human cancer tissues revealing the significant presence of CD8+ T cells that are not specific for the tumor antigens but instead recognizing viral antigens (such as EBV, flu or CMV). In other words, a significant fraction of the protective memory anti-viral T cell repertoire localizes to the tumor tissue, likely in response to chemotactic signals that are agnostic of specificity of the T cells.

Hence, we have investigated the opportunity to leverage the Immuno-STAT platform to generate therapeutic molecules to re-direct or “trick” the viral T cell repertoire present in the tumor environment to recognize and kill the cancer cells, including those that have lost the expression of HLA molecules or the ability to present antigen effectively. We believe this approach has several unique advantages: (i) it circumvents the tumor’s lack of HLA or antigen presentation; (ii) it harnesses a pre-existing robust anti-viral protective T cell repertoire within the host; (iii) it is an opportunity to alter the tumor microenvironment via localizing an active immune response; (iv) from a safety perspective, this approach is very distinct from other bispecific molecules that indiscriminately activate every T cell; and (v) it leverages the clinical de-risking provided by CUE-101, especially as it relates to the IL-2 molecules.

The schematic below describes the generation of viral-specific Immuno-STATs that can be tethered to a tumor cell via binding to tumor cell-surface antigens (e.g., Trop2, PSMA, mesothelin etc). Thus, in this manner the tumor is coated with a viral Immuno-STAT to make it appear like a virally-infected cancer cell, which can then be recognized by the anti-viral T cells that populate the host and the tumor tissue and become activated by the Immuno-STAT IL-2 to kill the tumor cell. Through rational protein engineering we have generated early proof of concept, or PoC, molecules that provide us confidence with the applicability of these unique bispecific Immuno-STATs for cancer immuno-therapy. We call these “re-directed” Immuno-STATs, or RDI-STATs.

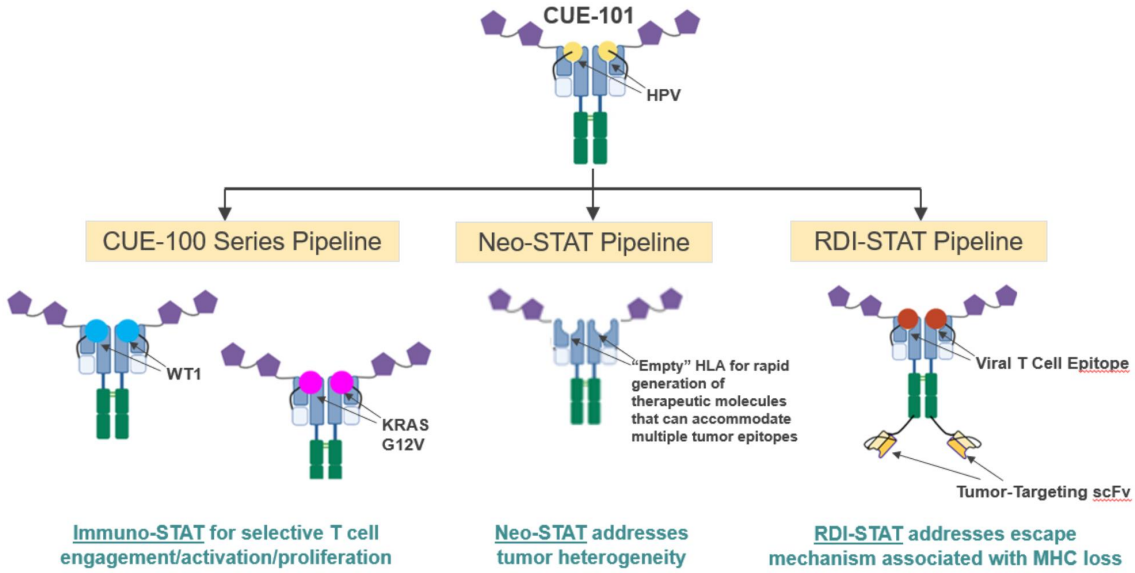
Viral T Cell Redirection via RDI STATs : Immuno-STAT Framework with Tumor Targeting TAA



Redirected Immuno-STATs (RDI-STATs) can leverage the patient's existing protective viral T cell repertoire to target tumors, regardless of the tumor HLA expression.

All of the above applications of the Immuno-STAT and Neo-STAT platform may benefit from the ongoing risk-reducing data generation via the current clinical studies with CUE-101, especially as it relates to the tolerability profile of the engineered IL-2 variant and this novel biologics platform. This is due to the fact that the core framework of the CUE-100 series remains essentially the same for each drug candidate, except for the targeting peptide epitope within the MHC pocket.

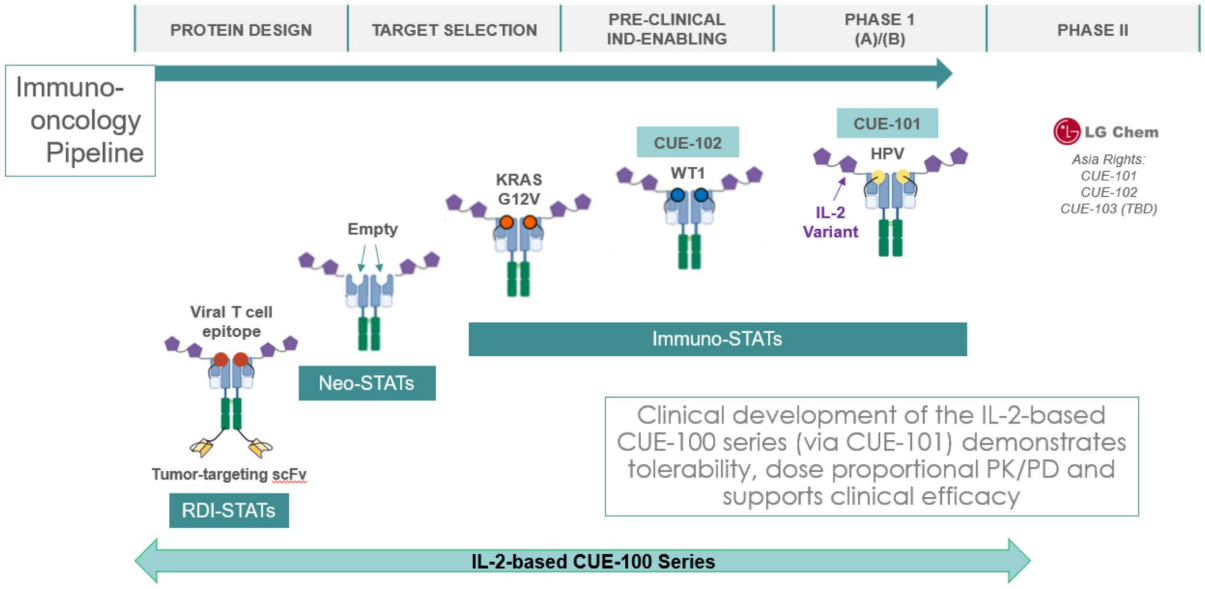
Clinical risk-reduction of CUE-100 Series via CUE-101 Clinical Studies Enables Broad Pipeline of Platform Opportunities



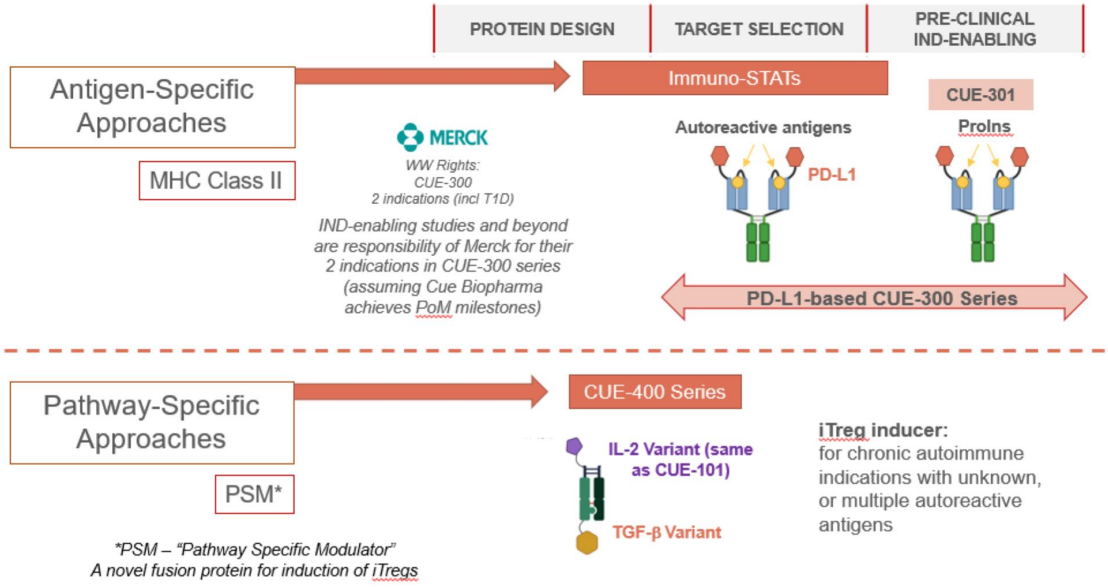
We have implemented a strategy of exploiting the potential applications of the CUE-100 series framework into multiple derivative constructs possessing specific properties and mechanistic activities to address diverse clinical conditions involving immune imbalance. Through this approach, we have designed and engineered various biologic constructs each

possessing desired activities with the potential for addressing underlying immune re-balancing to restore better health. Through this approach, as depicted in the figure below, we have exploited the CUE-100 series to develop a growing pipeline of Immuno-STATs for oncology, have created the derivative constructs of Neo-STAT and "re-directed" Immuno-STATs (or RDI-STATs) to address resistance mechanisms, and have utilized the frameworks modularity to engineer antigen-specific immune suppressors, (e.g, PD-L1) for treating autoimmune diseases (CUE-300 series) with known auto-antigens (such as T1D). We have also deployed the engineered IL-2 variant from the CUE-100 series to design a bi-specific molecule possessing both IL-2 and TGF-beta (CUE-400 series) for pathway specific modulation to stimulate iTregs in autoimmune diseases where the autoantigens are unknown or not well characterized. We believe these various derivatives have a reduced risk-profile due to the fact that CUE-101 has been well tolerated throughout the dose escalation Phase 1 study and, by implication, constructs designed/derivatized from this series have a lowered risk-profile.

Platform Development and Progress in Immuno-oncology



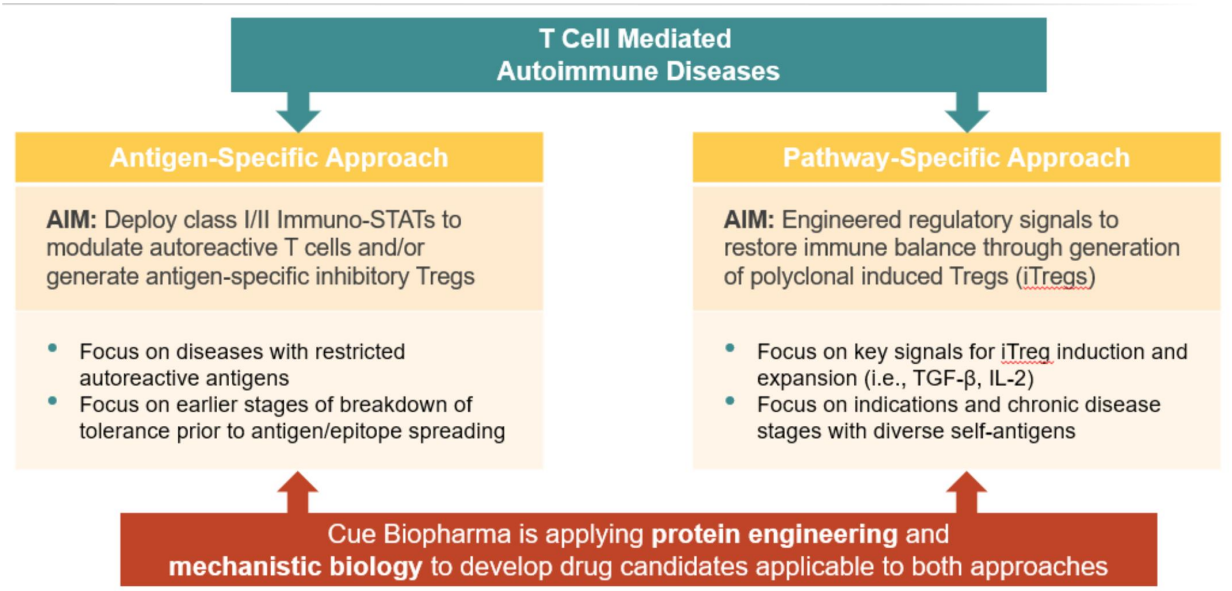
Platform Development and Progress in Auto-immune and inflammation



Autoimmune Disease

For applications in autoimmune, or AI, diseases, our strategy has focused on two broad themes of antigen-specific modulation and pathway-specific modulation for controlling autoreactive T cell responses. Both approaches complement each other and offer unique opportunities for selective immune re-set of the dysfunctional compartment. The antigen-specific approach is pertinent to diseases with restricted or well-characterized auto-antigens (such as type 1 diabetes, or T1D) and deploys the Immuno-STATs to directly modulate the autoreactive T cells. The pathway-specific approach exploits signals that can induce and sustain regulatory T cells, which can then control a broad population of autoreactive T cells. Hence, this approach may be more applicable to diseases with diverse unknown antigens. It is conceivable that the specific signals for antigen specific regulatory T cells, or Treg, induction could be deployed in an Immuno-STAT framework for generation of antigen-specific Tregs.

Approaches to Modulate Autoreactive T Cell Responses



Antigen-specific approach: CUE-300 Immuno-STAT Framework

The CUE-300 framework builds upon our antigen-specific approach for AI and has been focused on class II HLA alleles that are recognized by CD4+ T cells. It has the potential to target a broad range of addressable autoimmune diseases by selectively modulating disease-associated CD4+ T cells so that healthy cells and tissue are protected from immune attack.

To inhibit autoimmune disease associated T cells, Immuno-STATs are engineered to work via two general strategies:

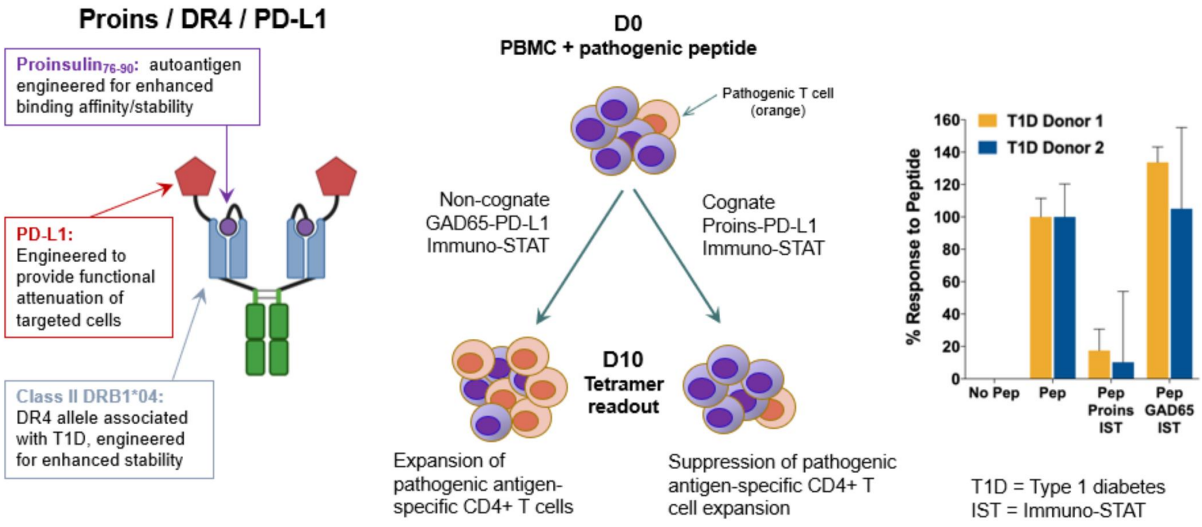
- Inhibition (or selective ablation) of autoreactive T cells by selectively delivering inhibitory signals; or
- Selective expansion of antigen specific Tregs to control aberrant activation of autoreactive T cells.

Immuno-STAT frameworks for AI disease will be designed to influence a subset of T cells known as CD4 T cells. CD4 T cells recognize peptides in the context of MHC class II proteins. Therefore, prototypic Immuno-STAT frameworks in autoimmunity would rely on MHC class II recognition by CD4 T cells. This is distinct from the MHC class I recognition by CD8 T cells that is the basis of our current oncology pipeline.

Consistent with our strategy to establish focused partnerships with leading pharmaceutical or biotechnology organizations to enhance capacity and further our development efforts on selected programs, in November 2017 we entered into a collaboration agreement with Merck for a partnership to research and develop proprietary biologics that focus on two autoimmune diseases, type 1 diabetes, or T1D, and an undisclosed indication. This agreement was recently extended through 2021 to support further development and identification of these targeted biologics. We view this collaboration agreement as a component of our development strategy since it will allow us to advance the CUE-300 series drug product candidates for selected autoimmune programs in partnership with a world class pharmaceutical company, while also providing us opportunities in autoimmune diseases beyond our partnered programs as well as continuing our focus on our more advanced cancer programs.

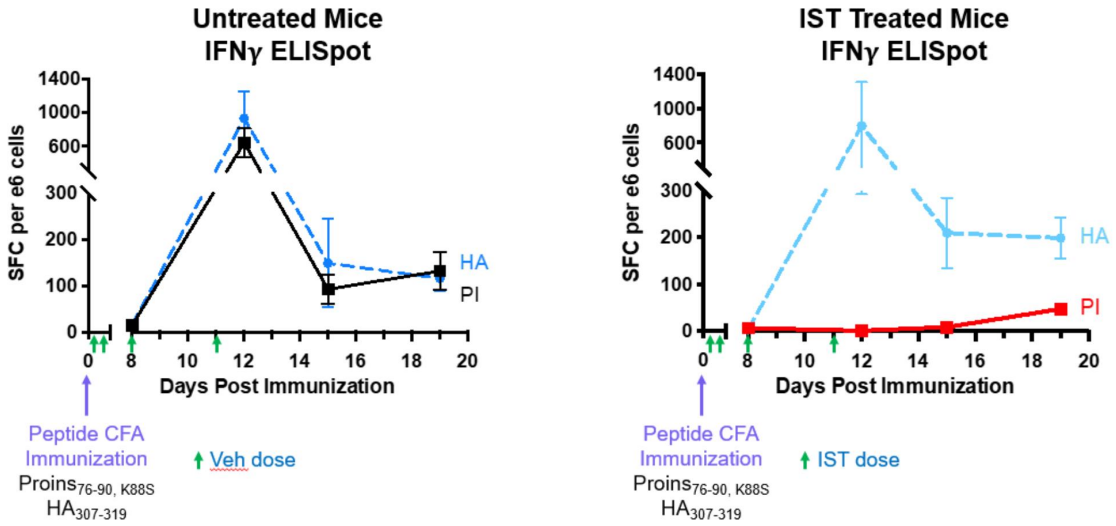
During 2021, we will continue to generate data to support proof-of-mechanism and inform the path forward for this program. CUE-301 is an example of an Immuno-STAT designed for the modulation of CD4+ T cells under the Merck collaboration agreement. In this instance Immuno-STATs with the human class II MHC molecule, HLA-DR0401, or DR4, were generated along with an epitope from pro-insulin (a known autoantigen in type 1 diabetes) and PD-L1 molecule for selective down-modulation of CD4+ T cells reactive to the pro-insulin peptide. The Pro-Insulin-DR4-PD-L1 Immuno-STATs (CUE-301) selectively inhibited the activation and expansion of insulin-specific T cells. In contrast, Immuno-STAT molecules harboring a peptide from glutamic acid decarboxylase, or GAD, another autoantigen in type 1 diabetes, had no effect, hence demonstrating selectivity and specificity. These data are summarized in the graphic shown below.

Framework and Selective Suppression of Proins-specific T cells In Vitro



LEGEND: CUE-301 is Cue's first Immuno-STAT targeting an autoimmune disease, Type 1 diabetes. The CUE-300 series differs from the CUE-100 series in that the pMHC module is comprised Class II MHC with a DRB1*04 HLA allele and an immune checkpoint ligand, programmed death receptor-1 ligand (PD-L1), as the co-regulatory (or co-inhibitory) module.

Recently, we have demonstrated the in vivo activity with CUE-301 (Proins-DR4-PDL1 IST), as shown in the figure below. HLA-DR0401 transgenic mice were immunized with a mixture of Proinsulin peptide (Proins $_{76\text{-}90,\ K88S}$) and a T cell epitope from the flu virus hemagglutinin protein ($HA_{307\text{-}319}$). Following immunization, mice were treated with a vehicle (left panel) or CUE-301 (right-panel, "IST dose"). T cell activation and expansion was determined at various days post-immunization/treatment via interferon-gamma ELISpot assay. As shown in the left panel, vehicle-treated mice raised comparable T cells to both Proins and HA. In contrast, as shown in the right panel, the mice treated with CUE-301 ("IST Treated Mice") showed selective abrogation of the Proins-specific T cells while still mounting a T cells response to HA. These in vivo data suggest that selective modulation of T cells with ISTs can be achieved for applications in AI diseases.



Additional mechanistic datasets that further extend in vitro and in vivo observations were recently presented at an autoimmune meeting in January 2021; https://www.cuebiopharma.com/wp-content/uploads/2021/01/20201223_ASIT-Summit-2021.pdf.

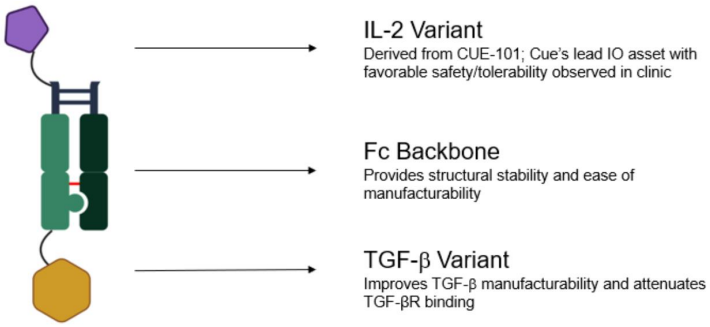
Pathway-specific approach: CUE-400 series

The CUE-400 series is focused on the generation of a novel bispecific molecule for differentiation and expansion of iTregs for applications in autoimmune diseases, graft versus host disease, or GVHD, and transplant rejection. The primary goals of developing the CUE-400 series of molecule is to harness signals that can generate large numbers of regulatory T cells, or Tregs, in the patient to control a broad repertoire of autoreactive and inflammatory T cells. This is especially important in controlling aberrant activation of autoreactive (or allo-reactive) T cells in those conditions where the antigen(s) are unknown or involves multiple antigens, or in chronic stages of autoimmune diseases with extensive epitope spreading involving many different antigens. We believe that harnessing Tregs is an attractive opportunity for re-setting immune balance and restoring functional tolerance.

Our focus has centered on expanding functional iTregs, which we believe offer untapped opportunities in autoimmune diseases and graft rejection. In contrast to natural Tregs, or nTregs, that are present in small numbers and constitutively express CD25 (IL-2R alpha), iTregs are derived from the vastly larger component of the normal CD4+ T cell repertoire that is CD25-negative. In contrast to CD25-biased IL-2 variants/muteins that are being pursued for nTregs, our approach incorporates both IL-2 and TGF-beta signals, which are needed for induction and expansion of iTregs. Importantly, the IL-2 signal in our approach is not biased to CD25 (IL-2R alpha) receptor subunit since the vast majority of the peripheral CD4+ T cell repertoire does not express CD25. We believe that harnessing iTregs over nTregs may have several key advantages: (i) the numbers of nTregs is limited (~2-5% of the CD4+ T cell compartment) since they come differentiated from the thymus with a fixed TCR repertoire, while iTregs can be readily generated from the vast majority of the conventional CD4+ T cell compartment that is diverse and adaptable to the local microenvironment; (ii) from a therapeutic manipulation perspective, we believe the opportunity to convert pathogenic autoreactive T cell into a regulatory phenotype is an attractive opportunity for immune re-set and restoration of immune balance; and (iii) the differentiation of iTregs can be achieved directly in the patient's body as long as the requisite two key modulators (IL-2 and TGF-beta) can co-localize to the same T cell. In chronic autoimmune diseases, autoreactive T cells are constantly recognizing self-antigens (i.e. Signal 1 of TCR engagement is perpetual), which provides us with an attractive opportunity to co-deliver the IL-2 and TGF-beta to these T cells to convert them into an iTreg phenotype.

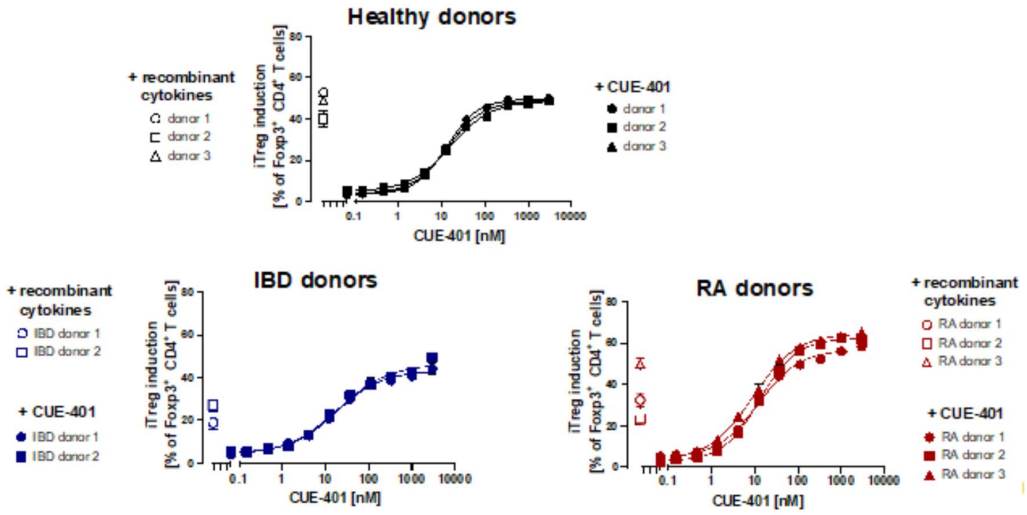
Harnessing structure-based rational protein engineering, we have generated the first molecule from our CUE-400 series, CUE-401, which is a novel IL-2-TGF-beta fusion protein. The structure of CUE-401 is shown below – it has one molecule of IL-2 fused to an Fc along with a masked TGF-beta molecule. Importantly, the IL-2 variant in CUE-401 has already demonstrated tolerability in the clinic since it is the same IL-2 variant that is present in our current clinical candidate CUE-101, albeit in a different valency (CUE-101 harbors 4 molecules of an affinity attenuated IL-2 along with bivalent tumor-peptide-HLA molecules to activate tumor-specific T cells).

CUE-401: Opportunity to Enhance Specificity and Selectivity



We have demonstrated that CUE-401 generated iTregs from conventional CD4+ T cells (as measured by robust induction of the master Treg transcription factor FoxP3). As shown below, we were able to generate iTregs from conventional CD4+ T cells from healthy subjects as well as from patients suffering from autoimmune diseases (RA -rheumatoid arthritis; IBD – inflammatory bowel disease). Importantly, in preclinical models, CUE-401 generated iTregs in equivalent or higher numbers when compared to the recombinant wild-type IL-2 and TGF-beta cytokines ("+recombinant cytokines", as noted in the figure below). Functional assessments have confirmed that these iTregs can suppress T cell responses. Ongoing studies in preclinical models provide additional support for in vivo conversion of iTregs upon single-dose administration of CUE-401.

Induction of iTregs in Healthy Subjects and Patients



In contrast to IL-2-directed approaches aiming to expand the limited number and repertoire of nTregs, we believe induction and conversion of the pathogenic autoreactive T cells into iTreg may offer a more meaningful and lasting benefit to the patient.

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 amended on October 30, 2018, 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, relating to Licensed Products that we may enter into. 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 creditable against any royalty payments we pay under the Einstein License. For the year ended December 31, 2020, we paid $75,000 to Einstein in license and license maintenance fees under the Einstein License.

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. As of December 31, 2020, we had paid to Einstein an aggregate amount of $150,000 in milestone payments.

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, 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.

Einstein may also terminate the Einstein License in the event we are convicted of certain felonies relating to the manufacture or use of Licensed Products.

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;

- submit an IND application to the FDA or similar foreign regulatory agency within a number of years from the Effective Date;
- 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 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 (30) 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 2 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 Merck

On November 14, 2017, we entered into an Exclusive Patent License and Research Collaboration Agreement, or the Merck Agreement, with Merck for a partnership to research and develop certain of the Company's proprietary biologics that target certain autoimmune disease indications, or the Initial Indications. We view this Merck Agreement as a component of our development strategy since it will allow us to advance our autoimmune programs in partnership with a world class pharmaceutical company, while also continuing our focus on our more advanced cancer programs. The research program outlined in the Merck Agreement entails (1) our research, discovery and development of certain Immuno-STAT drug candidates up to the point of demonstration of certain biologically relevant effects, or Proof of Mechanism, and (2) the further development by Merck of the Immuno-STAT drug product candidates that have demonstrated Proof of Mechanism, or the Proposed Drug Product Candidates, up to the point of demonstration of all or substantially all of the properties outlined in such Proposed Drug Product Candidates' profiles as described in the Merck Agreement.

For the purposes of this collaboration, we granted to Merck under the Merck Agreement an exclusive license under certain of our patent rights, including a sublicense of patent rights licensed from Einstein, to the extent applicable to the specific Immuno-STAT drug product candidates that are elected to be developed by Merck. In addition, so long as Merck continues product development on a Proposed Drug Product Candidate, we are restricted from conducting any development activities within the Initial Indication covered by such Proposed Drug Product Candidate other than pursuant to the Merck Agreement.

In exchange for the licenses and other rights granted to Merck under the Merck Agreement, we received a $2.5 million nonrefundable up-front payment and may be eligible to receive additional funding in developmental milestone payments, as well as tiered royalties if all research, development, regulatory and commercial milestones agreed upon by both parties are successfully achieved. Excluding the upfront payment described above, we are eligible to earn up to $101 million for the achievement of certain research and development milestones, $120 million for the achievement of certain regulatory milestones and $150 million for the achievement of certain commercial milestones, in addition to tiered royalties on sales, if all pre-specified milestones associated with multiple products across the primary disease indication areas are achieved. The Merck Agreement requires us to use the first $2.5 million milestone payment we receive under the agreement to fund contract research. The amount of the royalty payments is a percentage of product sales ranging in the single digits based on the amount of such sales. As of December 31, 2020, we recorded approximately $2.2 million in collaboration revenue related to this agreement.

The term of the Merck Agreement extends until the expiration of all royalty obligations following a product candidate's receipt of marketing authorization, at which point Merck's licenses and sublicenses granted under the agreement shall become fully paid-up, perpetual licenses and sublicenses, as applicable. Royalties on each product subject to the Merck Agreement shall continue on a country-by-country basis until the expiration of the later of: (1) the last-to-expire patent claiming the compound on which such product is based and (2) a period of ten years after the first commercial sale of such product in such country.

In November 2020, we extended the research collaboration terms of this agreement through December 31, 2021 to support further development and identification of targeted biologics for the treatment of autoimmune disease. Notwithstanding the foregoing, Merck may terminate the Merck Agreement at any time by providing us 30 days' notice. The Merck Agreement may also be terminated by either party if the other party is in breach of its obligations thereunder and fails to cure such breach within 90 days after notice or by either party if the other party files for bankruptcy or other similar insolvency proceedings.

Our Collaboration Agreement with LG Chem

Effective November 6, 2018, we entered into a Collaboration, License and Option Agreement, or the LG Chem Agreement, with LG Chem, related to the development of Immuno-STATs focused in the field of oncology.

Pursuant to the LG Chem Agreement, we granted LG Chem an exclusive license to develop, manufacture and commercialize our lead product, CUE-101, as well as Immuno-STATs that target T-cells against two additional cancer antigens, or 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. We retain rights to develop and commercialize all assets included in the LG Chem Agreement in the United States and in global markets outside of the LG Chem Territory. Under the LG Chem 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 commercialization 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 Agreement related to LG Chem's option for an Additional Immuno-STAT but generally does not become effective unless and until LG Chem exercises its option, other than certain select provisions including the length of the option period and representations, warranties and covenants of the parties. If LG Chem exercises this option, which expires on April 30, 2021, then the other provisions of the Global License and Collaboration Agreement, including the license to the Additional Immuno-STAT from us to LG Chem and the terms and conditions for such license, will become effective. We will retain an option to co-develop and co-commercialize the additional program worldwide. In an amendment effective November 5, 2020, we extended the time for LG Chem to exercise this option until April 30, 2021.

Under the terms of the LG Chem Agreement, LG Chem paid us a $5.0 million non-refundable, non-creditable upfront payment and purchased approximately $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 Agreement. We are also eligible to receive additional aggregate payments of approximately $400 million if certain research, development, regulatory and commercial milestones are successfully achieved. In addition, the LG Chem 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 Agreement.

Pursuant to the LG Chem 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. Furthermore, should the parties enter into a Global License and Collaboration Agreement for an Additional Immuno-STAT, LG Chem will pay us a one-time, non-refundable, non-creditable upfront payment and we will be eligible to receive up to approximately $470 to $675 million in fees and milestone payments as well as tiered royalty payments on future global sales that range from high-single digit to mid-double digit percentages in the United States and mid-single to low-double digit percentages outside of the United States. The amount of fees and milestone payments, as well as whether we receive royalty payments, will depend on when LG Chem nominates the Additional Immuno-STAT, the number of alleles selected by LG Chem and whether we exercise our option to co-develop and co-commercialize the additional program worldwide, in which case we would share costs and profits instead of receiving royalties and post-option-exercise milestones. As of December 31, 2020, we recorded approximately $5.5 million in collaboration revenue related to this agreement.

The LG Chem Agreement includes various representations, warranties, covenants, indemnities and other customary provisions. LG Chem may terminate the LG Chem 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 Agreement. Either party may terminate the LG Chem 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 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 Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the applicable royalty term.

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 licensor, 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, 2020, we owned or had licensed fifty-two issued patents, thirty-five pending patent applications in the United States (including thirteen pending U.S. provisional patent applications), eighteen pending international PCT applications and 147 pending foreign patent applications intended to protect the intellectual property underlying our technology. 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, as well as specific biologic molecules, drug product candidates and methods of treatment using our Immuno-STATs. 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. non-provisional priority filing date, subject to available extensions. They are thus set to expire no earlier than dates ranging from 2033 to 2040, although there can be no assurance that any of the patent applications will be granted.

Competition

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.

Furthermore, immunotherapy technologies are advancing at a rapid pace and we anticipate competing with companies developing bi-specific antibodies attempting to deliver T cell activating cytokines, such as IL-2 (e.g., Amgen Inc., or Amgen, Immunocore Holdings plc, or Immunocore, and Roche Holding AG, or Roche), cell therapies for activating or creating cancer-relevant T cells outside the patient’s body, i.e., ex vivo, (e.g., Bristol-Myers Squibb Company, or Bristol-Myers Squibb, Gilead Sciences, Inc., or Gilead, and Novartis AG, or Novartis), antibody-drug conjugates (e.g., Gilead, Roche, Seagen Inc., or Seattle Genetics), immune checkpoint inhibitors (e.g., Bristol-Myers Squibb, Merck, and Pfizer Inc., or Pfizer), and modified cytokines, such as pegylated IL-2 for slower-release (e.g., Bristol-Myers Squibb/Nektar, who recently announced a combination study of BEMPEG plus KEYTRUDA in a Phase 2/3 clinical trial in first-line squamous cell carcinoma of the head and neck), as a means of reducing the unwanted collateral adverse effects of wild type IL-2, genetically-modified IL-2 for ablating the alpha subunit activity to reduce CD4 activation in favor of CD8 (e.g. Neoleukin Therapeutics, Inc., or Neoleukin, Roche, and Sanofi), and antigen-specific targeting of cytokines through nanoparticles (e.g., Neximmune). [We believe that our approach provides Cue with the competitive advantage of antigen-specific targeting of cytokines, such as IL-2 by engineering proteins with a targeting moiety, i.e, peptide-MHC, coupled to genetically modified cytokines, such as not-alpha IL2 for enhancing CD8 activation and attenuated Beta-subunit for biasing the peptide-MHC/TCR affinity, thereby providing cancer antigen specificity.

We expect our lead product candidate, CUE-101, will compete with other product candidates for the treatment of HPV+ cancers. While there is currently no FDA-approved therapy that specifically targets HPV for HPV+ cancers, there are multiple product candidates in clinical development, including cell therapies (e.g., Gilead and Rubius Therapeutics, Inc., or Rubius), and cancer vaccines (e.g., BioNTech SE, or BioNTech, Hookipa Pharma Inc., or Hookipa Pharma, Inovio Pharmaceuticals, Inc., or Inovio, and ISA B.V., or ISA Pharma). Therapies not specific to HPV are also being developed to address HPV+ cancers, including immune checkpoint inhibitors as well as tumor infiltrating lymphocytes by Iovance Biotherapeutics, Inc., or Iovance Biotherapeutics.

Our corporate objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability, and safety. We expect any drug product candidate that we commercialize, either independently or with our strategic partners, will compete with existing, market-leading products.

There are many companies focused on the development of small molecules and antibodies for cancer treatment. Our core competitors include pharmaceutical and biotech organizations, as well as academic research institutions, clinical research laboratories and government agencies that are pursuing research activities in the same therapeutic area. 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 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, 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.

Licensure and Regulation of Biologics in the United States

In the United States, our candidate products would be 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 its implementing regulations and guidances. 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 an applicant to delays in the conduct of the study, regulatory review and approval, and/or administrative or judicial sanctions. An applicant 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 regulations;

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

- submission to the FDA of an 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 Biologic License Application, or 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 cGMP requirements and to assure that the facilities, methods, and controls 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 user Prescription Drug User Free Act, or PDUFA, securing FDA approval of the BLA and licensure of the new biologic product; 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 and Investigational New Drug Application

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. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application.

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 at any time during the IND process, 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 chemistry, manufacturing, and controls. 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 I 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.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain regulatory requirements of the FDA in order to use the trial as support for an IND or application for marketing approval. Specifically, the FDA requires that such trials be conducted in accordance with GCP, including review and approval by an independent ethics committee and informed consent from subjects. The GCP requirements encompass both ethical and data integrity standards for clinical trials. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign trials are conducted in a manner comparable to that required for clinical trials in the United States.

Further, 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 FDA, 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 safety monitoring board, or DSMB. 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 DSMB 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 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 post-approval trials are typically referred to as Phase 4 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 Phase 4 clinical trial requirement or to request a change in the product labeling. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Information about clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness 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 applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, 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 applicant may request an amendment to the plan at any time.

For products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, 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 applicant, 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. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Administration Safety and Innovation Act, or FDASIA. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. Congress amended the FDA Reauthorization Act of 2017, or FDARA. Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the Pediatric Research Equity Act. Under the amended section 505B, beginning on August 18, 2020, the submission of a pediatric assessment, waiver or deferral will be required for certain molecularly targeted cancer indications with the submission of an application or supplement to an application.

Compliance with cGMP Requirements

Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

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. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs 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.

Review and Approval 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 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 2021 is $2,875,842 for an application requiring clinical data. The sponsor of a licensed BLA is also subject to an annual program fee, which for fiscal year 2021 is $336,432. 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 has 60 days after submission of the application to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency’s threshold determination that it is sufficiently complete to permit substantive review. 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 applicant, 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 applicant otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure, and potent and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure, and potent. On the basis of the FDA’s evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of non-clinical and clinical trial sites to assure compliance with GCPs, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the application is not approved, the FDA will issue a complete response letter, 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 complete response letter 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 an applicant 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.

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.

If the FDA approves a new product, it 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 Phase 4 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-market 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.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it 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 product 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.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. 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 priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

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 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 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.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

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. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor’s agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product’s clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for drug product candidates approved under accelerated regulations are subject to prior review by the FDA.

Real-Time Oncology Review of Supplemental NDAs

Through its Oncology Center for Excellence, or 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 an applicant 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 and effectiveness. 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 applicant 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 applicant 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 applicant 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 applicant 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 cGMP 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 cGMP 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. 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.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. 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.

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 DOJ, or the Office of the Inspector General of the Department of Health and Human Services, 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.

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 and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor or the sponsor is unable to provide sufficient quantities.

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 marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. 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 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." As of January 1, 2021, the FDA has approved 29 biosimilar products for use in the United States. No interchangeable biosimilars, however, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidances are expected to be finalized by the FDA in the near term.

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.

Under the BPCIA, 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. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law. Since the passage of the BPCIA, many states have passed laws or amendments to laws, including laws governing pharmacy practices, which are state-regulated, to regulate the use of biosimilars.

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 a clinical investigation involving human beings is begun 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 USPTO 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.

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 applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2021, the standard fee is $365,657 and the small business fee is $91,414.

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.

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, an applicant 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 European Union 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 European Union.

Clinical Trial Approval

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will become directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State.

The Regulation was published on June 16, 2014 but has not yet become effective. As of January 1, 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020. In late 2020, the EMA indicated that it plans to focus on the findings of a system audit; improving the usability, quality and stability of the clinical trial information system; and knowledge transfer to prepare users and their organizations for the new clinical trial system. The EMA has indicated that the system will go live in December 2021.

Parties conducting certain clinical studies must, as in the U.S., post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the EU

In March 2016, the European Medicines Agency, or 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

Applicants 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 European Union regulatory system, an applicant must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in European Union Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, an applicant 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 European Union, 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 applicant 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.

Regulatory Data Protection in the European Union

In the European Union, 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.

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 applicant 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.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable by up to two years). On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of drug product candidates in the UK, as the UK legislation now has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact regulatory requirements for drug product candidates and products in the UK in the long-term. The MHRA has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK's regulatory position on medicinal products evolves over time.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the European Union's General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like an European Union member state in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected.

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 U.S., 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 will be 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.

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 the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians 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 ACA 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 2030 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.

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, which was signed by President Trump on December 22, 2017, 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 December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the PPACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the PPACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the PPACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden Administration withdrew DOJ's support for this lawsuit. A ruling by the Court is expected sometime this year. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the PPACA, including directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the PPACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the PPACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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 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.

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, 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 third countries that impose similar obligations.

Human Capital

As of December 31, 2020, we had 50 full-time employees and two part-time employees. Substantially all of our employees are in Cambridge, 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. 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 diversity; and employee health and safety.

We are committed to the health and safety of our employees. During 2020, as a result of COVID-19 pandemic, we implemented additional safety protocols intended to help minimize the risk of virus transmission to our employees, including the establishment of remote working standards, pausing all non-essential travel worldwide for our employees, and limiting employee attendance at industry events and in-person work-related meetings, to the extent those events and meetings are continuing.

Status as an Emerging Growth Company

We are an “emerging growth company” as that term is defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Section 102(b)(1) of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until. private companies (*i.e.*, those that have not had a registration statement declared effective under the Securities Act of 1933, as amended, or the Securities Act, or do not have a class of securities registered under the Securities Exchange Act of 1934, as amended, or the Exchange Act) are required to comply with such new or revised financial accounting standards. The JOBS Act also provides that an emerging growth company can elect to opt out of the extended transition period provided by Section 102(b)(1) of the JOBS Act and comply with the requirements that apply to non-emerging growth companies, but any such election to opt out is irrevocable. We have irrevocably elected to opt out of this extended transition period provided by Section 102(b)(1) of the JOBS Act. Even though we have elected to opt out of the extended transition period, we may still take advantage of all of the other provisions of the JOBS Act, which include, but are not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, the reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and the exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

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 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

We are a clinical-stage biopharmaceutical company, have no history of generating commercial revenue, have a history of operating losses, and we 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, 2020, we had an accumulated deficit of approximately $153.3 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 planned drug product candidates and find strategic collaborators that can incorporate our planned products candidates into new or existing drugs which can be successfully commercialized. There can be no assurance that we will ever generate commercial revenues or achieve 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 planned drug product candidates in the United States or in any foreign market. Therefore, any estimated timing for our planned drug product candidates to be commercialized would be highly speculative.

To date, we have invested substantial resources in an exclusive license with Einstein that forms the foundation for our planned 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. Therefore, 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 planned drug product candidates;
- regulatory approvals and marketing authorizations may not be achieved for our planned 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 program, 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 planned 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.

We are substantially dependent on the success of our drug product candidates, only one of which is 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.

Our main focus and the investment of a significant portion of our efforts and financial resources has been in the development of our lead product candidate, CUE-101, for which we are currently actively conducting Phase 1 clinical trials. Our other drug product candidates are all at a pre-clinical stage. We expect that additional trials of CUE-101 will be required in order to gain approval by the FDA. 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 such 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 therapeutics 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 product clinical candidates. Additionally, we have conducted limited clinical testing of one 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 an IND or a BLA to the FDA or similar submissions to initiate clinical trials or obtain marketing authorization to foreign regulatory authorities. We cannot be certain that current clinical trials will begin or be completed on time, if at all, that our planned clinical trials will begin 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, CROs, consultants and collaborators. Relying on third-party clinical investigators, CROs 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 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.

The outbreak of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19, could adversely impact our business, including our clinical trials and preclinical studies.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. In December 2019, a novel strain of coronavirus, SARS-CoV-2, which causes coronavirus disease 2019, or COVID-19, surfaced in Wuhan, China. Since then, COVID-19 has spread to countries around the world and has been declared a pandemic by the World Health Organization. The COVID-19 pandemic is evolving, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. Beginning in March 2020, we undertook precautionary measures to help minimize risk of virus transmission to our employees, including the establishment of remote working standards, pausing all non-essential travel worldwide for our employees, and limiting employee attendance at industry events and in-person work-related meetings, to the extent those events and meetings are continuing.

As a result of the COVID-19 outbreak, or similar pandemics, we may in the future experience disruptions that could severely impact our business, clinical trials and preclinical studies, including:

- supply chain disruptions, making it difficult to order and receive materials needed for development of our drug product candidates;
- delays or disruptions in the manufacture of our drug product candidates by contract manufacturing organizations and vendors along their supply chain;
- government responses, including orders that make it difficult to remain open for business, and other seen and unforeseen actions taken by government agencies;
- absenteeism or loss of employees at our Company, or at our collaborator companies, due to health reasons or government restrictions, that are needed to develop, validate, manufacture and perform other necessary functions for our operations;
- delays or difficulties in enrolling patients in our clinical trials;
- delays or disruptions in non-clinical experiments due to unforeseen circumstances at contract research organizations and vendors along their supply chain;

- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19, being forced to quarantine, or otherwise;
- interruption of key clinical trial activities due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact approval timelines;
- equipment failures, loss of utilities and other disruptions that could impact our operations or render them inoperable; and
- effects of a local or global recession or depression that could harm the international banking system and limit our access to capital.

In January 2021, we were notified by our contract manufacturing organization, or CMO, that the manufacture of our cGMP material for the CUE-102 drug candidate would be delayed by approximately six weeks due to the invocation of the Defense Production Act, or DPA, which gives priority to the manufacture of vaccines and other drug products used to prevent or treat COVID-19. The delay in the manufacturing of our CUE-102 cGMP batch impacted the expected filing date of the CUE-102 IND that was planned for the fourth quarter of 2021. The CUE-102 IND is now expected to be filed in the first half of 2022 based on the revised CUE-102 cGMP manufacturing date provided by our CMO. Despite our efforts to manage and remedy these impacts, their ultimate impact depends on factors beyond our knowledge or control, including the duration and severity of the outbreak, as well as third-party actions taken to contain its spread and mitigate its public health effects. Additionally, the anticipated economic consequences of the COVID-19 pandemic have adversely impacted financial markets, resulting in high share price volatility, reduced market liquidity, and substantial declines in the market prices of the securities of many publicly traded companies. Volatile or declining markets for equities could adversely affect our ability to raise capital when needed through the sale of shares of common stock or other equity or equity-linked securities. If these market conditions persist when we need to raise capital, and if we are able to sell shares of our common stock under then prevailing market conditions, we might have to accept lower prices for our shares and issue a larger number of shares than might have been the case under better market conditions, resulting in significant dilution of the interests of our stockholders.

These and other factors arising from the COVID-19 pandemic could worsen in the United States or locally at the location of our offices or clinical trials, each of which could further adversely impact our business generally, and could have a material adverse impact on our operations and financial condition and results.

Our current or planned 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 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 conducting Phase 1 clinical trials for our lead product candidate, CUE-101, 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 planned drug product candidates in preclinical studies may not be observed in human clinical trials. If clinical trials of our planned 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 planned drug product candidates.

If significant adverse events or other side effects are observed in any of our 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 biotechnology industry 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 versus 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 product candidate development. Any such delays could materially and adversely affect our business, financial condition, results of operations and prospects.

We plan 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 14, 2017, we entered into the Merck Agreement under which Merck will partner with us in the development of specific Immuno-STATs targeting certain autoimmune diseases. Pursuant to the Merck Agreement, Merck will acquire rights to develop, commercialize and sell specific Immuno-STATs relating to certain autoimmune disease and, in exchange for such rights, has agreed to make payments to us that include a licensing fee, milestone payments and sales royalties. The Merck Agreement was amended in November 2020 to extend the research term through December 31, 2021.

Effective November 6, 2018, we entered into the LG Chem Agreement, for the development of our Immuno-STATs focused in the field of oncology. Pursuant to the LG Chem 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 a licensing fees, milestone payments and sales royalties. These agreements do not commit Merck or LG Chem to a long-term relationship, and they may disengage with us at any time.

Additionally, we plan to seek strategic alliances or collaborations with other third parties that we believe will complement or augment our development and commercialization efforts with respect to our planned 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 other alternative arrangements for our planned 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 planned drug product candidates as having the requisite potential to demonstrate safety, purity, and efficacy. If we are unable to establish additional strategic partnerships or other alternative arrangements 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 planned 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 managements' attention and our other resources;

- 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 or net income to justify such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to our planned drug product candidates could delay the development and commercialization of our planned drug product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition, and results of operations.

Our collaboration agreements with Merck and LG Chem contain exclusivity provisions that restrict our research and development activities.

We have granted to Merck under the Merck Agreement an exclusive license under certain of our patent rights, including a sublicense of patent rights licensed from Einstein, to the extent applicable to the specific Immuno-STAT that are elected to be developed by Merck for two initial indications. So long as Merck continues product development on a Proposed Drug Product Candidate for an initial indication, we are restricted from conducting any development activities within the initial indication covered by such Proposed Drug Product Candidate other than pursuant to the Merck Agreement.

Additionally, we have granted to LG Chem under the LG Chem Agreement an exclusive license to develop, manufacture and commercialize CUE-101, as well as the Drug Product Candidates, in the LG Chem Territory. Under the LG Chem Agreement, the Company 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 CMC process for the development and commercialization of Drug Product Candidates. In addition, LG Chem has the option to select one additional Immuno-STAT for an oncology target up to April 30, 2021 for an exclusive worldwide development and commercialization license.

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 development of certain drug product candidates; these decisions may prove to be wrong and may adversely affect our business.

Although we intend to 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 planned 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 will 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.

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results 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 bi-specific antibodies (e.g., Amgen, Immunocore and Roche), cell therapies (e.g., Bristol-Myers Squibb, Gilead and Novartis), antibody-drug conjugates (e.g., Gilead, Roche, Seattle Genetics), immune checkpoint inhibitors (e.g., Bristol-Myers Squibb, Merck and Pfizer), and targeted cytokines (e.g., Bristol Myers Squibb/Nektar, Neoleukin, Roche and Sanofi) 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, including Daniel Passeri, M.Sc., our Chief Executive Officer, Anish Suri, our President and Chief Scientific Officer, Kenneth Pienta, our Acting Chief Medical Officer, and other members of our scientific and clinical advisory team, including Steven Almo, Ph.D., the Chairman of our Scientific and Clinical Advisory Board. 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.

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 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 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 cGMP regulations. While we work closely with our CROs 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 CROs 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, 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, 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 cGMP 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 -- further discussed below under "*Risks Related to Intellectual Property and Other Legal Matters*" -- 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 sources of supply for our drug product candidates and any disruption in the chain of supply may cause delays in developing, obtaining approval for, and commercializing our drug product candidates.

Currently, we use Catalent as a sole source of supply for manufacturing clinical supply of our lead product candidate, CUE-101. If we experience multiple successive batch failures, or if supply from Catalent is otherwise interrupted, there could be a significant disruption in our product candidate 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. rely on sole sources of supply for the preclinical and clinical supply of materials.

The manufacturing processes for CUE-101 and our other drug product candidates are complex, and it may 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 is 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 identification of novel immunomodulators, novel epitopes, and novel immunotherapy drugs. 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 important 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. 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 having 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 therapeutic industry is 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. 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 will 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.

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

The price of our common stock may 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.

Risks Related to Government Regulation

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. The exercise of these "march-in" rights 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.

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.

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 drug 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. 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 medicine not commercially viable.

Finally, disruptions at the FDA and other agencies may prolong the time necessary for new drugs 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, have had to furlough critical 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. The Trump Administration also took several executive actions that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities.

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.

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 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 or these third parties 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 medicines in any jurisdiction, which would materially impair our ability to generate revenue.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of drug product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing any drug product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for any drug product candidates, which could significantly and materially harm our business.

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.

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. Additionally, the fast-track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

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 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. A fast-track or breakthrough therapy designated drug 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 will delay revenue from their potential sales and will increase the capital necessary to fund these product development programs.

To obtain the necessary approval of our potential products, as a precondition, there will have to be conducted 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 therapeutic to be safe or effective;
- interpret data from preclinical and clinical testing differently than we do;
- not approve the manufacturing processes;
- conclude that our 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 medicine, 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, cGMP 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 medicine 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 medicine.

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 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 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.

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Product, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown problems with our medicines, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such medicines, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;
- restrictions on the distribution or use of a medicine;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- fines, restitution, or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our medicines;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any 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.

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 medicines 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 the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers 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 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 industry 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 the U.S. Department of Health and Human Services, 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, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. 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 2029 unless additional Congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030. 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.

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 December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020. On February 10, 2021, the Biden Administration withdrew the federal government's support for overturning the ACA. A ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

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

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for products. To those ends, President Trump issued several executive orders intended to lower the costs of prescription drug products. Certain of these orders are reflected in recently promulgated regulations, including an interim final rule implementing President Trump's most favored nation model, but such final rule is currently subject to a nationwide preliminary injunction. It remains to be seen whether these orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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.

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 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 European Economic Area, or EEA, in May 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 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.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. 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.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these 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 increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

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 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.

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 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 Owning Our Common Stock, Our Financial Results and Our Need for Financing

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 our first potential products and we are able to successfully commercialize them through sales and licensing. 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 planned 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 expect to require 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 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 planned and potential 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;
- 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 Einstein, employees, collaborators 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.

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

We are an "emerging growth company," or EGC, as defined in the JOBS Act. We will remain an EGC until the earlier of: (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of our initial public offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the last day of the first fiscal year in which the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- reduced disclosure obligations regarding executive compensation;
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved; and

- an exemption from compliance with the requirement of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on the financial statements.

In addition, the JOBS Act provides that an EGC may take advantage of an extended transition period for complying with new or revised accounting standards. This allows an EGC to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not EGCs.

We are also 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 common shares held by non-affiliates is more than $250 million 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 common shares held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations, such as an exemption from providing selected financial data and 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 investors may have difficulty selling their shares.

Our common stock is currently listed on the Nasdaq Capital Market under the symbol "CUE." The price of our common stock may 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 also be affected by:

- 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;
- result 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;
- release or expiry of lock-up or other transfer restrictions on our outstanding ordinary shares or our common stock;
- sales or perceived potential sales of additional ordinary shares or 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 and overall fluctuations in the U.S. equity markets.

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 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. We currently have one securities and industry analyst providing research coverage. If few analysts commence research coverage of us, or 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 potential products 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.

Our ability to use net operating loss carryforwards and research 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 carry forwards and Section 383 imposes an annual limitation on the amount of tax a corporation may offset with business credit (including the R&D credit) carry forwards.

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.

We incur significant costs as a result of being a public company that reports to the Securities and Exchange Commission and our management will be required to devote substantial time to meet compliance obligations.

As a public company reporting to the Securities and Exchange Commission, or the SEC, we incur significant legal, accounting and other expenses. We are subject to reporting requirements of the Exchange Act and 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 are expected to 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 may be filled only by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- 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 share acquisition. 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, subject to limited exceptions, that the Court of Chancery of the State of Delaware will, to the fullest extent permitted by law, be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders; (3) any action asserting a claim against us, any director or our officers and employees arising pursuant to any provision of the Delaware General Corporation Law, our Certificate of Incorporation or our Bylaws, or as to which the Delaware General Corporation Law confers exclusive jurisdiction on the Court of Chancery; or (4) any action asserting a claim against us, any director or our officers or employees that is governed by the internal affairs doctrine. The choice of forum provisions will not apply to claims arising under 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 an "emerging growth company," 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.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our principal office is located in Cambridge, Massachusetts. We currently lease approximately 19,800 square feet of office and laboratory space. We use this space as our principal executive offices and for general office, research and development, and laboratory uses. The monthly rent payments due under this lease agreement will be approximately $375,000 for the remainder of the lease term, which expires in June 2022. We also lease additional laboratory space consisting of three procedure and holding rooms. The monthly payments due under this lease agreement will be approximately $61,000 for the remainder of the lease term which expires in June 2022.

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 1, 2021, there were approximately 39 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. 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.

Item 6. Selected Financial Data

Not applicable.

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 engineering a novel class of injectable biologics to selectively engage and modulate targeted T cells directly within the patient's body. We believe our proprietary Immuno-STAT™ (Selective Targeting and Alteration of T Cells) platform will allow us to harness the fullest potential of an individual's intrinsic immune repertoire for restoring health while avoiding the deleterious side-effects of broad immune activation (for immuno-oncology or infectious immunity) or broad immune suppression (for autoimmunity and inflammation). In addition to the selective modulation of T cell activity, we believe Immuno-STATs offer several key points of potential differentiation over competing approaches, including modularity and versatility providing broad disease coverage, manufacturability, and convenient administration.

Through rational protein engineering, we leverage the modular and versatile nature of the Immuno-STAT platform to design drug product candidates for selective immune modulation in cancer, chronic infectious disease, and autoimmune disease. To address the needs of these clinical indications, we have developed four biologic series within the Immuno-STAT platform: CUE-100, CUE-200, CUE-300, and CUE-400, each specifically designed through rational engineering to possess distinct signaling modules for desired biological mechanisms that may be applied across many diseases. The CUE-100 series exploits rationally engineered IL-2 in context of the core Immuno-STAT framework for selective activation of targeted tumor-specific T cells, while the CUE-200 series is focused on cell surface receptors including CD80 and/or 4-1BBL to address T cell exhaustion associated with chronic infections. The CUE-300 series, being developed for autoimmune diseases, incorporates the inhibitory PDL1 co-modulator for selective inhibition of the autoreactive T cell repertoire. This approach is pertinent for autoimmune diseases with known, well characterized, limited or few autoantigens, such as type 1 diabetes. The CUE-400 series, for autoimmune diseases with diverse or unknown autoantigens, represents a novel class of bispecific molecules that can selectively and effectively expand induced regulatory T cells, or iTregs. We categorize these molecules as "pathway-specific modulators," or PSM. The first candidate, CUE-401, incorporates the two key biological signals that are necessary for generation of iTregs, namely IL-2 and TGF-beta. Based on structure-based rational protein engineering, both IL-2 and TGF-beta have been affinity tuned to maintain on-target engagement while minimizing systemic toxicities.

Our drug product candidates are in various stages of clinical and preclinical development, and while we believe that these candidates hold potential value, our activities are 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 additional capital to fund our growth and ongoing business operations.

Coronavirus (COVID-19) Pandemic

The COVID-19 outbreak, which the World Health Organization has classified as a pandemic, has prompted governments and regulatory bodies throughout the world to issue "stay-at-home" or similar orders, and enact restrictions on the performance of "non-essential" services, public gatherings and travel.

Beginning in March 2020, we undertook precautionary measures intended to help minimize the risk of virus transmission to our employees, including the establishment of remote working standards, pausing all non-essential travel worldwide for our employees, and limiting employee attendance at industry events and in-person work-related meetings, to the extent those events and meetings are continuing. We also established policies and procedures for all personnel who enter our company premises. The policies and procedures we implemented are consistent with the rules and guidelines recommended by the Centers for Disease Control and Prevention, Commonwealth of Massachusetts and the City of Cambridge. To date, we do not believe these actions have had a significant negative impact on our productivity or our operations. However, these actions or additional measures we may undertake may ultimately delay progress of our developmental goals or otherwise negatively affect our business. In addition, third-party actions taken to contain the spread of the novel coronavirus, SARS-CoV-2, and mitigate public health effects may negatively affect our business.

In January 2021, we were notified by our contract manufacturing organization, or CMO, that the manufacture of our cGMP material for the CUE-102 drug candidate would be delayed by approximately six weeks due to the invocation of the Defense Production Act, or DPA, which gives priority to the manufacture of vaccines and other drug products used to prevent or treat COVID-19. The delay in the manufacturing of our CUE-102 cGMP batch impacted the expected filing date of the CUE-102 IND that was planned for the fourth quarter of 2021. The CUE-102 IND is now expected to be filed in the first quarter of 2022 based on the revised CUE-102 cGMP manufacturing date provided by our CMO.

Plan of Operation

Our technology is in the development phase. We believe that our licensed platforms have the potential for creating a diverse pipeline of 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 research, testing, optimization, conducting pilot studies, performing early stage clinical development and potentially partnering 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 and our planned future activities will be devoted to furthering research and development.

A fundamental part of our corporate development strategy is to establish one or more strategic partnerships with leading pharmaceutical or biotechnology organizations that will allow us to more fully exploit the potential of our technology platform, such as those described below under the headings “Collaboration Agreement with Merck” and “Collaboration with LG Chem”.

Critical Accounting Policies and Significant Judgments and Estimates

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 the Company’s 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 as of December 31, 2020.

Revenue Recognition

We follow the provisions of Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers*. We generate revenue solely through collaboration arrangements with strategic partners for the development and commercialization of drug product candidates. The core principle of ASC 606 is that an entity should recognize revenue to depict the transfer of promised goods and/or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods and/or services. To determine the appropriate amount of revenue to be recognized for arrangements that we determine are within the scope of ASC 606, we perform the following steps: (i) identify the contract(s) with the customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract and (v) recognize revenue when (or as) each performance obligation is satisfied.

We recognize collaboration revenue under certain of our license or collaboration agreements that are within the scope of ASC 606. 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 judgement 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. 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 “most likely amount” method to estimate the amount of variable consideration, to predict the amount of consideration to which we will be entitled for our two open contracts. 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, we evaluate whether the associated event is considered probable of achievement and estimates the amount to be included in the transaction price using the most likely amount method. Currently, we have one contract with an option to acquire additional goods and/or services in the form of additional research and development services for additional drug product candidates.

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.

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 expense recognition is more appropriate. Other research and development expenses are charged to operations as incurred. Payments made pursuant to research and development contracts are initially recorded as research and development contract advances in our balance sheet and then charged to research and development expenses in our consolidated statements of operations and comprehensive loss as those contract services are performed. Expenses incurred under research and development contracts in excess of amounts advanced are recorded as research and development contract liabilities in our balance sheet, with a corresponding charge to research and development expenses in our consolidated statements of operations and comprehensive loss.

Nonrefundable advance payments for future research and development activities pursuant to an executory contractual arrangement are recorded as advances as described above. 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 charged to expense. 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 adjusts the carrying amounts and their classification on the balance sheet as appropriate.

Stock-Based Compensation

We periodically issue stock-based awards to officers, directors, employees, Scientific and Clinical Advisory Board members, non-employees and consultants for services rendered. Such issuances vest and expire according to terms established at the issuance date.

Stock-based payments to officers, directors, members of our Scientific and Clinical Advisory Board, non-employees and outside consultants and employees, 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. We also grant performance-based awards periodically to our officers. We recognize compensation costs related to performance awards over the requisite service period if and when we conclude 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 option-pricing model, which is affected by several variables, including the risk-free interest rate, the expected dividend yield, the life of the equity award, the exercise price of the stock option as compared to the fair value of the common stock on the grant date, and the estimated volatility of the common stock over the term of the equity award.

The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant. Until we have established a trading history for our common stock that approximates the expected term of the options, estimated volatility is based on the average historical volatilities of comparable public companies in a similar industry. The expected dividend yield is based on the current yield at the grant date; we have never declared or paid dividends and have no plans to do so for the foreseeable future. As permitted by Staff Accounting Bulletin No. 107, due to our lack of history and option activity, we utilize the simplified method to estimate the expected term of options at the date of grant. The fair value of common stock is determined by reference to either recent or anticipated cash transactions involving the sale of our common stock.

We recognize the fair value of stock-based compensation in general and administrative expenses and in research and development expenses in our consolidated statements of operations and comprehensive loss, depending on the type of services provided by the recipient of the equity award. We issue new shares of common stock to satisfy stock option exercises.

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.

Recent Accounting Pronouncements

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 amended on October 30, 2018, or the Einstein License, with Albert Einstein College of Medicine, or Einstein, for certain patent rights relating to our core technology platform for the engineering of biologics to control T cell activity, precision, immune-modulatory drug 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 covered by the Einstein License, including certain technology received from Einstein related thereto, or the Licensed Products. Under the Einstein License, we are required to:

- Pay royalties and amounts based on 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. At December 31, 2020, one of these milestones had been achieved, as we had filed an investigational new drug application, or IND, in 2019.
- Incur minimum product development costs per year until the first commercial sale of the first Licensed Product.

We were in compliance with our obligations under the Einstein License at December 31, 2020 and 2019.

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 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, 2020 and 2019, costs incurred with respect to the Einstein License aggregated $75,000 and $565,659, respectively. Such costs are included in research and development costs in the 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 the Annual Report on Form 10-K for additional discussion of the Einstein License.

Collaboration Agreement with Merck

On November 14, 2017, we entered into an Exclusive Patent License and Research Collaboration Agreement, or the Merck Agreement, with Merck Sharp & Dohme Corp., or Merck, for a partnership to research and develop certain of our proprietary biologics that target certain autoimmune disease indications, or the Initial Indications. We view the Merck Agreement as a component of our development strategy since it will allow us to advance our autoimmune programs in partnership with a world class pharmaceutical company, while also continuing our focus on our more advanced cancer programs. The research program outlined in the Merck Agreement entails (1) our research, discovery and development of certain Immuno-STAT drug candidates up to the point of demonstration of certain biologically relevant effects, or Proof of Mechanism, and (2) the further development by Merck of the Immuno-STAT drug candidates that have demonstrated Proof of Mechanism, or the Proposed Drug Product Candidates, up to the point of demonstration of all or substantially all of the properties outlined in such Proposed Drug Product Candidates' profiles as described in the Merck Agreement.

For the purposes of this collaboration, we granted to Merck under the Merck Agreement an exclusive license under certain of our patent rights, including a sublicense of patent rights licensed from Einstein, to the extent applicable to the specific Immuno-STAT that are elected to be developed by Merck. So long as Merck continues product development on a Proposed Drug Product Candidate, we are restricted from conducting any development activities within the Initial Indication covered by such Proposed Drug Product Candidate other than pursuant to the Merck Agreement.

In exchange for the licenses and other rights granted to Merck under the Merck Agreement, Merck paid to us a $2.5 million nonrefundable up-front payment. Additionally, we may be eligible to receive funding in developmental milestone payments, as well as tiered royalties, if all research, development, regulatory and commercial milestones agreed upon by both parties are successfully achieved. Excluding the up-front payment described above, we are eligible to earn up to $101 million for the achievement of certain research and development milestones, $120 million for the achievement of certain regulatory milestones and $150 million for the achievement of certain commercial milestones, in addition to tiered royalties on sales, if all pre-specified milestones associated with multiple products across the primary disease indication areas are achieved. The Merck Agreement requires us to use the first $2.5 million of milestone payments we receive under the agreement to fund contract research. The amount of the royalty payments is a percentage of product sales ranging in the single digits based on the amount of such sales. We recorded approximately $177,000 in revenue for the year ended December 31, 2020 related to the Merck Agreement, compared to $874,000 for the year ended December 31, 2019.

The term of the Merck Agreement extends until the expiration of all royalty obligations following a product candidate's receipt of marketing authorization, at which point Merck's licenses and sublicenses granted under the agreement shall become fully paid-up, perpetual licenses and sublicenses, as applicable. Royalties on each product subject to the Merck Agreement shall continue on a country-by-country basis until the expiration of the later of: (1) the last-to-expire patent claiming the compound on which such product is based and (2) a period of ten years after the first commercial sale of such product in such country.

On November 18, 2020, we entered into a First Amendment to the Merck Agreement, or the Amendment, with Merck. Pursuant to rights granted to Merck under the Merck Agreement, the Amendment extends the term of the research program under the Merck Agreement for an additional year, until December 31, 2021. Under the terms of the Amendment, Merck will reimburse us for specified expenses and provide additional financial research support to further study and develop preclinical biologics with the objective of identifying clinical candidates subject, in each case, to specified maximum amounts, with any amounts in excess of such maximum amounts to be borne by us. On November 18, 2020, we earned a milestone payment related to this Amendment in the amount of $300,000. The $300,000 milestone payment was recorded as a contract liability upon receipt. We will recognize revenue related to this milestone payment pursuant to our revenue recognition policy in relation to the performance of our obligations related to the development of Immuno-STAT drug candidates under the arrangement.

See “Our Collaboration Agreement with Merck” under Part I, Item 1 of the Annual Report on Form 10-K for additional discussion of the Merck Agreement.

Collaboration Agreement with LG Chem

Effective November 6, 2018, we entered into a collaboration agreement with LG Chem, Ltd., or LG Chem, which we refer to as the LG Chem Agreement, related to the development of Immuno-STATs focused in the field of oncology.

Pursuant to the LG Chem Agreement, we granted LG Chem an exclusive license to develop, manufacture and commercialize our lead product, CUE-101, as well as Immuno-STATs that target T cells against two additional cancer antigens, or 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. On December 20, 2018, we reported the selection of Wilms Tumor 1, or WT1, as the first target antigen for a Product Candidate under the LG Chem Agreement. We retain rights to develop and commercialize all assets included in the LG Chem Agreement in the United States and in global markets outside of the LG Chem Territory. Under the LG Chem 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. The LG Chem Agreement provided LG Chem with 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 commercialization 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 Agreement related to LG Chem’s option for an Additional Immuno-STAT but generally does not become effective unless and until LG Chem exercises its option, other than certain select provisions including the length of the option period and representations, warranties and covenants of the parties. If LG Chem exercises this option, which expires on April 30, 2021, then the other provisions of the Global License and Collaboration Agreement, including the license to the Additional Immuno-STAT from us to LG Chem and the terms and conditions for such license, will become effective. We will retain an option to co-develop and co-commercialize the additional program worldwide.

Under the terms of the LG Chem Agreement, LG Chem paid us a $5.0 million non-refundable, non-creditable upfront payment and purchased approximately $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 Agreement. We are also eligible to receive additional aggregate payments of approximately $400 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 U.S. Food and Drug Administration, or FDA’s, acceptance of the IND for our lead drug candidate, CUE-101, pursuant to the LG Chem Agreement. In addition, the LG Chem 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 Agreement. On December 7, 2020, we earned a $1.25 million milestone payment on the selection of a pre-clinical candidate pursuant to the LG Chem Agreement. The $1.25 million milestone payment was recorded as a contract liability upon receipt. We will recognize revenue related to this milestone payment pursuant to our revenue recognition policy in relation to the performance of our obligations related to the development of the selected pre-clinical candidate under the arrangement.

Pursuant to the LG Chem 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 royalty payments on the sales of Collaboration Products sold in all countries outside the LG Chem Territory. Furthermore, should LG Chem exercise its option for an Additional Immuno-STAT, LG Chem will pay us a one-time, non-refundable, non-creditable upfront payment and we will be eligible to receive up to approximately $470 to $675 million in fees and milestone payments as well as tiered royalty payments on future global sales that range from high-single digits to mid-double digit teens in the United States and mid-single to low-double digits outside of the United States. The amount of fees and milestone payments, as well as whether we receive royalty payments, will depend on when LG Chem nominates the Additional Immuno-STAT Biologic, the number of alleles selected by LG Chem and whether we exercise our option to co-develop and co-commercialize the additional program worldwide, in which case we would share costs and profits instead of receiving royalties and post-option-exercise milestones. For the years ended December 31, 2020 and 2019, we recognized approximately $2,978,000 and $2,584,000, respectively, in collaboration revenue related to this agreement.

See “Our Collaboration Agreement with LG Chem” under Part I, Item 1 of the Annual Report on Form 10-K for additional discussion of the LG Chem Agreement.

Results of Operations

Collaboration Revenue

We have not generated commercial revenue from product sales. To date, we have generated collaboration revenue from the Merck Agreement and LG Chem Agreement.

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, trademark, 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 increase in future periods as we add personnel and incur additional expenses related to an expansion of our research and development activities and our operation as a public company, including higher legal, accounting, insurance, compliance, compensation and other expenses.

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 research and development expenses to increase in the future as we increase our efforts to develop technology for potential future products based on our technology and research.

Years Ended December 31, 2020 and 2019

Our consolidated statements of operations and comprehensive loss for the years ended December 31, 2020 and 2019, as discussed herein are presented below.

	Years Ended December 31,	
	2020	**2019**
Collaboration revenue	$ 3,154,325	$ 3,458,331
Operating expenses:		
General and administrative	14,651,205	12,740,093
Research and development	33,545,705	27,487,485
Total operating expenses	48,196,910	40,227,578
Loss from operations	(45,042,585)	(36,769,247)
Other income:		
Interest income, net	463,914	482,790
Total other income	463,914	482,790
Loss before provision for income taxes	(44,578,671)	(36,286,457)
Provision for income taxes	(206,250)	(412,500)
Net loss	$ (44,784,921)	$ (36,698,957)

Collaboration Revenue

Collaboration revenue totaled $3,154,325 and $3,458,331 for the years ended December 31, 2020 and 2019, respectively. This decrease was due to a revised estimate of our progress under the LG Chem Agreement during the year ended December 31, 2020, which resulted in a decrease to collaboration revenue of approximately $47,000 during the fourth quarter of 2020. Upon the preclinical candidate selection of A02 Allele pursuant to the LG Chem Agreement, we reimbursed LG Chem final costs of approximately $68,000 related to the termination of the A24 Allele funding. We also recorded a decrease to collaboration revenue of approximately $79,000 during the fourth quarter of 2020 related to the Merck Amendment, which extended the term and revised budgeted costs for an additional year through December 31, 2021.

General and Administrative

General and administrative expenses totaled approximately $14,651,000 and $12,740,000 for the years ended December 31, 2020 and 2019, respectively. This increase of approximately $1,911,000 was due primarily to higher stock-based compensation related to executive management and legal fees offset by a decrease in travel expenses as the COVID-19 pandemic continued to hamper business travel throughout 2020. We expect our general and administrative expenses to increase as we continue to expand our operations. General and administrative expenses for the year ended December 31, 2020 included expenses related to employee and board compensation of $3,875,000, professional and consulting fees of $4,483,000, rent of $1,082,000, insurance of $256,000, stock-based compensation of $4,094,000, investor relations of $275,000, travel of $31,000, depreciation and amortization of $97,000, and other expenses of $458,000.

General and administrative expenses for the year ended December 31, 2019 included expenses related to employee and board compensation of approximately $3,547,000, professional and consulting fees of $4,663,000, rent of $965,000, insurance of $448,000, stock-based compensation of $2,109,000, investor relations of $200,000, travel of $179,000, depreciation and amortization of $115,000, and other expenses of $514,000.

Research and Development

Research and development expenses totaled approximately $33,546,000 and $27,487,000 for the years ended December 31, 2020 and 2019, respectively. This increase of approximately $6,059,000 was due primarily to higher laboratory and drug substance manufacturing costs, stock-based compensation expense and clinical expenses, offset by a decrease in travel expenses as the COVID-19 pandemic continued to hamper business travel. We expect our research and development expenses to continue to increase as we expand our development activities. Research and development expenses for the year ended December 31, 2020 included expenses related to employee and Scientific and Clinical Advisory Board compensation of $7,886,000, depreciation and amortization of $960,000, stock-based compensation of $6,387,000, research and laboratory expenses of $8,420,000, rent of $3,511,000, licensing fees of $99,000, other professional fees of $531,000, clinical expenses of $4,264,000, travel of $27,000, insurance expense of $666,000, and other expenses of $795,000.

Research and development expenses for the year ended December 31, 2019 included expenses related to employee and Scientific and Clinical Advisory Board compensation of $6,997,000, depreciation and amortization of $885,000, stock-based compensation of $4,412,000, research and laboratory expenses of $6,500,000, rent of $3,509,000, licensing fees of $658,000, other professional fees of $1,271,000, clinical expenses of $2,053,000, travel of $128,000, insurance expense of $234,000, and other expenses of $840,000.

Interest Income

Interest income was $463,914 for the year ended December 31, 2020, as compared to $482,790 for the year ended December 31, 2019. The decrease in interest income was from higher amortization of discounts received on certain of our marketable securities offset by interest income earned on the investment of an increased portion of our cash in cash equivalents and marketable securities during 2020. Interest income for the year ended December 31, 2020 included $80,110 in expense resulting from amortization of discounts received on certain of our marketable securities, compared to $64,078 of other income for the year ended December 31, 2019.

Foreign Withholding Taxes

Provision for income tax for the year ended December 31, 2020 was comprised of $206,250 in foreign income tax expense on the LG Chem milestone payment, compared to the year ended December 31, 2019 comprised of $412,500.

Net Loss

As a result of the foregoing, our net loss was $44,784,921 for the year ended December 31, 2020, as compared to $36,698,957 for the year ended December 31, 2019.

Liquidity and Capital Resources

We have financed our working capital requirements primarily through private and public offerings of equity securities and cash received from Merck and LG Chem under their respective collaboration agreements. At December 31, 2020 and December 31, 2019, we had unrestricted cash, cash equivalents and marketable securities totaling $84,868,683 and $59,409,955, 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 report.

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 January 4, 2019, we filed a universal shelf registration statement on Form S-3 with the SEC, or the 2019 Shelf, to register for sale from time to time up to $150 million of our common stock, preferred stock, debt securities, warrants and/or units in one or more offerings (File No. 333-229140). This registration statement became effective on February 3, 2019.

In June 2019, we entered into an "at-the-market", or ATM, equity offering sales agreement, or the June 2019 Sales Agreement, with Stifel Nicolaus & Company, Inc., or Stifel, to sell shares of our common stock for aggregate gross proceeds of up to $30 million, from time to time, through an "at-the-market" equity offering program under which Stifel acts as sales agent. As of December 31, 2020, we had sold a total of 3,584,945 shares of common stock under the June 2019 Sales Agreement for proceeds of approximately $29.4 million, net of commissions paid, but excluding estimated transaction expenses. Due to the issuance and sale of all the shares of common stock subject thereto, the June 2019 Sales Agreement terminated in accordance with its terms.

In November 2019, we entered into an ATM equity offering sales agreement, or the November 2019 Sales Agreement, with Stifel to sell shares of our common stock for aggregate gross proceeds of up to $20 million, from time to time, through an "at-the-market" equity offering program under which Stifel acts as sales agent. As of December 31, 2020, we had sold a total of 1,729,110 shares of common stock under the November 2019 Sales Agreement for proceeds of approximately $19.6 million, net of commissions paid, but excluding estimated transaction expenses. Due to the issuance and sale of all the shares of common stock subject thereto, the November 2019 Sales Agreement terminated in accordance with its terms.

In March 2020, we entered into an ATM equity offering sales agreement, or the March 2020 Sales Agreement, with Stifel to sell shares of our common stock for aggregate gross proceeds of up to $35 million, from time to time, through an "at-the-market" equity offering program under which Stifel acts as sales agent. As of December 31, 2020, we had sold a total of 1,824,901 shares of common stock under the March 2020 Sales Agreement for proceeds of approximately $34.3 million, net of commissions paid, but excluding estimated transaction expenses. Due to the issuance and sale of all the shares of common stock subject thereto, the March 2020 Sales Agreement terminated in accordance with its terms.

The shares of common stock sold under the June 2019 Sales Agreement, November 2019 Sales Agreement and the March 2020 Sales Agreement were made pursuant to the 2019 Shelf.

On June 22, 2020, we filed a registration statement on Form S-3ASR, which became automatically effective upon filing with the SEC (File No. 333-239357), or the 2020 Shelf, to register for sale from time to time up to $300 million of our common stock, preferred stock, debt securities, warrants, rights and/or units in one or more offerings.

In June 2020, we entered into an ATM equity offering sales agreement, or the June 2020 Sales Agreement, with Stifel to sell shares of our common stock for aggregate gross proceeds of up to $40 million, from time to time, through an "at-the-market" equity offering program under which Stifel acts as sales agent. The sales agreement will terminate upon the earliest of (a) the sale of $40 million of shares of our common stock or (b) the termination of the June 2020 Sales Agreement by us or Stifel. As of December 31, 2020, we had sold 1,192,000 shares of common stock under the June 2020 Sales Agreement for proceeds of approximately $22.4 million, net of commissions paid, but excluding estimated transaction expenses. The shares of common stock sold under the June 2020 Sales Agreement are made pursuant to the 2020 Shelf.

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

The following table summarizes our changes in cash, cash equivalents, and restricted cash for the year ended December 31, 2020 and 2019:

	December 31,	
	2020	2019
Net cash provided by (used in):		
Operating activities	$ (32,494,034)	$ (30,796,910)
Investing activities	4,455,874	3,446,823
Financing activities	58,614,263	50,789,765
Net increase in cash, cash equivalents, and restricted cash	$ 30,576,103	$ 23,439,678

Operating Activities

During the year ended December 31, 2020, we used cash of approximately $32,494,000 in operating activities, as compared to $30,797,000 of cash used in operating activities during the year ended December 31, 2019. Cash used during the year ended December 31, 2020 consisted primarily of our net loss of approximately $44,785,000, and increases of approximately $662,000 in accounts receivable, $563,000 in other non-cash charges, $381,000 in prepaid expenses, $5,000 in other assets, and $4,203,000 in operating lease right-of-use asset. Cash used was partially offset by increases of approximately $503,000 in research and development contract liabilities, $4,679,000 in operating lease liability, $741,000 in accounts payable, and $560,000 in accrued expenses, as well as non-cash charges of approximately $1,057,000 in depreciation and amortization, $10,481,000 in stock-based compensation expense, and $84,000 in amortization of premium/discount on purchased securities.

Cash used during the year ended December 31, 2019 of approximately $30,797,000 consisted primarily of our net loss of approximately $36,699,000, increases of approximately $755,000 in accounts receivable, and $1,560,000 in deposits, decreases of approximately $1,153,000 in accounts payable, and $4,278,000 in operating lease liability, and a non-cash charge of $72,000 in amortization of premium/discount on purchased securities. Cash used was partially offset by decreases of approximately $487,000 in prepaid expenses and other current assets, $4,355,000 in operating lease right-of-use assets, and $124,000 in other assets, increases of approximately $439,000 in accrued expenses, and $929,000 in research and development contract liabilities, and non-cash charges of approximately $811,000 in depreciation and amortization, $6,521,000 in stock based compensation, and $54,000 for loss on disposal of fixed assets.

Investing Activities

During the year ended December 31, 2020, we generated cash of approximately $4,456,000 from investing activities, compared to approximately $3,447,000 generated by investing activities during the year ended December 31, 2019. Cash generated during the year ended December 31, 2020 consisted primarily of approximately $15,000,000 for the redemption of short-term investments offset by the purchase of property and equipment of approximately $595,000 and the purchase of marketable securities of $9,949,000. We generated cash during the year ended December 31, 2019, of approximately $3,447,000 which consisted primarily of approximately $18,500,000 for the redemption of short-term investments, and $127,500 cash received for the sale of lab equipment, offset by the purchase of property and equipment of approximately $46,000 and the purchase of short-term investments of $15,134,000.

Financing Activities

During the year ended December 31, 2020, we generated cash from financing activities of approximately $58,614,000, compared to approximately $50,790,000 generated in financing activities during the year ended December 31, 2019. Cash generated during the year ended December 31, 2020 consisted primarily of cash proceeds from the common stock sold through our ATM sales agreements with Stifel of approximately $56,682,000, net of underwriting commissions and fees, and the exercise of common stock options of approximately $2,203,000, and restricted stock awards net of taxes withheld of $271,000. Compared to cash generated during the year ended December 31, 2019 primarily of cash proceeds from the common stock sold through our ATM sales agreements with Stifel of approximately $48,999,000, net of underwriting commissions and fees, and the exercise of common stock options of approximately $1,882,000, and restricted stock awards net of taxes withheld of $91,000.

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, 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 the clinical development of CUE-101;
- leverage our programs to advance our other drug product candidates into preclinical and clinical development;
- seek regulatory approvals for any drug product candidates that 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;
- hire additional clinical, quality control and scientific personnel;
- expand our manufacturing, operational, financial and management systems;
- increase personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- 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.

We believe that our existing cash resources as of December 31, 2020 will enable us to fund our operating requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

We will need to raise additional capital or incur indebtedness to continue to fund our operations in the future. 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 research, development and commercialization of 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 planned and potential 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;
- 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 Einstein, employees, collaborators 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 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 January 18, 2018, we entered into an operating lease agreement for our laboratory and office space in Cambridge, Massachusetts for the period from May 1, 2018 through April 30, 2021, or the Laboratory and Office Lease. The lease contains escalating payments during the lease period. Upon execution of this lease agreement, 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. We also prepaid seven and one half months’ rent pursuant to an amendment to the lease agreement executed on June 18, 2018. We record monthly rent expense on a straight-line basis, equal to the total of the lease payments over the lease term divided by the number of months of the lease term.

On June 18, 2018, we entered into an amendment to the Laboratory and Office Lease that provide us with a reduction in rental fees for our office and laboratory space in exchange for prepayment of a portion of the fees. This amendment was effective beginning on May 15, 2018 and expires on April 14, 2021. The monthly rent payment due under the Laboratory and Office Lease is currently $330,550 until April 2021 and will increase to $375,174 for the remainder of the term.

On September 20, 2018, we entered into an operating lease for additional laboratory space at 21 Erie Street, Cambridge, Massachusetts for the period from October 15, 2018 through April 14, 2021, or the Additional Laboratory Lease. The lease contains escalating payments during the lease period. The monthly rental rate under the Additional Laboratory Lease was $72,600 for the first 12 months and $78,600 for the remainder of the term. Upon execution of this lease agreement, we prepaid 12 months' rent pursuant to the lease agreement executed on September 20, 2018.

On September 19, 2019, we entered into a second amendment to the Additional Laboratory Lease that removed one holding room from the additional laboratory space. The amendment was effective beginning on October 1, 2019 and expires on April 14, 2021. The monthly rental rate under the Additional Laboratory Lease decreased from $78,600 to $58,995 for the remainder of the lease term.

On June 24, 2020, we entered into a second amendment to the Laboratory and Office Lease. Pursuant to the amendment (1) the term of the lease was extended to June 14, 2022 and (2) the monthly rental rate for the last 14 months of the lease term was increased to $375,174. We determined that the amendment should be accounted for as a lease modification under Accounting Standards Codification 842, *Leases*, or ASC 842, not as a separate contract, with an effective date of lease modification of May 14, 2020. At the effective date of modification, we recorded an adjustment to the right-of-use asset and lease liability in the amount of approximately $4,826,000.

On July 20, 2020, we entered into a third amendment to the Additional Laboratory Lease. Pursuant to the amendment the term of the lease was extended to June 14, 2022. We determined that the amendment should be accounted for as a lease modification under ASC 842, not as a separate contract, with an effective date of lease modification of August 4, 2020, when the agreement was fully executed. At the effective date of modification, we recorded an adjustment to the right-of-use asset and lease liability in the amount of approximately $813,000.

Einstein License Agreement

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

Off-Balance Sheet Transactions

At December 31, 2020, we did not have any transactions, obligations or relationships that could be considered off-balance sheet arrangements.

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 we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's 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, 2020, our disclosure controls and procedures were effective.

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 Exchange Act Rule 13a-15(f). 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, 2020, 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, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

This annual report does not include an attestation report of our registered public accounting firm due to the transition period established by the JOBS Act for emerging growth companies.

Item 9B. Other Information.

On March 4, 2021, we entered into a third amended and restated employment agreement with Mr. Passeri, our Chief Executive Officer, or the Passeri Employment Agreement, which amends and restates the second amended and restated employment agreement dated February 10, 2020 and pursuant to which, among other things, the parties agreed to remove the annual renewal provision and the right of Mr. Passeri to receive a severance payment if he resigns during the first renewal period. The Passeri Employment Agreement provides that Mr. Passeri shall continue to be employed as our Chief Executive Officer. The term of the Passeri Employment Agreement continues in effect until terminated in accordance with its terms. Mr. Passeri's employment under the Passeri Employment Agreement shall terminate on the first to occur of the following (i) upon 10 days' prior written notice by us to Mr. Passeri of termination due to Mr. Passeri's disability (as defined in the Passeri Employment Agreement), (ii) automatically upon Mr. Passeri's death, (iii) immediately upon written notice by us to Mr. Passeri of a termination for cause (as defined in the Passeri Employment Agreement), (iv) upon written notice by Mr. Passeri to us of a termination for good reason (as defined in the Passeri Employment Agreement), (v) immediately upon written notice by us to Mr. Passeri of an involuntary termination without cause (other than for death or disability) or (vi) upon 60 days' prior written notice by Mr. Passeri to us of Mr. Passeri's voluntary termination without good reason.

The Passeri Employment Agreement provides that Mr. Passeri shall receive an initial annual base salary of $515,000 and is eligible to receive an annual incentive bonus of up to 50% of his base salary based upon achievement of performance-based objectives established by our board of directors. The Passeri Employment Agreement also provides that Mr. Passeri received an option to purchase 150,000 shares of common stock and 150,000 restricted stock units, which represent the contingent right to receive an equal number of shares of common stock, under our 2016 Omnibus Incentive Plan.

The payments and other benefits that Mr. Passeri is eligible to receive upon termination of his employment pursuant to the Passeri Employment Agreement are the same as those described in "Compensation and Other Information Concerning Directors and Officers—Employment Agreements and Change of Control Arrangements—Employment Agreements—Daniel R. Passeri" in our definitive proxy statement filed with the SEC on May 29, 2020. Our obligation to make those payments and provide those benefits is conditioned upon Mr. Passeri signing and delivering a release of claims and agreement not to compete with us for 12 months post-employment.

Mr. Passeri executed a non-competition agreement in the form attached to the Passeri Employment Agreement as a condition of his continued employment.

A copy of the Passeri Employment Agreement is filed as Exhibit 10.26 to this Annual Report on Form 10-K, and the foregoing description of the terms of the Passeri Employment Agreement is qualified in its entirety by reference to such exhibit.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item is incorporated by reference to our Definitive Proxy Statement on Schedule 14A relating to our 2021 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 is incorporated by reference to our Proxy Statement on Schedule 14A relating to our 2021 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 is incorporated by reference to our Proxy Statement on Schedule 14A relating to our 2021 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 is incorporated by reference to our Proxy Statement on Schedule 14A relating to our 2021 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 is incorporated by reference to our Proxy Statement on Schedule 14A relating to our 2021 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.

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, 2020 and 2019, 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, 2020 and 2019, 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.

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.

/s/ RSM US LLP

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

Boston, Massachusetts
March 9, 2021

CUE BIOPHARMA, INC.

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2020	**2019**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 74,866,133	$ 44,290,030
Marketable securities	10,002,550	15,119,925
Accounts receivable	1,417,482	754,898
Prepaid expenses and other current assets	1,241,239	860,107
Total current assets	87,527,404	61,024,960
Property and equipment, net	2,108,024	1,846,922
Operating lease right-of-use	6,774,229	5,337,026
Deposits	2,572,476	2,572,476
Restricted cash	150,000	150,000
Other long term assets	401,667	673,625
Total assets	$ 99,533,800	$ 71,605,009
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,070,303	$ 882,666
Accrued expenses	2,787,211	2,227,352
Research and development contract liability, current portion	6,681,025	4,097,443
Operating lease liability, current portion	4,777,427	4,447,787
Total current liabilities	16,315,966	11,655,248
Research and development contract liability, net of current portion	1,937,575	4,017,894
Operating lease liability, net of current portion	2,368,787	1,347,971
Total liabilities	20,622,328	17,021,113
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; authorized – 100,000,000 shares; issued and outstanding – 30,351,366 shares and 26,562,178 shares at December 31, 2020 and 2019, respectively	30,351	26,562
Additional paid in capital	232,159,029	163,067,773
Accumulated other comprehensive income (loss)	7,131	(10,321)
Accumulated deficit	(153,285,039)	(108,500,118)
Total stockholders' equity	78,911,472	54,583,896
Total liabilities and stockholders' equity	$ 99,533,800	$ 71,605,009

See accompanying notes to consolidated financial statements.

CUE BIOPHARMA, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Years Ended December 31,	
	2020	**2019**
Collaboration revenue	$ 3,154,325	$ 3,458,331
Operating expenses:		
General and administrative	14,651,205	12,740,093
Research and development	33,545,705	27,487,485
Total operating expenses	48,196,910	40,227,578
Loss from operations	(45,042,585)	(36,769,247)
Other income:		
Interest income, net	463,914	482,790
Total other income	463,914	482,790
Loss before provision for income taxes	$ (44,578,671)	$ (36,286,457)
Provision for income taxes	(206,250)	(412,500)
Net loss	(44,784,921)	(36,698,957)
Unrealized gains from available-for-sale securities	17,452	637
Comprehensive loss	$ (44,767,469)	$ (36,698,320)
Net loss per common share – basic and diluted	$ (1.56)	$ (1.66)
Weighted average common shares outstanding – basic and diluted	28,688,625	22,041,792

See accompanying notes to consolidated financial statements.

CUE BIOPHARMA, INC.

CONSOLIDATED STATEMENT OF STOCKHOLDERS' EQUITY
Years Ended December 31, 2020 and 2019

	Common Stock					
	Shares	Par Value	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
Balance, December 31, 2018	20,697,453	$ 20,697	$ 105,762,891	$ (10,958)	$ (71,801,161)	$ 33,971,469
Issuance of common stock from public offerings, net of underwriter commissions and fees	5,314,055	5,314	48,993,593	—	—	48,998,907
Stock-based compensation	—	—	6,520,982	—	—	6,520,982
Exercise of stock options	485,105	485	1,881,388	—	—	1,881,873
Issuance of common stock upon cashless exercise of warrants, net of shares withheld	44,319	45	(45)	—	—	—
Restricted stock awards	33,333	33	(21)	—	—	12
Repurchase of restricted stock awards	(12,087)	(12)	(91,015)	—	—	(91,027)
Unrealized gains from available-for-sale securities	—	—	—	637	—	637
Net loss	—	—	—	—	(36,698,957)	(36,698,957)
Balance, December 31, 2019	26,562,178	26,562	163,067,773	(10,321)	(108,500,118)	54,583,896
Issuance of common stock from public offerings, net of underwriter commissions and fees	3,016,901	3,017	56,679,219	—	—	56,682,236
Stock-based compensation	—	—	10,480,782	—	—	10,480,782
Exercise of stock options	454,497	454	2,202,607	—	—	2,203,061
Issuance of common stock upon cashless exercise of warrants, net of shares withheld	278,179	278	(278)	—	—	—
Restricted stock awards	56,665	57	(40)	—	—	17
Repurchase of restricted stock awards	(17,054)	(17)	(271,034)	—	—	(271,051)
Unrealized gains from available-for-sale securities	—	—	—	17,452	—	17,452
Net loss	—	—	—	—	(44,784,921)	(44,784,921)
Balance, December 31, 2020	30,351,366	$ 30,351	$ 232,159,029	$ 7,131	$ (153,285,039)	$ 78,911,472

See accompanying notes to consolidated financial statements.

CUE BIOPHARMA, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years Ended December 31,	
	2020	**2019**
Cash flows from operating activities:		
Net loss	$ (44,784,921)	$ (36,698,957)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,057,458	810,782
Stock-based compensation	10,480,782	6,520,982
Loss on disposal of fixed asset	—	54,274
Other non cash charges	(563,232)	—
Amortization of premium/discount on purchased securities	83,694	(72,464)
Changes in operating assets and liabilities:		
Account receivable	(662,584)	(754,898)
Prepaid expenses and other current assets	(381,132)	487,182
Operating lease right-of-use asset	(4,202,480)	4,354,810
Other assets	(4,971)	123,437
Deposits	—	(1,559,704)
Accounts payable	741,265	(1,152,688)
Accrued expenses	559,859	439,290
Research and development contract liability	503,263	928,588
Operating lease liability	4,678,965	(4,277,544)
Net cash used in operating activities	(32,494,034)	(30,796,910)
Cash flows from investing activities:		
Purchases of property and equipment	(595,259)	(46,353)
Redemption of short term investments	15,000,000	18,500,000
Purchases of marketable securities	(9,948,867)	(15,134,324)
Cash received from sale of fixed asset	—	127,500
Net cash provided by investing activities	4,455,874	3,446,823
Cash flows from financing activities:		
Proceeds from the public offering of common stock, net of underwriter's commission and fees	56,682,236	48,998,907
Issuance of restricted stock awards	17	12
Restricted stock repurchase at vesting to cover taxes	(271,051)	(91,027)
Proceeds from the exercise of stock options	2,203,061	1,881,873
Net cash provided by financing activities	58,614,263	50,789,765
Net increase in cash, cash equivalents, and restricted cash	30,576,103	23,439,678
Cash, cash equivalents, and restricted cash at beginning of year	44,440,030	21,000,352
Cash, cash equivalents, and restricted cash at end of year	$ 75,016,133	$ 44,440,030
Supplemental disclosures of cash flow information:		
Cash paid for –		
Income taxes	$ —	$ 412,500
Purchases of property and equipment in accounts payable or accrued expenses	$ 446,372	$ —
Operating lease modification	$ 5,639,000	$ —

See accompanying notes to consolidated financial statements.

1. Organization and Basis of Presentation

Cue Biopharma, Inc. (the "Company") was incorporated in the State of Delaware on December 31, 2014 under the name Imagen Biopharma, Inc., and completed its organization, formation and initial capitalization activities effective as of January 1, 2015. In October 2016, the Company changed its name to Cue Biopharma, Inc. The Company's corporate office and research facilities are located in Cambridge, Massachusetts.

The Company is a clinical-stage biopharmaceutical company engineering a novel class of injectable biologics to selectively engage and modulate targeted T cells within the patient's body to treat a broad range of cancers, chronic infectious diseases, and autoimmune disorders.

The Company is in the development stage and has incurred recurring losses and negative cash flows from operations. As of December 31, 2020, the Company had unrestricted cash, cash equivalents and marketable securities of approximately $84.9 million. Management believes that current cash, cash equivalents and marketable securities on hand at December 31, 2020 are sufficient to fund operations for at least the next twelve months from the date of issuance of these financial statements; however, the future viability of the Company is dependent on its ability to raise additional capital to finance its operations and to fund increased research and development costs in order to seek approval for commercialization of its drug product candidates. 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 the Company's drug product candidates in order to generate future revenue streams.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements for the years ended December 31, 2020 and 2019, 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 Corporation, Inc., 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

In June 2019, the Company entered into an "at-the-market" ("ATM") equity offering sales agreement (the "June 2019 ATM Agreement") with Stifel Nicolaus & Company, Inc. ("Stifel") to sell shares of the Company's common stock for aggregate gross proceeds of up to $30 million, from time to time, through an ATM equity offering program under which Stifel acted as sales agent. As of December 31, 2020, the Company had sold 3,584,945 shares of common stock under the June 2019 ATM Agreement for proceeds of approximately $29.4 million, net of commissions paid, but excluding transaction expenses, and terminated this equity offering upon completion.

In November 2019, the Company entered into an ATM equity offering sales agreement with Stifel (the "November 2019 ATM Agreement") to sell shares of the Company's common stock for aggregate gross proceeds of up to $20 million, from time to time, through an ATM equity offering program under which Stifel acted as sales agent. As of December 31, 2020, the Company had sold 1,729,110 common shares under the November 2019 ATM Agreement for proceeds of approximately $19.6 million, net of commissions paid, but excluding estimated transaction expenses, and terminated this equity offering upon completion.

In March 2020, the Company entered into an ATM equity offering sales agreement with Stifel (the "March 2020 ATM Agreement") to sell shares of the Company's common stock for aggregate gross proceeds of up to $35 million, from time to time, through an ATM equity offering program under which Stifel would act as sales agent. As of December 31, 2020, the Company had sold a total of 1,824,901 shares of common stock under the March 2020 ATM Agreement for proceeds of approximately $34.3 million, net of commissions paid, but excluding estimated transaction expenses. Due to the issuance and sale of all the shares of common stock subject thereto, the March 2020 ATM Agreement terminated in accordance with its terms.

In June 2020, the Company entered into an ATM equity offering sales agreement with Stifel (the "June 2020 ATM Agreement") to sell shares of the Company's common stock for aggregate gross proceeds of up to $40 million, from time to time, through an ATM equity offering program under which Stifel acts as sales agent. The June 2020 ATM Agreement will terminate upon the earliest of (a) the sale of $40 million of shares of the Company's common stock or (b) the termination of the June 2020 ATM Agreement by the Company or Stifel. As of December 31, 2020, the Company had sold 1,192,000 shares of common stock under the June 2020 ATM Agreement for proceeds of approximately $22.4 million, net of commissions paid, but excluding estimated transaction expenses.

Consolidation

The accompanying consolidated financial statements include the Company and its wholly owned subsidiary, Cue Biopharma Securities Corporation, Inc. The Company has eliminated all intercompany transactions for the years presented.

Reclassifications

Certain prior year amounts have been reclassified for consistency with the current year presentation. These reclassifications had no effect on the reported results of operations.

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 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 a financial institution in Federally-insured accounts and may periodically have cash balances in excess of insurance limits. The Company maintains its accounts with a financial institution with a high credit rating. The Company has not experienced any losses to date and believes that it is not exposed to any significant credit risk on cash.

Cash and Cash Equivalents

The Company considers all liquid investments with a maturity of three months or less at the date of purchase to be cash equivalents. The Company currently 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 balance sheet date. 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 are recognized and are included in other comprehensive income (loss). Realized gains are recognized and determined on a specific identification basis and are included in other income (loss) on the income statement. Amortization and accretion of discounts and premiums is recorded in interest income. The Company currently invests in United States Treasury obligations.

Restricted Cash

The Company purchased a $150,000 certificate of deposit to collateralize a credit card account with a commercial bank that was classified as short-term certificate of deposit as of December 31, 2020.

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 disposition 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 in and 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.

As the Company can renew the underlying rights to the CUE BIOLOGICS Mark indefinitely at nominal cost, this acquired intangible asset has been classified as a component of other long term assets, having a useful life of 15 years. The Company recorded $11,666 and $11,667 in amortization related to the trademark at December 31, 2020 and 2019, respectively.

Revenue Recognition

The Company follows the provisions of Accounting Standards Codification 606, *Revenue from Contracts with Customers* ("ASC 606"). The Company generates revenue solely through collaboration arrangements with strategic partners for the development and commercialization of drug product candidates. The core principle of ASC 606 is that an entity should recognize revenue to depict the transfer of promised goods and/or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods and/or services. To determine the appropriate amount of revenue to be recognized for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following steps: (i) Identify the contract(s) with the customer, (ii) Identify the performance obligations in the contract, (iii) Determine the transaction price, (iv) Allocate the transaction price to the performance obligations in the contract and (v) Recognize revenue when (or as) each performance obligation is satisfied.

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 judgement 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 "most likely amount" 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 most likely amount method. Currently, the Company has one contract with an option to acquire additional goods and/or services in the form of additional research and development services for additional drug product candidates which it evaluated and determined that it was not a material right related to the LG Chem agreement.

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 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.

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 balance sheet 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 operations as incurred. For the years ended December 31, 2020 and 2019, patent expenses were $1,879,000 and $1,934,000, respectively. Patent expenses are included in general and administrative expenses in the Company's consolidated statements of operations and comprehensive loss.

Licensing Fees and Costs

Licensing fees and costs consist primarily of costs relating to the acquisition of the Company's license agreement with Einstein, including related royalties, maintenance fees, milestone payments and product development costs. Licensing fees and costs are charged to operations as incurred.

Long-Lived Assets

The Company reviews long-lived assets, consisting of property and equipment and a trademark, for impairment at each fiscal year end or 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 balance sheet 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. During the year ended December 31, 2019, the Company sold lab equipment with a net book value of approximately $181,000 that was being decommissioned and recognized a loss of approximately $54,000. There were no sales of lab equipment or capital equipment during the year ended December 31, 2020.

Leases

In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standard Update ("ASU") 2016-02, Leases (ASC 842) ("ASU-2016-02"), which supersedes the existing guidance for lease accounting, Leases (ASC 840). ASU 2016-02 requires a lessee to record a right-of-use asset and a corresponding lease liability, for most lease arrangements on the balance sheet. Under the standard, disclosure of key information about leasing arrangements to assist users of the financial statements to assess the amount, timing and uncertainty of cash flows arising from leases are required. The standard is effective for fiscal years beginning after December 15, 2018.

The adoption of ASC 842 on January 1, 2019 resulted in the recognition of approximately $9,692,000 of right-of-use asset and $9,347,000 of lease liabilities on the Company's balance sheet. The adoption did not have a material net impact on the Company's consolidated statements of operations or accumulated deficit. Please refer to Note 14 for more detail.

Stock-Based Compensation

The Company periodically issues stock-based awards to officers, directors, employees, Scientific and Clinical Advisory Board members, non-employees and consultants for services rendered. Such issuances vest and expire according to terms established at the issuance date.

Stock-based payments to officers, directors, members of the Company's Scientific and Clinical Advisory Board, non-employees and outside consultants and employees, 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 option-pricing model, which is affected by several variables, including the risk-free interest rate, the expected dividend yield, the life of the equity award, the exercise price of the stock option as compared to the fair value of the common stock on the grant date, and the estimated volatility of the common stock over the term of the equity award.

The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant. Until the Company has established a trading history for its common stock that approximates the expected term of the options, estimated volatility is based on the average historical volatilities of comparable public companies in a similar industry. 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 statements of operations, 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.

The Company recognized approximately, $206,250 and $412,500 of income tax expense related to the foreign taxes withheld from an upfront payment received from LG Chem, Ltd. ("LG Chem") pursuant to a collaboration agreement with LG Chem (the "LG Chem Agreement") during the year ended December 31, 2020 and 2019, respectively.

The Company recognizes interest accrued relative to unrecognized tax benefits in interest expense and penalties in operating expense. During the years ended December 31, 2020 and 2019, 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, 2020 and 2019.

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 loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive loss in all periods presented, other than its net loss, was unrealized gains and losses 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.

At December 31, 2020 and 2019, the Company excluded the outstanding securities summarized below, which entitle the holders thereof to acquire shares of common stock, from its calculation of earnings per share, as their effect would have been anti-dilutive.

	December 31,	
	2020	**2019**
Common stock warrants	861,969	1,189,827
Common stock options	5,030,899	4,793,253
Nonvested restricted stock units	230,002	66,667
Total	6,122,870	6,049,747

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.

Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company has determined that its financial assets are currently classified within Level 1 and that its financial liabilities are currently all classified within Level 3 in the fair value hierarchy. In determining the appropriate levels, the Company performs an analysis of the assets and liabilities at each reporting period end.

The Company had $72,943,275 in cash equivalents and $10,002,550 in short-term marketable securities that were measured and recorded at fair value on the Company's balance sheet at December 31, 2020. The Company had $39,303,609 in cash equivalents and $15,119,925 in short-term marketable securities that were measured and recorded at fair value on the Company's balance sheet at December 31, 2019.

The carrying value of financial instruments (consisting of cash, a certificate of deposit, 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

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments- Credit Losses: Measurement of Credit Losses on Financial Instruments (ASC 326) (CECL). The standard requires entities to measure all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions and reasonable and supportable forecasts. The standard is effective for annual reporting periods beginning after December 15, 2022, including interim reporting periods within each annual reporting period, for smaller reporting companies. The Company is still evaluating the impact of ASU 2016-13 on the Company's consolidated financial statements, if any.

In December 2019, the FASB issued ASU No. 2019-12, "*Income Taxes (ASC 740): Simplifying the Accounting for Income Taxes*," which is intended to simplify various aspects related to accounting for income taxes. The pronouncement is effective for fiscal years, and for interim periods within those fiscal years, beginning after December 15, 2020, with early adoption permitted. ASU No. 2019-12 is effective for us beginning in the fiscal year ending December 31, 2021. The Company is currently in the process of evaluating the effects of this pronouncement on the 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 generally accepted accounting principles 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, 2020 and 2019 and indicate the level of the fair value hierarchy utilized to determine such fair value:

	Fair Value Measurements as of December 31, 2020			
	Level 1	Level 2	Level 3	Fair Value
Cash equivalents	$ 72,943,275	$ —	$ —	$ 72,943,275
Marketable securities	—	10,002,550	—	10,002,550
Total	$ 72,943,275	$ 10,002,550	$ —	$ 82,945,825

	Fair Value Measurements as of December 31, 2019			
	Level 1	Level 2	Level 3	Fair Value
Cash equivalents	$ 39,303,609	$ —	$ —	$ 39,303,609
Marketable securities	—	15,119,925	—	15,119,925
Total	$ 39,303,609	$ 15,119,925	$ —	$ 54,423,534

As of December 31, 2020 and 2019, the Company's cash equivalents that are invested in money market funds valued using Level 1 inputs for identical securities. The Company measures the fair value of marketable securities that are invested in United States Treasury securities using Level 2 inputs and primarily relies on quoted prices in active markets for similar marketable securities. During the year ended December 31, 2020 and 2019, there were no transfers between Level 2 and Level 3.

4. Marketable Securities

As of December 31, 2020 and 2019, the fair value of available-for-sale marketable securities by type of security was as follows:

	December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Treasury Securities	$ 9,995,419	$ 7,131	$ —	$ 10,002,550
	$ 9,995,419	$ 7,131	$ —	$ 10,002,550

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Treasury Securities	$ 15,130,246	$ —	$ (10,321)	$ 15,119,925
	$ 15,130,246	$ —	$ (10,321)	$ 15,119,925

At December 31, 2020, marketable securities consisted of $10,002,550 of investments that mature within twelve months. The Company recorded an unrealized gain on investments of $17,452 for the year ended December 31, 2020. At December 31, 2019, the Company marketable securities consisted of $15,119,925 of investments that mature within twelve months. The Company recognized an unrealized gain on investments of $637 for the year ended December 31, 2019.

5. Property and Equipment

Property and equipment as of December 31, 2020 and 2019 is summarized as follows:

	December 31,	
	2020	2019
Laboratory equipment	$ 4,148,426	$ 3,587,559
Furniture and fixtures	93,321	93,321
Computer equipment	267,837	192,092
Construction in progress	405,019	—
	4,914,603	3,872,972
Less accumulated depreciation	(2,806,579)	(2,026,050)
Net property and equipment	$ 2,108,024	$ 1,846,922

Depreciation expense for the year ended December 31, 2020 was included in the consolidated statements of operations and comprehensive loss as follows, excluding trademark amortization of $11,666 and amortization of capitalized license expenses of $265,263. Depreciation expense for the year ended December 31, 2019 was included in the consolidated statements of operations and comprehensive loss as follows, excluding trademark amortization of $11,667.

	Years Ended December 31,	
	2020	2019
General and administrative	$ 20,301	$ 60,974
Research and development	760,228	738,140
Total	$ 780,529	$ 799,114

During the year ended December 31, 2019, the Company sold lab equipment with an acquisition cost of $320,778 and accumulated depreciation of $139,003, and realized a loss of $54,274. The Company did not sell lab equipment or other capital equipment during the year ended December 31, 2020.

6. Accrued Expenses

Accrued expenses as of December 31, 2020 and 2019 is summarized as follows:

	December 31,	
	2020	2019
Accrued compensation	$ 1,963,983	$ 1,575,821
Contract manufacturing services	108,880	150,250
Professional Services	326,028	383,910
Contract research services	388,320	117,371
	$ 2,787,211	$ 2,227,352

7. Einstein License and Service Agreement

License Agreement

On January 14, 2015, the Company entered into a license agreement, as amended on June 2, 2015 (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 candidates, and two supporting technologies that enable the discovery of costimulatory signaling molecules (ligands) and T-cell targeting peptides. On July 31, 2017, the Company entered into an amended and restated license agreement which modified certain obligations of the parties under the Einstein License.

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 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, 2020, $150,000 had been paid by the Company towards 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, 2020 and 2019.

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 the costs incurred in connection with the Einstein License in accordance with ASC 730, *Research and Development*. For the years ended December 31, 2020 and 2019, costs aggregated $75,000 and $565,659, respectively resulting from LG milestone payments earned with respect to the Einstein License. For the years ended December 31, 2020 and 2019, $75,000 and $50,000 were included in research and development expenses in the consolidated statements of operations and comprehensive loss. As of December 31, 2020, the Company capitalized $416,855 net of amortization with respect to the Einstein License pursuant to ASC 606 and ASC 340-40, *Other Assets and Deferred Costs: Contracts with Customers* in prepaid expenses and other current assets. As of December 31, 2019, the Company capitalized $525,554 with respect to the Einstein License pursuant to ASC 606 and ASC 340. The Company recorded $265,262 and $260,292 in prepaid expenses and other current assets and other long term assets, respectively.

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 provide 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, 2020, the Company granted stock options to purchase 981,800 shares of the Company's common stock and 220,000 restricted stock units. At December 31, 2020, stock options for 4,459,301 shares of common stock and 320,000 restricted stock units had been granted and 750,325 shares of common stock were reserved for future grants under the Omnibus Plan, and stock options for 481,600 shares of common stock had been granted and 5,400 shares of common stock were reserved for future grants under the Non-Employee Plan. In the aggregate, at December 31, 2020, stock options for a total of 4,940,901 shares of common stock and 320,000 restricted stock units had been granted and 755,725 shares of common stock were reserved for future grants. Such grants are accounted for as share-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, 2020 and 2019, the fair value of each stock option award was estimated using the Black-Scholes option-pricing model utilizing the following assumptions:

	December 31,	
	2020	**2019**
Risk-free interest rate	0.38 to 1.56%	1.75 to 2.58%
Expected dividend yield	0%	0%
Expected volatility	93.4-99.6%	88.0-94.0%
Expected life	5.5 to 6.25 years	4.0 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 volatilities of comparable companies in a similar industry; 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, 2020 is as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in Years)
Stock options outstanding at December 31, 2018	4,540,321	$ 7.08	5.16
Granted	1,288,100		
Exercised	(485,105)		
Cancelled	(550,063)		
Stock options outstanding at December 31, 2019	4,793,253	$ 7.10	5.64
Granted	981,800	17.31	
Exercised	(454,497)	4.86	
Cancelled	(289,657)	10.14	
Stock options outstanding at December 31, 2020	5,030,899	$ 9.10	5.51
Stock options exercisable at December 31, 2020	2,920,318	$ 7.05	4.03

The Company recognized, $8,861,760 and $6,208,949, in stock-based compensation during the years ended December 31, 2020 and 2019, respectively related to stock option activity. As of December 31, 2020, total unrecognized stock-based compensation was approximately $15,605,021, which is expected to be recognized as an operating expense in the Company’s consolidated statements of operations and comprehensive loss through June 2022.

The aggregate intrinsic value of exercisable but unexercised in-the-money stock options at December 31, 2020 was approximately $16,869,399 based on a weighted average exercise price of $7.05 per share. The aggregate intrinsic value of options is calculated as the difference of the market close price of $12.51 on December 31, 2020, and the weighted average exercise price of $7.05, with a weighted average remaining contractual term of 4.03 years.

The aggregate intrinsic value of exercisable but unexercised in-the-money stock options at December 31, 2019 was approximately $19,471,155, based on a weighted average exercise price of $6.26 per share at December 31, 2019.

Option Amendments- Modification of Incentive Stock Options

During the year ended December 31, 2020, the following event resulted in the amendment to terms of outstanding stock option awards:

On January 22, 2020, an employee who was employed for a particular role pursuant to an employment agreement that prescribed certain separation benefits to the employee was separated from that role. Per the employment agreement, upon termination (i) all unvested stock options would accelerate and become vested as of the termination date, and (ii) the options would remain exercisable, to the extent applicable, following the date of termination for the period prescribed in the equity award plan. As of January 21, 2020, the terminated employee held outstanding options to purchase an aggregate of 215,000 shares of the Company's common stock at a weighted average exercise price of $6.22 per share, including unvested options to purchase 94,375 shares at a weighted average exercise price of $7.83 per share. On January 21, 2020, the unvested portion of the outstanding options vested, and the post-employment option exercise period was extended from 90 days, as prescribed to the equity award plan, to 12 months from the date of the termination. In May 2020, the final separation agreement was amended to extend the post-employment option exercise period from 12 months to 36 months.

The Company calculated the change in stock-based compensation cost associated with the previously described stock option modifications pursuant to the applicable guidance in ASC 718. The change in compensation cost was determined by calculating the difference between (a) the estimated fair value of each option award immediately prior to the modifications and (b) the estimated fair value of each option award immediately after the modifications. The fair value of each option award immediately prior to and immediately after modification was estimated using the Black-Scholes option-pricing model to determine an incremental fair value, consistent with and in accordance with the Company’s existing accounting policy for stock compensation. The total additional compensation cost associated with the previously described modifications was determined to be approximately $344,850, which was expensed in the year ended December 31, 2020.

Restricted Stock Units

On October 3, 2019, the Company granted 100,000 restricted stock units ("RSUs") with time-based vesting conditions to certain executives. During the year ended December 31, 2019, the Company awarded 100,000 RSUs at an average grant date fair value of $7.53 per share. The RSUs vest in three substantially equal installments beginning on grant date, and annually thereafter. Compensation expense is recognized on a straight-line basis.

On February 5, 2020, the Company granted 150,000 RSUs with time-based vesting conditions to an executive officer. One-half of the RSUs vest on September 30, 2021, and the balance vest on March 31, 2022, subject to the recipient's continued service on each applicable vesting date. On March 31, 2020, the Company granted 50,000 RSUs with time-based vesting conditions to an executive officer. The RSUs vest in three substantially equal installments beginning on the grant date, and annually thereafter, subject to the recipient's continued service on each applicable vesting date. Compensation expense is recognized on a straight-line basis.

On August 21, 2020, the Company granted 20,000 RSUs with time-based vesting conditions to an executive officer. The RSUs vest in three substantially equal installments beginning on the grant date, and annually thereafter, subject to the recipient's continued service on each applicable vesting date. Compensation expense is recognized on a straight-line basis.

The following table summarizes the RSU activity for the under the Omnibus Plan for the year ending December 31, 2020:

Restricted Securities	Number of Shares	Weighted Average Grant Date Fair Value Per Share
Nonvested balance as of December 31, 2019	66,667	$ 7.53
Granted	220,000	17.96
Vested/Released	(56,665)	10.94
Forfeited	—	—
Nonvested balance at December 31, 2020	230,002	$ 16.66

The Company recognized $1,619,022 and $312,032 in stock-based compensation during the years ended December 31, 2020 and 2019, respectively, related to restricted stock unit activity. As of December 31, 2020, total unrecognized stock-based compensation was approximately $2,772,845, which is expected to be recognized as an operating expense in the Company's consolidated statements of operations and comprehensive loss through June 2022.

Stock-based Compensation

Stock-based compensation for the years ended December 31, 2020 and 2019 was included in the consolidated statements of operations and comprehensive loss as follows:

	December 31,	
	2020	2019
General and administrative	$ 4,093,542	$ 2,109,335
Research and development	6,387,240	4,411,647
Total	$ 10,480,782	$ 6,520,982

9. Warrants

The Company has two tranches of common stock warrants outstanding at December 31, 2020. The first tranche was exercisable for 370,370 shares of common stock issued on June 15, 2015 with an exercise price of $2.70 per share. These warrants were issued with a 7 year term and expire on June 15, 2022. The second tranche was exercisable for 882,071 shares of common stock issued on December 27, 2017 with an exercise price of $9.38 per share. These warrants were issued with a 5 year term and expire on December 26, 2022. The intrinsic value of exercisable but unexercised in-the-money common stock warrants at December 31, 2020 was approximately $3,187,000 based on a fair value of $12.51 per share on December 31, 2020.

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 following table summarizes common stock warrant activity for the year ended December 31, 2020:

	Warrant Issued June 15, 2015 Tranche 1	Warrant Issued December 27, 2017 Tranche 2	Total
Balance at December 31, 2019	322,259	867,568	1,189,827
Issued via cashless exercises	(227,184)	(50,995)	(278,179)
Withheld as payment to cover issued shares	(22,464)	(27,215)	(49,679)
Balance at December 31, 2020	72,611	789,358	861,969

10. Revenue Recognition

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 judgement 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, (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 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 "most likely amount" 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 contact 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 judgement 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 the 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.

On November 14, 2017, the Company entered into a collaboration agreement (the "Merck Agreement") with Merck Sharp & Dohme Corp. ("Merck") for a partnership to research and develop certain of the Company's proprietary biologics that target certain autoimmune disease indications (the "Initial Indications"). The Company views the Merck Agreement as a component of its development strategy since it will allow the Company to advance its autoimmune programs in partnership with a world class pharmaceutical company, while also continuing its focus on its more advanced cancer programs. The research program outlined in the Merck Agreement entails (1) the Company's research, discovery and development of certain Immuno-STAT™ drug candidates up to the point of demonstration of certain biologically relevant effects ("Proof of Mechanism") and (2) the further development by Merck of the Immuno-STAT drug candidates that have demonstrated Proof of Mechanism (the "Proposed Drug Product Candidates") up to the point of demonstration of all or substantially all of the properties outlined in such Proposed Drug Product Candidates' profiles as described in the Merck Agreement.

In exchange for the licenses and other rights granted to Merck under the Merck Agreement, Merck paid to the Company a $2.5 million nonrefundable up-front payment. Additionally, the Company may be eligible to receive funding in developmental milestone payments, as well as tiered royalties, if all research, development, regulatory and commercial milestones agreed upon by both parties are successfully achieved. Excluding the up-front payment described above, the Company is eligible to earn up to $101 million for the achievement of certain research and development milestones, $120 million for the achievement of certain regulatory milestones and $150 million for the achievement of certain commercial milestones, in addition to tiered royalties on sales, if all pre-specified milestones associated with multiple products across the primary disease indication areas are achieved. The Merck Agreement requires the Company to use the first $2.5 million milestone payment it receives under the agreement to fund contract research. The amount of the royalty payments is a percentage of product sales ranging in the single digits based on the amount of such sales.

As it relates to the Merck Agreement, the Company recognized the upfront payment associated with its one open contract 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. Amounts expected to be recognized as revenue within the twelve months following the balance sheet date are classified in current liabilities. Amounts not expected to be recognized as revenue within the twelve months following the balance sheet date are classified as contract liabilities, net of current portion. The Company determined that there was one performance obligation: consisting of the license and research development services. Thus, the transaction price of $2.5 million was allocated to the single performance obligation.

On November 18, 2020, the Company entered into a First Amendment to the Merck Agreement (the "Amendment") with Merck. Pursuant to rights granted to Merck under the Merck Agreement, the Amendment extends the term of the research program under the Merck Agreement for an additional year, until December 31, 2021. Under the terms of the Amendment, Merck will reimburse the Company for specified expenses and provide additional financial research support to further study and develop preclinical biologics with the objective of identifying clinical candidates subject, in each case, to specified maximum amounts, with any amounts in excess of such maximum amounts to be borne by the Company. On November 18, 2020, the Company earned a milestone payment related to this Amendment in the amount of $300,000. The $300,000 milestone payment was recorded as a contract liability upon receipt. The Company will recognize revenue related to this milestone payment pursuant to its revenue recognition policy in relation to the performance of its obligations related to the development of Immuno-STAT drug candidates under the arrangement.

Aside from the $300,000 milestone payment earned to date, the Company does not believe that any variable consideration should be included in the transaction price at December 31, 2020. 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 by assessing the effort and expense expended during the period. For the year ended December 31, 2020, the Company recognized approximately $177,000 in collaboration revenue related to this agreement and recorded short and long-term research and development liabilities on its balance sheet dated December 31, 2020 of $606,771 and $0, respectively. For the year ended December 31, 2019, the Company recognized approximately $874,000 in collaboration revenue related to this agreement and recorded short and long-term research and development liabilities on its balance sheet dated December 31, 2019 of $483,515 and $0, respectively.

On November 6, 2018, the Company entered into the LG Chem Agreement with LG Chem related to the development of the Company's Immuno-STATs focused in the field of oncology. Pursuant to the LG Chem Agreement, the Company granted LG Chem an exclusive license to develop, manufacture and commercialize the Company's lead product, CUE-101, as well as Immuno-STATs that target T cells against two additional cancer antigens, in certain Asian countries (the "LG Chem Territory"). Pursuant to a global license and collaboration agreement, dated December 18, 2019, as amended on November 5, 2020, LG Chem has the option to elect one additional Immuno-STAT for an oncology target on or prior to April 30, 2021 for a worldwide development and commercialization license, and the Company will retain an option to co-develop and co-commercialize the additional program worldwide. The Company retains rights to develop and commercialize all assets included in the agreement in the United States and in global markets outside of Asia. In exchange for the licenses and other rights granted to LG Chem under the LG Chem Agreement, LG Chem made a $5.0 million equity investment in common stock of the Company and a $5.0 million nonrefundable upfront cash payment. The Company is also eligible to receive up to an additional $400 million in research, development, regulatory and sales milestones. In addition, the LG Chem 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 FDA acceptance of the IND for the Company's lead drug candidate, CUE-101, pursuant to the LG Chem 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, approximately $412,500 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 $1.25 million milestone payment on the selection of a pre-clinical candidate pursuant to the LG Chem Agreement. The $1.25 million milestone payment was recorded as a contract liability upon receipt. Revenue related to this milestone payment will be 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 pre-clinical candidate. Of the $1.25 million milestone payment, approximately $206,250 was withheld as payment of foreign tax withholding and shown as income tax expense on the consolidated statement of operations and comprehensive loss.

The Company recorded short and long-term research and development liabilities on its balance sheet dated of $6,074,254 and $1,937,575, respectively, for the year ended December 31, 2020.

Aside from the $3.75 million 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, 2020. 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, 2020 and 2019, the Company recognized revenue of approximately $2,978,000 and $2,584,000, respectively, related to the LG Chem Agreement.

The Company considered the capitalization of contract costs under the guidance in ASC 340. There were no contract costs identified in the Merck Agreement. As it related to the LG Chem Agreement, the Company capitalized license expenses of approximately $907,600 as of December 31, 2020, pursuant to the Einstein License which requires the Company to pay a percentage of sublicenses related to the Company's patent rights for components of its core technology that is licensed from Einstein. This amount is comprised of approximately $438,000 of capitalized license expenses related to the upfront payment received from LG Chem in December 2018, approximately $313,000 in capitalized license expenses related to the milestone payment received in June 2019, and approximately $156,600 in capitalized license expenses related to the milestone payment received in December 2020, net of accumulated amortization of approximately $490,700. For the year ended December 31, 2020, approximately $416,900 was included in prepaid expenses and other short-term assets and $0 is included in other long-term assets.
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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, 2020 and 2019. 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 100,000,000 shares of common stock, par value $0.001 per share, of which 30,351,366 shares and 26,562,178 shares were issued and outstanding at December 31, 2020 and 2019, respectively.

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 reported a $206,250 tax provision for the year ended December 31, 2020 related to foreign withholding taxes paid.

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, 2020 and 2019 are as follows:

	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 34,539,000	$ 23,348,000
Research and other credits	2,312,000	2,069,000
Reserves and accruals	7,446,000	5,281,000
Other	—	3,000
Total gross deferred tax assets	44,297,000	30,701,000
Less valuation allowance	(42,321,000)	(29,095,000)
Total deferred tax assets	1,976,000	1,606,000
Deferred tax liability:		
Depreciation	(1,974,000)	(1,606,000)
Other	(2,000)	—
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, 2020, and 2019, 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, 2020, 2019, and 2018, 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, 2020, 2019, and 2018 is as follows:

	Years Ended December 31,	
	2020	2019
U. S. Federal statutory tax rate	(21)%	(21)%
State Taxes	(7)%	(6)%
Change in valuation allowance	30%	27%
Tax credits	(1)%	(2)%
Stock based compensation	(2)%	1%
Tax reform	0%	0%
Foreign withholding taxes	0%	1%
Other	1%	1%
Effective tax rate	0%	1%

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, 2020 and 2019, the Company had unrecognized tax benefits related to Federal and state research tax credits of approximately $1,675,000 and $1,334,000, respectively. The Company is subject to Federal and state income tax examinations by tax authorities for all years since its incorporation in 2014. The Company is currently not under examination by any tax authority.

At December 31, 2020, the Company has available net operating loss carryforwards for Federal and state income tax purposes of approximately $126,941,033 and $126,360,676, respectively, which, if not utilized earlier, will begin to expire in 2035. Approximately, $98,429,255 of the federal net operating losses have an indefinite carryforward. The Company has Federal research credits of approximately $2,993,000, which, if not utilized earlier, will begin to expire in 2035, and state research credits of approximately $1,151,000, which, if not utilized earlier, will begin to expire in 2031. At December 31, 2020 the Company recorded $250,000 in research credits as prepaid to be offset against payroll tax liabilities associated with research and development personnel in 2020 in addition to the approximately $250,000 in research and development credits remaining in prepaid from 2019.

Ownership changes, as defined in the Internal Revenue Code, including those resulting from the issuance of common stock in connection with our 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. We have performed an analysis of ownership changes through December 31, 2020. Based on this analysis, we do not believe that any of our 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, 2020 and 2019:

	Year Ended December 31,	
	2020	**2019**
Balance at the beginning of year	$ 1,334,000	$ 972,000
Additions for current year tax provisions	341,000	294,000
Additions for prior year tax provisions	—	81,000
Reductions of prior year tax provisions	—	(13,000)
Balance as of end of year	$ 1,675,000	$ 1,334,000

14. Commitments and Contingencies

Einstein License and Service Agreement

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 Merck

See discussion of the Merck Agreement in Note 10.

Collaboration Agreement with LG Chem Life Sciences

See discussion of the LG Chem Agreement in Note 10.

Leased Facilities

The Company leases approximately 19,900 square feet of office space in Cambridge, Massachusetts under a lease that began in May 2018 and is scheduled to expire on April 14, 2021 (the "Lease"), as discussed further below. Upon adoption of ASU 2016-02, the Company recorded a right-of-use asset and corresponding lease liability for the Lease on January 1, 2019, by calculating the present value of lease payments, discounted at 6%, the Company's estimated incremental borrowing rate annually, over the 2.3-year remaining term.

On January 18, 2018, the Company entered into an operating lease agreement for its laboratory and office space in Cambridge, Massachusetts for the period from May 1, 2018 through April 30, 2021 (the "Laboratory and Office Lease"). The lease contains escalating payments during the lease period. Upon execution of this lease agreement the Company prepaid three months of rent, two of which will be held in escrow and credited against future rent payments and that the other of which was applied to the first months' rent. The Company also prepaid seven and one half months' rent pursuant to an amendment to the lease agreement executed on June 18, 2018. These amounts were recorded to deposits and prepaid expenses, respectively, at December 31, 2020.

On June 18, 2018, the Company entered into an amendment to the Laboratory and Office Lease that provided the Company with a reduction in rental fees for its office and laboratory space in exchange for prepayment of a portion of the fees. This amendment was effective beginning on May 15, 2018 and expires on April 14, 2021.

The monthly rent payment due under the Laboratory and Office Lease is currently $330,550 until April 2021 and will increase to $375,174 for the remainder of the term.

On September 20, 2018, the Company entered into an operating lease for additional laboratory space at 21 Erie Street, Cambridge, Massachusetts for the period from October 15, 2018 through April 14, 2021(the "Additional Laboratory Lease"). The lease contains escalating payments during the lease period. The monthly rental rate under the Additional Laboratory Lease was $72,600 for the first 12 months and $78,600 for the remainder of the term. Upon execution of this lease agreement the Company prepaid 12 months' rent pursuant to the lease agreement executed on September 20, 2018.

On September 19, 2019, the Company entered into a second amendment to the Additional Laboratory Lease that removed one holding room from the additional laboratory space. The amendment was effective beginning on October 1, 2019 and expires on April 14, 2021. The monthly rental rate under the Additional Laboratory Lease decreased from $78,600 to $58,995, for the remainder of the lease term. The partial termination of the lease did not change the classification of the lease and remained accounted for as an operating lease. The weighted-average discount rate remained the same at 6%. The Company accounted for the lease modification under ASC 842 that removed one holding room by electing Approach 1, which remeasured the right-of-use asset on the basis of the amount of the liability change. The modification of the partial termination resulted in a reduction to right-of-use asset and lease liability of $335,465 and $327,079, respectively. The difference of $8,386 was recorded as a loss to the right-of-use asset as of December 31, 2019.

On June 24, 2020, the Company entered into a second amendment to the Laboratory and Office Lease. Pursuant to the amendment (1) the term of the lease was extended to June 14, 2022 and (2) the monthly rental rate for the last 14 months of the lease term was increased to $375,174. The Company determined that the amendment should be accounted for as a lease modification applicable under ASC 842, not as a separate contract, with an effective date of lease modification of May 14, 2020. At the effective date of modification, the Company recorded an adjustment to the right-of-use asset and lease liability in the amount of approximately $4,826,000.

On July 20, 2020, the Company entered into a third amendment to the Additional Laboratory Lease. Pursuant to the amendment the term of the lease was extended to June 14, 2022. The Company determined that the amendment should be accounted for as a lease modification applicable under ASC 842, not as a separate contract, with an effective date of lease modification of August 4, 2020, when the agreement was fully executed. At the effective date of modification, the Company recorded an adjustment to the right-of-use asset and lease liability in the amount of approximately $813,000.

At December 31, 2020, the Company recorded approximately $6,774,000 to operating right-of-use asset, and approximately $4,777,000 and $2,369,000 to short and long-term operating lease liability, respectively. At December 31, 2020 the remaining lease term was 1.46 years.

Future minimum lease payments under these leases at December 31, 2020 are as follows:

Year	
2021	5,079,642
2022	2,407,692
Total lease payments	7,487,334
Less: present value discount	(341,121)
Present value of lease payments	$ 7,146,213

Total rent expense of approximately $4,593,000 and $4,474,000 was included in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2020 and 2019, respectively.

Contingencies

The Company accrues for 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, 2020, 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. 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 did not make any contributions to the Plan during the year ended December 31, 2020 or 2019.

16. Subsequent Events

The Company has evaluated subsequent events through the date on which the consolidated financial statements were issued, to ensure that this submission includes appropriate disclosure of events both recognized in the consolidated financial statements and events which occurred subsequently but were not recognized in the consolidated financial statements.

PART IV

Item 15. Exhibits, Financial Statements and 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:

Exhibit Number	Exhibit Description	Incorporated by Reference				
		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	11/09/20	005-90232
3.2	Amended and Restated Bylaws of the Registrant		S-1	3.5	12/05/17	333-220550
4.1	Specimen Certificate representing shares of common stock of the Registrant		S-1	4.1	12/05/17	333-220550
4.2	Warrant to Purchase Common Stock issued to the placement agent in the Registrant's 2015 private placement offering		S-1	4.3	09/21/17	333-220550
4.3	Form of Warrant issued to the underwriter in the Registrant's 2017 initial public offering		10-K	4.3	03/29/18	001-38327
4.4	Description of Common Stock of the Registrant Registered Pursuant to Section 12 of the Securities Exchange Act of 1934		10-K	4.4	03/12/2020	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	09/21/17	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	09/21/17	333-220550
10.3#	First Amendment to Collaboration, License and Option Agreement, dated March 15, 2019, between the Registrant and LG CHEM LTD.	X				
10.4#	Second Amendment to Collaboration, License and Option Agreement, dated August 5, 2019, between the Registrant and LG CHEM LTD.	X				
10.5#	Third Amendment to Collaboration, License and Option Agreement, dated October 29, 2019, between the Registrant and LG CHEM LTD.	X				
10.6#	Fourth Amendment to Collaboration, License and Option Agreement, dated December 18, 2019, between the Registrant and LG CHEM LTD.	X				
10.7#	Fifth Amendment to Collaboration, License and Option Agreement, dated January 10, 2020, between the Registrant and LG CHEM LTD.	X				

10.8#	Sixth Amendment to Collaboration, License and Option Agreement, dated February 14, 2020, between the Registrant and LG CHEM LTD.	X				
10.9#	Seventh Amendment to Collaboration, License and Option Agreement, dated May 14, 2020, between the Registrant and LG CHEM LTD.	X				
10.10#	Eighth Amendment to Collaboration, License and Option Agreement, dated December 7, 2020, between the Registrant and LG CHEM LTD.	X				
10.11	Form of Indemnification Agreement between the Registrant and its directors and officers		S-1	10.10	09/21/17	333-220550
10.12†	Amended and Restated License Agreement by and between the Registrant and Albert Einstein College of Medicine dated July 31, 2017		S-1	10.11	12/13/17	333-220550
10.13*	Cue Biopharma, Inc. 2016 Omnibus Incentive Plan, as amended and restated		S-1	10.13	09/21/17	333-220550
10.14*	Form of stock option award under 2016 Omnibus Incentive Plan		S-1	10.14	09/21/17	333-220550
10.15*	Cue Biopharma, Inc. 2016 Non-Employee Equity Incentive Plan		S-1	10.15	09/21/17	333-220550
10.16*	Form of stock option award under 2016 Non-Employee Equity Incentive Plan		S-1	10.16	09/21/17	333-220550
10.17*	Director Compensation Policy dated October 30, 2018		10-K	10.10	03/14/2019	001-38327
10.18†	Exclusive Patent License and Research Collaboration Agreement between the Registrant and Merck Sharp & Dohme Corp. dated November 14, 2017		S-1	10.21	12/04/17	333-220550
10.19*	Executive Employment Agreement between the Registrant and Colin G. Sandercock dated as of November 15, 2017		S-1	10.22	12/04/17	333-220550
10.20	License Agreement between the Registrant and MIL 21 E, LLC dated January 19, 2018		10-K	10.21	03/29/18	001-38327
10.21	First Amendment to the License Agreement between Registrant and MIL 21E, LLC dated June 18, 2018		8-K	10.1	06/20/18	001-38327
10.22	Second Amendment to License Agreement between the Registrant and MIL 21E, LLC dated June 24, 2020.		8-K	10.1	06/26/20	001-38327
10.23†	Collaboration, License and Option Agreement between the Registrant and LG Chem, Ltd. dated November 6, 2018		8-K	10.1	12/26/18	001-38327
10.24*	Amendment No. 1 to Cue Biopharma, Inc. 2016 Omnibus Incentive Plan		10-K	10.16	03/12/2020	001-38327
10.25*	Amended and Restated Executive Employment Agreement between the Registrant and Anish Suri dated October 3, 2019		8-K	10.1	10/07/19	001-38327
10.26	Third Amended and Restated Executive Employment Agreement dated March 4, 2021 between the Company and Daniel Passeri	X				

10.27	Executive Employment Agreement dated August 21, 2020 between Registrant and Kerri-Ann Millar		8-K	10.1	08/24/20	001-38327
10.28#	First Amendment to the Exclusive Patent License and Research Collaboration Agreement with Merck Sharp & Dohme Corp. dated November 9, 2020	X				
10.29	Third Amendment to Vivarium Agreement, dated July 20, 2020, between the Registrant and MIL 21E, LLC		10-Q	10.2	11/09/20	001-38327
10.30#	First Amendment to the Amended and Restated License Agreement with Albert Einstein College of Medicine dated October 30, 2018	X				
21	List of Subsidiaries	X				
23.1	Consent of RSM Inc., 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				
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 portions of this exhibit, indicated by asterisks, have been omitted.
# 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 9, 2021

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 our true and lawful attorney, with full power to him 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 9, 2021
/s/ Kerri-Ann Millar Kerri-Ann Millar	Chief Financial Officer (Principal Financial and Accounting Officer)	March 9, 2021
/s/ Aaron Fletcher Aaron Fletcher	Director	March 9, 2021
/s/ Cameron Gray Cameron Gray	Director	March 9, 2021
/s/ Peter A. Kiener Peter A. Kiener	Director	March 9, 2021
/s/ Barry Simon Barry Simon	Director	March 9, 2021
/s/ Frederick Driscoll Frederick Driscoll	Director	March 9, 2021
/s/ Frank Morich Frank Morich	Director	March 9, 2021
/s/ Tamar Howson Tamar Howson	Director	March 9, 2021

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXHIBIT 10.3

FIRST AMENDMENT

TO COLLABORATION, LICENSE AND OPTION AGREEMENT

This First Amendment ("**First Amendment**"), dated as of March 15, 2019 (the "**First Amendment Effective Date**"), to the Collaboration, License and Option Agreement, dated November 6, 2018 (for purposes of this First Amendment only, the "**Original Agreement**", and as amended hereby, the "**Agreement**"), by and between **Cue Biopharma, Inc.**, a Delaware corporation, having an address of 21 Erie Street, Cambridge, MA 02139 ("**Cue**"), and **LG Chem Ltd.**, with its principal place of business at LG Twin Towers, 128, Yeoui-daero, Yeongdeungpo-gu, Seoul, 07336, Republic of Korea ("**LGC**"). **Cue** and **LGC** may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

Whereas, Section 2.11(b) of the Original Agreement establishes a term for the Parties to negotiate and agree upon a form of a Global License and Collaboration Agreement that may be executed by the Parties upon exercise by LGC of the Global Option;

Whereas, Section 4.19 of the Original Agreement establishes a term for the Parties to enter into a pharmacovigilance agreement and

Whereas, the Parties desire to extend the terms provided in Section 2.11(b) and Section 4.19;

Now, Therefore, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and LGC hereby agree as follows:

1. Section 2.11(b) of the Original Agreement is hereby deleted in its entirety and replaced with the following in lieu thereof:

(b) Global License and Collaboration Agreement. Within [**], the Parties shall negotiate in good faith a form of license and collaboration agreement substantially in accordance with the term sheet attached hereto as Exhibit C (the "**Global License and Collaboration Agreement Term Sheet**"), setting forth the terms and conditions of the Global Product License and each Party's rights and responsibilities relating to the Global Products that will be executed by the Parties upon LGC's exercise of the Global Option in accordance with Section 2.11(c) ("**Global License and Collaboration Agreement**").

2. Section 4.19 of the Original Agreement is hereby deleted in its entirety and replaced with the following in lieu thereof:

Adverse Event Reporting; Pharmacovigilance Agreement. As between the Parties: (a) Cue shall be responsible for the timely reporting of all relevant adverse drug reactions/experiences, product quality, product complaints and Safety Data relating to Collaboration Compounds and Collaboration Products to the appropriate Regulatory Authorities in the Cue Territory; and (b) LGC shall be responsible for the timely reporting of all relevant adverse drug reactions/experiences, product quality, product complaints and Safety Data relating to Collaboration Compounds and Collaboration Products to the appropriate Regulatory

Authorities in the LGC Territory, in each case in accordance with Applicable Laws of the relevant countries and Regulatory Authorities. Cue shall be responsible for preparing, reporting and maintaining global pharmacovigilance system and the core safety data sheet. The Parties shall cooperate with each other with respect to their respective pharmacovigilance responsibilities, and LGC shall comply with all pharmacovigilance requirements necessary to support Development and Commercialization of Collaboration Products in the Cue Territory and Cue shall comply with all pharmacovigilance requirements necessary to support Development and Commercialization of Collaboration Products in the LGC Territory. Each Party shall be solely responsible for all costs it incurs to conduct its respective pharmacovigilance responsibilities. Within nine (9) months after the Effective Date, the Parties shall enter into a pharmacovigilance agreement on terms that comply with ICH guidelines, including: (i) providing detailed procedures regarding the maintenance of core safety information and the exchange of Safety Data relating to Collaboration Compounds and Collaboration Products worldwide within appropriate timeframes and in an appropriate format to enable each Party to meet both expedited and periodic regulatory reporting requirements; and (ii) ensuring compliance with the reporting requirements of all applicable Regulatory Authorities on a worldwide basis for the reporting of Safety Data in accordance with standards stipulated in the ICH guidelines, and all applicable regulatory and legal requirements regarding the management of Safety Data.

3. Except as amended hereby, all other terms and conditions of the Original Agreement shall remain in full force and effect, and are unmodified by this First Amendment.

IN WITNESS WHEREOF the Parties hereto have caused this First Amendment to be executed and entered into by their duly authorized representatives as of the First Amendment Effective Date.

[The Remainder of this page is intentionally left blank. Signatures appear on following page.]

CUE BIOPHARMA, INC.	**LG CHEM LTD.**
By: /s/ Daniel Passeri	By: /s/ Jeewoong Son
Name: Daniel Passeri	Name: Jeewoong Son
Title: CEO	Title: President

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXHIBIT 10.4

SECOND AMENDMENT

TO COLLABORATION, LICENSE AND OPTION AGREEMENT

This Second Amendment ("**Second Amendment**"), dated as of August 5, 2019 (the "**Second Amendment Effective Date**"), to the First Amendment to Collaboration, License and Option Agreement, dated March 15, 2019 (for purposes of this Second Amendment only, the "First Amended **Agreement**", and as amended hereby, the "**Agreement**"), by and between **Cue Biopharma, Inc.**, a Delaware corporation, having an address of 21 Erie Street, Cambridge, MA 02139 ("**Cue**"), and **LG Chem Ltd.**, with its principal place of business at LG Twin Towers, 128, Yeoui-daero, Yeongdeungpo-gu, Seoul, 07336, Republic of Korea ("**LGC**"). **Cue** and **LGC** may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

Whereas, Section 2.11(b) of the First Amended Agreement establishes a term for the Parties to negotiate and agree upon a form of a Global License and Collaboration Agreement that may be executed by the Parties upon exercise by LGC of the Global Option; and

Whereas, the Parties desire to further extend the term provided in Section 2.11(b);

Now, Therefore, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and LGC hereby agree as follows:

1. Section 2.11(b) of the First Amended Agreement is hereby deleted in its entirety and replaced with the following in lieu thereof:

(b) Global License and Collaboration Agreement. Within [**], the Parties shall negotiate in good faith a form of license and collaboration agreement substantially in accordance with the term sheet attached hereto as Exhibit C (the "**Global License and Collaboration Agreement Term Sheet**"), setting forth the terms and conditions of the Global Product License and each Party's rights and responsibilities relating to the Global Products that will be executed by the Parties upon LGC's exercise of the Global Option in accordance with Section 2.11(c) ("**Global License and Collaboration Agreement**").

2. Except as amended hereby, all other terms and conditions of the First Amended Agreement shall remain in full force and effect, and are unmodified by this First Amendment.

IN WITNESS WHEREOF the Parties hereto have caused this Second Amendment to be executed and entered into by their duly authorized representatives as of the Second Amendment Effective Date.

[The Remainder of this page is intentionally left blank. Signatures appear on following page.]

CUE BIOPHARMA, INC.	**LG CHEM LTD.**
By: /s/ Daniel Passeri	By: /s/ Jeewoong Son
Name: Daniel Passeri	Name: Jeewoong Son
Title: CEO	Title: President

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXHIBIT 10.5

THIRD AMENDMENT

TO COLLABORATION, LICENSE AND OPTION AGREEMENT

This Third Amendment to the Collaboration, License and Option Agreement (the **"Third Amendment"**) is entered into as of October 29, 2019 (the "**Third Amendment Effective Date"**) by and between **Cue Biopharma, Inc.**, a Delaware corporation, having an address of 21 Erie Street, Cambridge, MA 02139 ("**Cue**"), and **LG Chem Ltd.**, with its principal place of business at LG Twin Towers, 128, Yeoui-daero, Yeongdeungpo-gu, Seoul, 07336, Republic of Korea ("**LGC**"). **Cue** and **LGC** may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

Whereas, the Parties entered into a Collaboration, License and Option Agreement as of November 6, 2018 (the **"Original Agreement"**) that was subsequently amended on March 15, 2019 and August 5, 2019 (the **"First Amendment"** and "**Second Amendment"**, and the Original Agreement, collectively the **"Agreement"**);

Whereas, Section 4.3(c) of the Agreement establishes a term for the Parties to (i) select a Collaboration Antigen and Initial Collaboration Alleles for the CUE-103 Program, and (ii) prepare and approve a CUE-103 Initial Research Plan; and

Whereas, the Parties desire to further extend the terms provided in Section 4.3(c);

Now, Therefore, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and LGC hereby agree as follows:

1. Section 4.3(c) of the Agreement is hereby deleted in its entirety and replaced with the following in lieu thereof:

(c) CUE-103 Program.

(i) Antigen and Allele Selection. No later than [**] and no sooner than [**] (the "**CUE-103 Program Selection Period**"), (i) the Parties, through the JSC, shall jointly choose one (1) Collaboration Antigen (other than a Cue Reserved Antigen) for the CUE-103 Program, (ii) LGC shall select one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program, and (iii) following LGC's selection, Cue shall select one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program (whether the same or different from the Initial Collaboration Allele elected by LGC). Each Party may select no more than one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program, provided that if at any time the JSC determines that [**], the applicable Party [**].

(ii) Research Plan. No later than [**] but after the Parties' selection of the Collaboration Antigen for the CUE-103 Program and each Party's selection of its Initial Collaboration Alleles for the CUE-103 Program, the Parties, through the JRC, shall jointly draft,

review, discuss and send to the JSC for approval (with neither Party unreasonably withholding its approval) the initial Research Plan (including an initial Research Budget) for the Initial Collaboration Alleles in the CUE-103 Program (such Research Plan (including the Research Budget), a "**CUE-103 Initial Research Plan**"). The CUE-103 Initial Research Plan shall, at a minimum, unless the Parties agree otherwise, be reasonably designed to include Research activities for CUE-103 Compounds containing the Initial Collaboration Allele(s) reasonably required to accomplish the filing of an IND [**] and shall be consistent with the Template Initial Research Plan. The CUE-103 Initial Research Plan shall be updated and amended by the JRC as it deems appropriate, and in any event promptly after any LGC Additional Allele, Cue Additional Allele [**] is added to the CUE-103 Program in accordance with the terms of Section 4.3(e).

2. Except as amended hereby, all other terms and conditions of the Agreement shall remain in full force and effect, and are unmodified by this Third Amendment.

IN WITNESS WHEREOF the Parties hereto have caused this Third Amendment to be executed and entered into by their duly authorized representatives as of the Third Amendment Effective Date.

[The Remainder of this page is intentionally left blank. Signatures appear on following page.]

CUE BIOPHARMA, INC.

By: /s/ Daniel Passeri

Name: Daniel Passeri

Title: CEO

LG CHEM LTD.

By: /s/ Jeewoong Son

Name: Jeewoong Son

Title: President

EXECUTION VERSION

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXHIBIT 10.6

FOURTH AMENDMENT

TO COLLABORATION, LICENSE AND OPTION AGREEMENT

This Fourth Amendment to the Collaboration, License and Option Agreement (the "**Fourth Amendment**") is entered into as of December 18, 2019 (the "**Fourth Amendment Effective Date**"), by and between **Cue Biopharma, Inc.**, a Delaware corporation, having an address of 21 Erie Street, Cambridge, MA 02139 ("**Cue**"), and **LG Chem Ltd.**, with its principal place of business at LG Twin Towers, 128, Yeoui-daero, Yeongdeungpo-gu, Seoul, 07336, Republic of Korea ("**LGC**"). Cue and LGC may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

Whereas, the Parties entered into a Collaboration, License and Option Agreement as of November 6, 2018 (the "**Original Agreement**") that was subsequently amended on March 15, 2019 (the "**First Amendment**"), August 5, 2019 (the "**Second Amendment**") and October 29, 2019 (the "**Third Amendment**" and collectively with the Original Agreement, the First Amendment and the Second Amendment, the "**Agreement**");

Whereas, the Parties entered into a Global License and Collaboration Agreement on even date herewith (the "**Global Agreement**"); and

Whereas, the Parties desire to make the following changes to certain provisions of the Agreement.

Now, Therefore, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and LGC hereby agree as follows:

1. All capitalized terms not separately defined in this Fourth Amendment shall have the meaning ascribed to them in the Agreement.

2. The first three sentences of Section 4.15 of the Agreement are hereby deleted and replaced with the following:

> "In order to facilitate the Development and Manufacturing activities contemplated by this Agreement, Cue shall, at LGC's cost, provide to LGC certain available biological materials or chemical compounds in Cue's possession and Controlled by Cue that are relevant to Collaboration Compounds or Collaboration Products (collectively, "**Materials**") for use by LGC in furtherance of activities under a Research Plan, Development Plan, Manufacturing Plan, Commercialization Plan or otherwise under this Agreement. Except as otherwise provided for under this Agreement, all such Materials delivered will remain the sole property of Cue. LGC shall use such Materials only in furtherance of activities conducted in accordance with this Agreement or the Global

License and Collaboration Agreement, as applicable, and the Materials will not be used or delivered for any other purpose, or to or for the benefit of any Third Party, except for Sublicensees and subcontractors, without the prior written consent of Cue, and will be used in compliance with all Applicable Laws."

3. The third sentence of Section 9.1(b) of the Agreement is hereby deleted and replaced with the following:

"Except as granted herein or in the Global License and Collaboration Agreement, LGC shall have no rights in the Cue Background IP or involvement in any actions taken by Cue with respect to Cue Background IP, and Cue shall have no rights in the LGC Background IP or involvement in any actions taken by LGC with respect to LGC Background IP."

4. The second sentence of Section 13.1 of the Agreement is hereby deleted and replaced with the following:

"Upon expiration (but not termination) of this Agreement with respect to any Collaboration Product in any country within the LGC Territory or Cue Territory, (a) LGC's license under Section 2.1 with respect to such Collaboration Product in such country, including LGC's right to use related Materials provided by Cue under Section 4.15 under such license, will become fully paid-up and royalty free and (b) Cue's license under Section 2.4 with respect to such Collaboration Product in such country will become fully paid-up and royalty free."

5. Section 15.6(d)(i) of the Agreement is hereby deleted and replaced with the following:

"(A) following closing of a Change of Control, Transferee shall require that [**], in each case, [**] and are not [**], and the Transferee does not [**] and (B) following closing of a Change of Control, Transferee shall [**]; provided that if the requirements of either Section 15.6(d)(i)(A) or (B) are not met, [**]"

6. **Entire Agreement; Modification.** Except as expressly amended by this Fourth Amendment, all other terms and conditions of the Agreement shall remain in full force and effect, and are unmodified by this Fourth Amendment. The Agreement, as modified by this Fourth Amendment, contains the entire agreement of the Parties with regard to the subject matter set forth herein and supersedes all prior and contemporaneous agreements and communications, whether oral, written or otherwise, concerning any and all matters contained herein; provided, however, that the Global Agreement shall continue in full force and effect in accordance with its terms. This Fourth Amendment may only be modified or supplemented in a writing expressly stated for such purpose and signed by the Parties.

7. **Counterparts; Electronic or Facsimile Signatures.** This Fourth Amendment may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument. This Fourth Amendment may be executed and delivered electronically or by facsimile and upon such delivery such electronic or facsimile signature will be deemed to have the same effect as if the original signature had been delivered to the other Party.

[Signature Page Follows]

In Witness Whereof, the Parties hereto have caused this **Fourth Amendment** to be executed and entered into by their duly authorized representatives as of the Fourth Amendment Effective Date.

Cue Biopharma, Inc.		**LG Chem Ltd.**	
By:	/s/ Daniel Passeri	By:	/s/ Jeewoong Son
Name:	Daniel Passeri	Name:	Jeewoong Son
Title:	CEO	Title:	President

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXHIBIT 10.7

FIFTH AMENDMENT

TO COLLABORATION, LICENSE AND OPTION AGREEMENT

This Fifth Amendment to the Collaboration, License and Option Agreement (the **"Fifth Amendment"**) is entered into as of January 15, 2020 (the "**Fifth Amendment Effective Date"**) by and between **Cue Biopharma, Inc.**, a Delaware corporation, having an address of 21 Erie Street, Cambridge, MA 02139 ("**Cue**"), and **LG Chem Ltd.**, with its principal place of business at LG Twin Towers, 128, Yeoui-daero, Yeongdeungpo-gu, Seoul, 07336, Republic of Korea ("**LGC**"). **Cue** and **LGC** may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

Whereas, the Parties entered into a Collaboration, License and Option Agreement as of November 6, 2018 (the **"Original Agreement"**) that was subsequently amended on March 15, 2019 (the "**First Amendment**"), August 5, 2019 (the "**Second Amendment**"), October 29, 2019 (the "**Third Amendment**") and December 18, 2019 (the "**Fourth Amendment**" and collectively with the Original Agreement, the First Amendment, the Second Amendment and the Third Amendment, the **"Agreement"**);

Whereas, Section 4.3(c) of the Agreement establishes a term for the Parties to (i) select a Collaboration Antigen and Initial Collaboration Alleles for the CUE-103 Program, and (ii) prepare and approve a CUE-103 Initial Research Plan; and

Whereas, the Parties desire to further extend the terms provided in Section 4.3(c);

Now, Therefore, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and LGC hereby agree as follows:

1. Section 4.3(c) of the Agreement is hereby deleted in its entirety and replaced with the following in lieu thereof:

(c) CUE-103 Program.

(i) Antigen and Allele Selection. No later than [**] and no sooner than [**] (the "**CUE-103 Program** Selection **Period**"), (i) the Parties, through the JSC, shall jointly choose one (1) Collaboration Antigen (other than a Cue Reserved Antigen) for the CUE-103 Program, (ii) LGC shall select one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program, and (iii) following LGC's selection, Cue shall select one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program (whether the same or different from the Initial Collaboration Allele elected by LGC). Each Party may select no more than one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program, provided that if at any time the JSC determines that [**], the applicable Party [**].

(ii) Research Plan. No later than [**] but after the Parties' selection of the Collaboration Antigen for the CUE-103 Program and each Party's selection of its Initial Collaboration Alleles for the CUE-103 Program, the Parties, through the JRC, shall jointly draft, review, discuss and send to the JSC for approval (with neither Party unreasonably withholding its approval) the initial Research Plan (including an initial Research Budget) for the Initial Collaboration Alleles in the CUE-103 Program (such Research Plan (including the Research Budget), a "**CUE-103 Initial Research Plan**"). The CUE-103 Initial Research Plan shall, at a minimum, unless the Parties agree otherwise, be reasonably designed to include Research activities for CUE-103 Compounds containing the Initial Collaboration Allele(s) reasonably required to accomplish the filing of an IND [**] and shall be consistent with the Template Initial Research Plan. The CUE-103 Initial Research Plan shall be updated and amended by the JRC as it deems appropriate, and in any event promptly after any LGC Additional Allele, Cue Additional Allele [**] is added to the CUE-103 Program in accordance with the terms of Section 4.3(e).

2. Except as amended hereby, all other terms and conditions of the Agreement shall remain in full force and effect, and are unmodified by this Fifth Amendment.

IN WITNESS WHEREOF the Parties hereto have caused this Fifth Amendment to be executed and entered into by their duly authorized representatives as of the Fifth Amendment Effective Date.

[The Remainder of this page is intentionally left blank. Signatures appear on following page.]

CUE BIOPHARMA, INC.

By: /s/ Daniel Passeri

Name: Daniel Passeri

Title: CEO

LG CHEM LTD.

By: /s/ Jeewoong Son

Name: Jeewoong Son

Title: President

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXHIBIT 10.8

SIXTH AMENDMENT

TO COLLABORATION, LICENSE AND OPTION AGREEMENT

This Sixth Amendment to the Collaboration, License and Option Agreement (the **"Sixth Amendment"**) is entered into as of February 14, 2020 (the "**Sixth Amendment Effective Date"**) by and between **Cue Biopharma, Inc.**, a Delaware corporation, having an address of 21 Erie Street, Cambridge, MA 02139 ("**Cue**"), and **LG Chem Ltd.**, with its principal place of business at LG Twin Towers, 128, Yeoui-daero, Yeongdeungpo-gu, Seoul, 07336, Republic of Korea ("**LGC**"). **Cue** and **LGC** may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

Whereas, the Parties entered into a Collaboration, License and Option Agreement as of November 6, 2018 (the **"Original Agreement"**) that was subsequently amended on March 15, 2019 (the "**First Amendment**"), August 5, 2019 (the "**Second Amendment**"), October 29, 2019 (the "**Third Amendment**"), December 18, 2019 (the "**Fourth Amendment**") and January 15, 2020 (the "**Fifth Amendment**" and collectively with the Original Agreement, the First Amendment, the Second Amendment, the Third Amendment and the Fourth Amendment, the **"Agreement"**);

Whereas, Section 4.3(c) of the Agreement establishes a term for the Parties to (i) select a Collaboration Antigen and Initial Collaboration Alleles for the CUE-103 Program, and (ii) prepare and approve a CUE-103 Initial Research Plan; and

Whereas, the Parties desire to further extend the terms provided in Section 4.3(c);

Now, Therefore, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and LGC hereby agree as follows:

1. Section 4.3(c) of the Agreement is hereby deleted in its entirety and replaced with the following in lieu thereof:

(c) CUE-103 Program.

(i) Antigen and Allele Selection. No later than [**] and no sooner than [**] (the "**CUE-103 Program Selection Period**"), (i) the Parties, through the JSC, shall jointly choose one (1) Collaboration Antigen (other than a Cue Reserved Antigen) for the CUE-103 Program, (ii) LGC shall select one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program, and (iii) following LGC's selection, Cue shall select one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program (whether the same or different from the Initial Collaboration Allele elected by LGC). Notwithstanding anything in this Agreement to the contrary, the Parties may discuss in good faith and agree to [**] for the CUE-103 Program. For clarity, although the Parties may discuss in good faith and agree to [**] for the CUE-103 Program, neither party is required, in its own discretion, to move forward with any agreement to [**] as the CUE-103

Program, and either Party may decline for any reason or no reason to amend the Agreement to [**] for the CUE-103 Program. Each Party may select no more than one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program, provided that if at any time the JSC determines that [**], the applicable Party [**].

(ii) Research Plan. No later than [**] but after the Parties' selection of the Collaboration Antigen for the CUE-103 Program and each Party's selection of its Initial Collaboration Alleles for the CUE-103 Program, the Parties, through the JRC, shall jointly draft, review, discuss and send to the JSC for approval (with neither Party unreasonably withholding its approval) the initial Research Plan (including an initial Research Budget) for the Initial Collaboration Alleles in the CUE-103 Program (such Research Plan (including the Research Budget), a "**CUE-103 Initial Research Plan**"). The CUE-103 Initial Research Plan shall, at a minimum, unless the Parties agree otherwise, be reasonably designed to include Research activities for CUE-103 Compounds containing the Initial Collaboration Allele(s) reasonably required to accomplish the filing of an IND [**] and shall be consistent with the Template Initial Research Plan. The CUE-103 Initial Research Plan shall be updated and amended by the JRC as it deems appropriate, and in any event promptly after any LGC Additional Allele, Cue Additional Allele [**] is added to the CUE-103 Program in accordance with the terms of Section 4.3(e).

2. Except as amended hereby, all other terms and conditions of the Agreement shall remain in full force and effect, and are unmodified by this Sixth Amendment.

IN WITNESS WHEREOF the Parties hereto have caused this Sixth Amendment to be executed and entered into by their duly authorized representatives as of the Sixth Amendment Effective Date.

[The Remainder of this page is intentionally left blank. Signatures appear on following page.]

CUE BIOPHARMA, INC.

By: /s/ Daniel Passeri

Name: Daniel Passeri

Title: CEO

LG CHEM LTD.

By: /s/ Jeewoong Son

Name: Jeewoong Son

Title: President

Exhibit 10.9

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

SEVENTH AMENDMENT

TO COLLABORATION, LICENSE AND OPTION AGREEMENT

This Seventh Amendment to the Collaboration, License and Option Agreement (the **"Seventh Amendment"**) is entered into as of May 14, 2020 (the "**Seventh Amendment Effective Date"**) by and between **Cue Biopharma, Inc.**, a Delaware corporation, having an address of 21 Erie Street, Cambridge, MA 02139 ("**Cue**"), and **LG Chem Ltd.**, with its principal place of business at LG Twin Towers, 128, Yeoui-daero, Yeongdeungpo-gu, Seoul, 07336, Republic of Korea ("**LGC**"). **Cue** and **LGC** may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

Whereas, the Parties entered into a Collaboration, License and Option Agreement as of November 6, 2018 (the **"Original Agreement"**) that was subsequently amended on March 15, 2019, August 5, 2019, October 29, 2019, December 18, 2019, January 15, 2020 and February 20, 2020 (the "**First Amendment**", "**Second Amendment**", "**Third Amendment**", "**Fourth Amendment**" , "**Fifth Amendment**" and "**Sixth Amendment**" and with the Original Agreement, collectively the **"Agreement"**);

Whereas, Section 4.3(c) of the Agreement establishes a term for the Parties to (i) select a Collaboration Antigen and Initial Collaboration Alleles for the CUE-103 Program, and (ii) prepare and approve a CUE-103 Initial Research Plan; and

Whereas, the Parties desire to further extend the terms provided in Section 4.3(c);

Now, Therefore, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and LGC hereby agree as follows:

1. Section 4.3(c) of the Agreement is hereby deleted in its entirety and replaced with the following in lieu thereof:

(c) CUE-103 Program.

(i) Antigen and Allele Selection. No later than [**] (the "**CUE-103 Program Selection Period**"), (i) the Parties, through the JSC, shall jointly choose one (1) Collaboration Antigen (other than a Cue Reserved Antigen) for the CUE-103 Program, (ii) LGC shall select one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program, and (iii) following LGC's selection, Cue shall select one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program (whether the same or different from the Initial Collaboration Allele elected by LGC). Notwithstanding anything in this Agreement to the contrary, the Parties may discuss in good faith and agree to [**] for the CUE-103 Program. For clarity, although the Parties may discuss in good faith and agree to [**] for the CUE-103 Program, neither party is required, in its own discretion, to move forward with any agreement to [**] as the CUE-103 Program, and either

Party may decline for any reason or no reason to amend the Agreement to [**] for the CUE-103 Program. Each Party may select no more than one (1) Allele as its Initial Collaboration Allele for the CUE-103 Program, provided that if at any time the JSC determines that [**], the applicable Party [**].

(ii) Research Plan. No later than [**] but after the Parties' selection of the Collaboration Antigen for the CUE-103 Program and each Party's selection of its Initial Collaboration Alleles for the CUE-103 Program, the Parties, through the JRC, shall jointly draft, review, discuss and send to the JSC for approval (with neither Party unreasonably withholding its approval) the initial Research Plan (including an initial Research Budget) for the Initial Collaboration Alleles in the CUE-103 Program (such Research Plan (including the Research Budget), a "**CUE-103 Initial Research Plan**"). The CUE-103 Initial Research Plan shall, at a minimum, unless the Parties agree otherwise, be reasonably designed to include Research activities for CUE-103 Compounds containing the Initial Collaboration Allele(s) reasonably required to accomplish the filing of an IND [**] and shall be consistent with the Template Initial Research Plan. The CUE-103 Initial Research Plan shall be updated and amended by the JRC as it deems appropriate, and in any event promptly after any LGC Additional Allele, Cue Additional Allele [**] is added to the CUE-103 Program in accordance with the terms of Section 4.3(e).

2. Except as amended hereby, all other terms and conditions of the Agreement shall remain in full force and effect, and are unmodified by this Seventh Amendment.

IN WITNESS WHEREOF the Parties hereto have caused this Seventh Amendment to be executed and entered into by their duly authorized representatives as of the Seventh Amendment Effective Date.

[The Remainder of this page is intentionally left blank. Signatures appear on following page.]

CUE BIOPHARMA, INC.

By: /s/ Daniel Passeri

Name: Daniel Passeri

Title: CEO

LG CHEM LTD.

By: /s/ Jeewoong Son

Name: Jeewoong Son

Title: President

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXHIBIT 10.10

EIGHTH AMENDMENT

TO COLLABORATION, LICENSE AND OPTION AGREEMENT

This Eighth Amendment to the Collaboration, License and Option Agreement (the "**Eighth Amendment**") is entered into as of December 7, 2020 (the "**Eighth Amendment Effective Date**"), by and between **CUE BIOPHARMA, INC.**, a Delaware corporation, having an address of 21 Erie Street, Cambridge, MA 02139 ("**Cue**"), and **LG CHEM LTD.**, with its principal place of business at LG Twin Towers, 128, Yeoui-daero, Yeongdeungpo-gu, Seoul, 07336, Republic of Korea ("**LGC**"). Cue and LGC may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

WHEREAS, the Parties entered into a Collaboration, License and Option Agreement as of November 6, 2018 (the "**Original Agreement**") that was subsequently amended on March 15, 2019, August 5, 2019, October 29, 2019, December 18, 2019, January 10, 2020, February 14, 2020 and May 14, 2020 (the "**First Amendment**", "**Second Amendment**", "**Third Amendment**", "**Fourth Amendment**" , "**Fifth Amendment**", "**Sixth Amendment**" and "**Seventh Amendment**" with the Original Agreement, collectively the "**Agreement**");

WHEREAS, pursuant to Section 4.3(b)(i) of the Agreement, on [**], LGC [**] and on [**], Cue [**];

WHEREAS, pursuant to the terms of the Agreement, the Parties engaged in Research in accordance with Research Plans for [**] for the CUE-102 Program (respectively, the [**]**Research Program**");

WHEREAS, LGC notified Cue [**];

WHEREAS, the Parties now desire to set down in writing the Parties' understanding that LGC [**];

WHEREAS, the Parties desire to further state the Parties' understanding that, subject to the [**] specified herein, LGC [**]; and

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and LGC hereby agree as follows:

1. All capitalized terms not separately defined in this Eighth Amendment shall have the meaning ascribed to them in the Agreement.

2. "**[**] LGC Know-How**" means all Know-How Controlled by LGC or its Affiliates as of the [**] that pertains to the Research, Development, Manufacture or Commercialization of any [**] Compound or [**] Product that is disclosed in [**].

3. "**[**] LGC Patent Rights**" means (a) [**], and (b) any Patent Rights Controlled by LGC or its Affiliates claiming priority to either or both of such applications.

4. "**[**] LGC Technology**" means the [**] LGC Know-How and the [**] LGC Patent Rights.

5. Notwithstanding [**] CUE-102 Program, as of the [**] shall be deemed [**] for the CUE-102 Program. From and after the [**] shall not be considered [**] by LGC for any purpose under the Agreement, including under Section [**].

6. The Parties acknowledge that the JSC selected a pre-clinical candidate for the CUE-102 [**] Research Program on [**]. As a result of [**] pursuant to this Eighth Amendment, LGC shall pay Cue the Milestone Payment under Section 7.5(a)(i)(1) of $1,250,000 with respect to the CUE-102 Program within [**] of the Eighth Amendment Effective Date. Such payment in accordance with this Paragraph 6 shall constitute full and timely satisfaction of LGC's obligation to pay the Milestone Payment under Section 7.5(a)(i)(1) of the Agreement for the CUE-102 Program.

7. Subject to Section 7.3 of the Agreement, the Parties shall share Research Costs for all payment obligations that accrued under the Agreement relating to the CUE-102 [**] Research Program up to the [**]. For clarity, LGC shall receive no reimbursement of any amounts accrued following [**] for the CUE-102 [**] Research Program and Cue shall receive no reimbursement of any amounts accrued following the [**] for the CUE-102 [**] Research Program.

8. As of the [**], solely for the purposes of Section [**] of the Agreement and as otherwise expressly set forth in this Eighth Amendment, [**] shall be [**] and it shall be deemed that LGC has elected, [**]. Notwithstanding anything to the contrary in the Agreement, (a) except as expressly set forth in this Eighth Amendment, [**] under the Agreement and (b) unless and until LGC [**] in accordance with Section [**] of the Agreement, the [**] of the Agreement [**].

9. Rights and Obligations Prior to [**]. Notwithstanding anything to the contrary in the Agreement, after the [**] and prior to the earlier of (i) [**] in accordance with Section [**] of the Agreement and (ii) any [**] (as defined in Paragraph 14 below):

    (a) Subject to the provisions of Paragraph 9(b) below, Cue shall use Commercially Reasonable Efforts to conduct the CUE-102 [**] Research Program in accordance with the high-level objectives of the Research Plan for the CUE-102 Program agreed upon by the JSC as it has been deemed approved by the Parties in accordance with Section 4.3(f)(iii)(1) of the Agreement;

    (b) Cue shall be solely responsible, in its own discretion (without any review, coordination, direction, oversight, discussion or approval by LGC or any Committee), for determining all activities, timelines and Research Costs relating to

the CUE-102 [**] Research Program after [**]. Cue shall reasonably inform LGC (through the JRC) of the progress and timelines of Research activities and for IND submission relating to the CUE-102 [**] Research Program;

(c) Pursuant to Section [**] of the Agreement, all Data generated [**] from the Research of the [**], CUE-102 [**] Compounds and CUE-102 [**] Products shall be deemed Excluded Data unless and until [**]; and

(d) Cue shall provide information (including copies of all then available data and an accounting of all Research Costs spent to date) relating to the CUE-102 [**] Research Program to LGC in accordance with the provisions of Section [**] of the Agreement, including written notice (through the JRC) of intended IND submission by Cue to be provided no later than [**] prior to IND submission.

10. Rights and Obligations if LGC [**]. Pursuant to Section [**] of the Agreement, if and after LGC [**] with respect to the [**], LGC shall pay Cue [**] of the Research Costs incurred by or on account of Cue in the period between the [**] and the date of such [**] in performing Research for the CUE-102 [**] Compounds and CUE-102 [**] Products in the CUE-102 [**] Research Program in accordance with the applicable Research Plan. If LGC [**] with respect to the [**] pursuant to Section [**] of the Agreement, then on the date of such [**]: (a) the [**] shall be deemed a [**] for the CUE-102 Program pursuant to Section [**] of the Agreement for all purposes under the Agreement; (b) the [**] LGC Patent Rights, [**] LGC Know-How and [**] LGC Technology shall be deemed LGC Sole Collaboration Patent Rights, LGC Sole Collaboration Know-How and LGC Sole Collaboration Technology, respectively, and Paragraph 12 of this Eighth Amendment shall have no further effect with respect to prosecution and maintenance of such LGC Sole Collaboration Patent Rights after such date; and (c) the option or any license granted by LGC to Cue pursuant to Paragraph 14 of this Eighth Amendment shall terminate. Notwithstanding anything to the contrary in the Agreement, except as set forth in Paragraph 13 of this Eighth Amendment, unless and until LGC [**] with respect to the [**], the licenses granted by LGC to Cue under the Agreement do not include the [**], CUE-102 [**] Compounds or CUE-102 [**] Products, or any rights under the [**] LGC Patent Rights or [**] LGC Know-How.

11. Rights and Obligations After [**]. Notwithstanding anything to the contrary in the Agreement, subject to Paragraphs 12, 13 and 14 of this Eighth Amendment, if and after any [**]:

(a) Cue shall be solely responsible, in its own expense and discretion (without any review, coordination, direction, oversight, discussion or approval by any Committee), for determining all Research Plans (and Research Budgets), Cue Territory Development Plans, Manufacturing Plans and Cue Territory Commercialization Plans (and, in each case, any amendments thereto), for (x) any compound that consists of a CUE-102 Compound having both (1) the [**] and (2) an epitope of the Collaboration Antigen for the CUE-102 Program (collectively, the "**CUE-102 [**] Compounds**") and (y) any pharmaceutical product consisting of or containing a CUE-102 [**] Compound (collectively, the "**CUE-102 [**] Products**"); provided that, in each case, such plan does not include any obligations on LGC that are not agreed upon in writing by LGC;

(b) Cue shall be solely responsible, in its own expense and discretion (without any review, coordination, direction, oversight, discussion or approval from any Committee and without any obligation to provide any information to any Committee), for all further Research, Development, Manufacture and Commercialization of the [**], CUE-102 [**] Compounds and CUE-102 [**] Products;

(c) Pursuant to [**] of the Agreement, all Data generated after the [**] from the Research of the [**], CUE-102 [**] Compounds and CUE-102 [**] Products shall continue to be deemed Excluded Data;

(d) Cue shall not have any diligence obligations pursuant to Sections 4.1, 4.6(b) and 4.10(b) of the Agreement and Paragraph 13 of this Eighth Amendment, in each case, with respect to the Research or Development of the [**], CUE-102 [**] Compounds or CUE-102 [**] Products; and

(e) LGC shall have no obligation to conduct any [**] relating to CUE-102 [**] Compounds and CUE-102 [**] Products and, as between the Parties, Cue shall have the sole right to conduct (or have conducted by a CMO selected in Cue's sole discretion) all [**] relating to CUE-102 [**] Compounds and CUE-102 [**] Products independently at Cue's cost and provided that such [**] are conducted without using LGC's Know-How (other than [**] LGC Know-How), Cue shall have no obligation to make [**] royalty payments to LGC pursuant to Section 7.7(a)(i) of the Agreement with respect to any CUE-102 [**] Compounds or CUE-102 [**] Products.

12. Following the Eighth Amendment Effective Date, notwithstanding anything to the contrary in the Agreement, LGC shall be the Lead Prosecution Party for all [**] LGC Patent Rights. Subject to the provisions set forth below, the Parties shall follow the procedures set forth in Section 9.2(a)(ii) of the Agreement ("**LGC is Lead Prosecution Party for Collaboration Patent Rights**") for all such [**] LGC Patent Rights.

(a) LGC shall be the Lead Prosecution Party in all cases for [**] LGC Patent Rights, including for any Paris Convention, non-Paris Convention, PCT National Phase, continuation, and divisional filings for [**] LGC Patent Rights in the Cue Territory.

(b) Until such time as LGC [**] pursuant to Section [**] of the Agreement with respect to the [**] or if LGC [**] for the [**], notwithstanding anything to the contrary in the Agreement, the following provisions (i)-(iv) shall apply for the [**] LGC Patent Rights.

(i) Cue shall be solely responsible for all out-of-pocket costs incurred with respect to preparation and filing of any priority patent applications (e.g., provisional patent applications) and PCT applications claiming priority thereto and for all fees and costs (including prosecution fees and costs) incurred with respect to any Paris Convention, non-Paris Convention, PCT National Phase, continuation, and divisional filings (i) in any country in the Cue Territory in which Cue requests LGC to file such applications,

and (ii) in any country in the LGC Territory in which Cue requests LGC to file such applications (such filings, the "**Cue-Requested Filings**"). On a Calendar Quarterly basis, LGC will invoice Cue for the costs relating to the Cue-Requested Filings and Cue will pay LGC's invoice within [**] after receipt thereof.

(ii) Cue shall notify LGC at least [**] prior to the relevant filing deadline of all Paris Convention, non-Paris Convention, and PCT National Phase filings if Cue desires that LGC file any such Paris Convention, non-Paris Convention, and/or PCT National Phase filing in any country in the Cue Territory or LGC Territory.

(iii) At least [**] prior to the relevant filing deadline, LGC shall notify Cue if LGC desires any additional Paris Convention, non-Paris Convention, and PCT National Phase filings in any country in the Cue Territory or LGC Territory beyond the filings that Cue desires to make (such additional filings the **"LGC Additional Filings"**). LGC shall make the LGC Additional Filings and LGC shall be solely responsible for all costs relating to such LGC Additional Filings (all patent costs relating to the Cue-Requested Filings and LGC Additional Filings, collectively, the "**[**] LGC Patent Costs**").

(iv) For clarity, LGC shall use LGC's own patent counsel for filing, prosecution and maintenance of the for [**] LGC Patent Rights, including the Cue-Requested Filings and the LGC Additional Filings, and Cue shall timely provide all necessary cooperation for all such patent activities, including, e.g., reviewing all patent application filings, including all PCT applications relating to [**] LGC Patent Rights.

(c) After LGC [**] pursuant to Section [**] of the Agreement with respect to the [**], the Parties shall be responsible for all [**] LGC Patent Costs incurred after such [**] according to the Agreement. In such event, LGC also shall reimburse Cue for all [**] LGC Patent Costs expenses incurred by Cue as follows: [**]% for all costs relating to any PCT applications, and [**]% of any costs relating to filings in the LGC Territory.

13. License Grant to Cue. Subject to the terms and conditions of the Agreement (including Section 13.2(b) of the Agreement), LGC hereby grants to Cue an exclusive (even as to LGC and its Affiliates), royalty-bearing license, with the right to grant sublicenses through multiple tiers (subject to Section 2.2(b) and 2.8 of the Agreement, as applicable, with such provisions applying *mutatis mutandis* to CUE-102 [**] Compounds and CUE-102 [**] Products), under the [**] LGC Technology to Research, Develop, import, use, Manufacture and Commercialize and otherwise exploit CUE-102 [**] Compounds and CUE-102 [**] Products in the Field in the Cue Territory. In recognition of LGC's contributions to the CUE-102 [**] Research Program prior to the [**], Cue shall make Calendar Quarterly royalty payments to LGC equal to [**]% of Net Sales of CUE-102 [**] Products (interpreted *mutatis mutandis* as if CUE-102 [**] Products were Collaboration Products) in the Cue Territory if, at the time of such sale, on a country-by-country and CUE-102 [**] Product-by CUE-102 [**] Product basis, such CUE-102 [**] Product (or the CUE-102 [**] Compound included therein) is covered by a Valid

Claim (interpreted *mutatis mutandis* as if CUE-102 [**] Products were Collaboration Products) of [**] LGC Patent Rights in such country. Cue royalty payments and associated reporting to LGC and audit rights of LGC will be executed in accordance with the procedures set forth in Article VIII of the Agreement, applied *mutatis mutandis* to the payment obligations under this Paragraph 13.

14. If LGC provides written notice to Cue that [**] for the [**] or if LGC [**] for the [**] within the [**] period for [**] specified pursuant to Section [**] of the Agreement (each, an "**[**]**"), then, notwithstanding anything to the contrary in the Agreement, subject to commercially reasonable terms, (a) the forbearance obligations in Section 2.9(a) of the Agreement shall not limit or prohibit Cue or its Affiliates from directly or indirectly, alone or with or through any Third Party, Researching, Developing, importing, using, Manufacturing or Commercializing any CUE-102 [**] Compounds or CUE-102 [**] Products in the Field in the LGC Territory, and (b) for up to [**] after the date of the [**] LGC hereby grants Cue an exclusive option to receive an exclusive (even as to LGC and its Affiliates), royalty-bearing license, with the right to grant sublicenses through multiple tiers, under the [**] LGC Technology to Research, Develop, import, use, Manufacture and Commercialize CUE-102 [**] Compounds and CUE-102 [**] Products in the Field in the LGC Territory. The Parties shall negotiate in good faith for a period of [**] after the date of the [**] to come to commercially reasonable terms for the rights granted pursuant to the provisions of this Paragraph 14. If the Parties are unable to agree upon such terms, including commercially reasonable financial terms, during such [**] period, then such dispute shall be determined pursuant to Section 14.3 of the Agreement.

15. Except as expressly specified otherwise in this Eighth Amendment, unless and until LGC [**] for the [**] in accordance with Section [**] of the Agreement: (a) Cue shall not acquire any license or other intellectual property interest, by implication or otherwise, under or to any [**] LGC Technology; and (b) after the [**], LGC shall have no further obligations under the Agreement in relation to the CUE-102 [**], CUE-102 [**] Compounds or CUE-102 [**] Products.

16. Notwithstanding anything to the contrary in the Agreement or this Eighth Amendment, LGC shall have no obligations under Section 11.2 of the Agreement with respect to any act, omission, event or occurrence in relation to the [**] or any CUE-102 [**] Compound or CUE-102 [**] Product that takes place after the [**] and prior to the date of [**] by LGC of the [**] for the [**] in accordance with Section [**] of the Agreement, or any Losses related to any of the foregoing.

17. LGC hereby represents and warrants to Cue, as of the Eight Amendment Effective Date, that LGC has not granted, and will not grant during the Term, any right to any Third Party under the [**] LGC Technology that would conflict with the rights granted to Cue hereunder.

18. Except as expressly amended by this Eighth Amendment, all other terms and conditions of the Agreement shall remain in full force and effect, and are unmodified by this Eighth Amendment. The Agreement, as modified by this Eighth Amendment, contains the entire agreement of the Parties with regard to the subject matter set forth herein and supersedes all prior and contemporaneous agreements and communications, whether oral, written or otherwise, concerning any and all matters contained herein; provided, however, that the Global

Agreement shall continue in full force and effect in accordance with its terms. This Eighth Amendment may only be modified or supplemented in a writing expressly stated for such purpose and signed by the Parties.

19. This Eighth Amendment may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument. This Eighth Amendment may be executed and delivered electronically or by facsimile and upon such delivery such electronic or facsimile signature will be deemed to have the same effect as if the original signature had been delivered to the other Party.

[Signature Page Follows]

In Witness Whereof, the Parties hereto have caused this **Eighth Amendment** to be executed and entered into by their duly authorized representatives as of the Eighth Amendment Effective Date.

Cue Biopharma, Inc.		**LG Chem Ltd.**	
By:	/s/ Daniel Passeri	By:	/s/ Jeewoong Son
Name:	Daniel Passeri	Name:	Jeewoong Son
Title:	CEO	Title:	President

EXHIBIT 10.26

CUE BIOPHARMA, INC.

THIRD AMENDED AND RESTATED EXECUTIVE EMPLOYMENT AGREEMENT

This Third Amended and Restated Executive Employment Agreement ("**Agreement**"), dated as of March 4, 2021 (the "**Effective Date**"), is made by and between Cue Biopharma, Inc., a Delaware corporation ("**Cue**" or the "**Company**") and Daniel Passeri ("**Executive**," and together with Cue, the "**Parties**").

WHEREAS, the Company and Executive are parties to an Amended and Restated Employment Agreement dated as of October 3, 2019 (the "Original Agreement"), as amended by the Second Amended and Restated Executive Employment Agreement; and

WHEREAS, the Company and Executive desire to enter into this Agreement to amend and restate the Original Agreement in its entirety and to set forth in this Agreement the conditions under which the Employee is to be employed by the Company.

NOW, THEREFORE, in consideration of the foregoing, of the mutual promises contained herein and of other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

1. POSITION AND DUTIES.

(a) As of the Effective Date, Cue shall continue to employ Executive as its Chief Executive Officer ("**CEO**"). In his role as CEO, Executive shall have such duties and authority commensurate with the positions of CEO, and such other duties commensurate with the positions that may be assigned by the Board of Directors of Cue (the "**Board**").

(b) Executive shall report directly to the Chairman of the Board.

(c) Executive, upon being duly elected, shall also serve as a member of the Board or as an officer or director of any Affiliate (as defined below) for no additional compensation.

(d) Executive shall devote all of Executive's business time, energy, judgment, knowledge and skill and Executive's best efforts to the performance of Executive's duties with Cue, *provided* that the foregoing shall not prevent Executive from (i) participating in charitable, civic, educational, professional, community or industry affairs or (ii) managing Executive's passive personal investments, so long as such activities in the aggregate do not interfere or conflict with Executive's duties hereunder or create a potential business or fiduciary conflict.

2. TERM. This Agreement shall begin on the Effective Date and continue in effect until terminated in accordance with Section 8 below (the "**Term**").

3. BASE SALARY. Cue shall pay Executive a base salary ("**Base Salary**") at the rate of $42,916.66 per month, which equates to an annual rate of $515,000 during the Term, in accordance with the regular payroll practices of Cue. The Base Salary shall be subject to annual review and

adjustment at the sole discretion of the Board, provided however, that the Base Salary shall not be reduced during the Term unless mutually agreed by the Parties.

4. ANNUAL BONUS. Each year during the Term, Executive shall be eligible to receive an annual incentive bonus (the "**Annual Bonus**") of up to 50% of the Base Salary, subject to achievement of key performance indicators for Cue, with the level of achievement determined by the Board in its sole discretion. The Compensation Committee of the Board (the "**Committee**") shall establish such key performance indicators for each year after consultation with Executive. The terms of the Annual Bonus developed by the Committee shall govern any Annual Bonus that may be paid. Any Annual Bonus shall be paid in all events within two and one-half months after the end of the year in which such Annual Bonus becomes earned, *provided* that no Annual Bonus shall be considered earned until the Board makes all necessary determinations with respect to the Annual Bonus.

5. STOCK OPTIONS. Prior to the Effective Date, Executive was granted an Option (as defined in the Cue Biopharma, Inc. 2016 Omnibus Incentive Plan (the "**Plan**")) to purchase 150,000 shares of Cue's Common Stock (the "**Option**"). The exercise price per share of the Option was equal to the Fair Market Value (as defined in the Plan) of a share of Common Stock as of the Grant Date (as defined in the Plan). The Option has a term that expires ten years from the Grant Date. The Option is subject to the terms and conditions applicable to Options granted under the Plan, as described in the Plan and the applicable Award Agreement (as defined in the Plan). The Option shall become exercisable over four years in equal, semi-annual installments beginning six months from the Grant Date, subject to the terms and conditions of the Plan and the applicable Award Agreement, but in all cases subject to accelerated vesting and post-termination exercise provisions as provided for herein. The Option and any other stock option granted to you by the Company during the Term shall be exercisable by your estate or the beneficiary that you designate (on a form provided for such purpose by the Company) following your death through the expiration of the Option or such other stock option as set forth in the plan and award agreement pursuant to which such Option or such other stock option is granted.

6. RESTRICTED STOCK UNITS. Prior to the Effective Date, Executive was granted 150,000 Restricted Stock Units (as defined in the Plan) (the "**RSUs**"). The RSUs are subject to the terms and conditions applicable to RSUs granted under the Plan, as described in the Plan and the applicable Award Agreement. The RSUs vest as follows: One half of the RSUs shall vest on September 30, 2021 and the balance shall vest on March 31, 2022, subject to the terms and conditions of the Plan and the applicable Award Agreement, but would not be subject to accelerated vesting pursuant to **Section 9(c)**. The Award Agreement for the RSUs provides that Executive shall have the right to elect to meet any tax withholding requirement by having withheld shares with a Fair Market Value (as defined in the Plan) equal to the amount of any taxes required to be withheld.

7. EMPLOYEE BENEFITS.

(a) **BENEFIT PLANS.** During the Term, Executive shall be entitled to participate in any employee benefit plans that Cue has adopted or may adopt, maintains or contributes to for the benefit of its employees generally, subject to satisfying the applicable eligibility requirements,

except to the extent such plans are duplicative of the benefits otherwise provided to Executive hereunder. Executive's participation shall be subject to the terms of the applicable plan documents and generally applicable Cue policies. Notwithstanding the foregoing, Cue may modify or terminate any employee benefit plan at any time.

(b) **VACATIONS.** During the Term, Executive shall be entitled to paid vacation time in accordance with Cue's policy applicable to senior management employees as in effect from time to time (the "**Vacation Policy**"). Since vacation time is not accrued, unused vacation time may not be carried forward from one calendar year to any subsequent calendar year and shall not be paid out upon termination.

(c) **BUSINESS EXPENSES.** Upon presentation of reasonable substantiation and documentation as Cue may require from time to time, Executive shall be reimbursed in accordance with Cue's expense reimbursement policy, for all reasonable out-of-pocket business expenses incurred and paid by Executive during the Term and in connection with the performance of Executive's duties hereunder.

8. TERMINATION. Executive's employment under this Agreement shall terminate on the first to occur of the following:

(a) **DISABILITY.** Upon 10 days' prior written notice by Cue to Executive of termination due to Disability. "**Disability**" shall mean Executive is unable to perform each of the essential duties of Executive's position by reason of a medically determinable physical or mental impairment that is potentially permanent in character or that can be expected to last for a continuous period of not less than 12 months.

(b) **DEATH.** Automatically upon the death of Executive.

(c) **CAUSE.** Immediately upon written notice by Cue to Executive of a termination for Cause. "**Cause**" shall mean:

(i) the commission of any act by Executive constituting financial dishonesty against Cue or its Affiliates (which act would be chargeable as a crime under applicable law);

(ii) Executive's engaging in any other act of dishonesty, fraud, intentional misrepresentation, moral turpitude, illegality or harassment that would (a) materially adversely affect the business or the reputation of Cue or any of its Affiliates with their respective current or prospective customers, suppliers, lenders or other third parties with whom such entity does or might do business or (b) expose Cue or any of its Affiliates to a risk of civil or criminal legal damages, liabilities or penalties;

(iii) the repeated failure by Executive to follow the directives of the Board;

(iv) any material misconduct, violation of Cue's or Affiliates' policies, or willful and deliberate non-performance of duty by Executive in connection with the business affairs of Cue or its Affiliates; or

(v) Executive's material breach of this Agreement.

Executive shall be given written notice detailing the specific Cause event and a period of 10 days following Executive's receipt of such notice to cure such event (if susceptible to cure) to the reasonable satisfaction of the Board. Notwithstanding anything to the contrary contained herein, Executive's right to cure as set forth in the preceding sentence shall not apply if there are habitual or repeated breaches by Executive. A termination for Cause shall be deemed to include a determination by the Board or its designee following Executive's termination of service that circumstances existing prior to such termination would have entitled Cue to have terminated Executive for Cause. All rights Executive has or may have under this Agreement shall be suspended automatically during the pendency of any investigation by the Board or its designee, or during any negotiations between the Board or its designee and Executive, regarding any actual or alleged act or omission by Executive of the type described in this definition of Cause.

(d) **GOOD REASON.** Upon written notice by Executive to Cue of a termination for Good Reason. "**Good Reason**" shall mean the occurrence of any of the following events, without the consent of Executive, unless such events are fully corrected in all material respects by Cue within 30 days following written notification by Executive to Cue of the occurrence of one of the events:

(i) a material diminution in Executive's Base Salary or Annual Bonus opportunity;

(ii) a material diminution in Executive's authority or duties set forth in **Section 1** above, other than temporarily while physically or mentally incapacitated, as required by applicable law;

(iii) a relocation of Executive's primary work location by more than 25 miles from its then current location other than any such relocation that is recommended or approved by Executive in his role as CEO and is within 50 miles of the then current location;

(iv) a material breach by Cue of a material term of this Agreement.

Executive shall provide Cue with a written notice detailing the specific circumstances alleged to constitute Good Reason within 30 days after the first occurrence of such circumstances, and actually terminate employment within 30 days following the expiration of Cue's 30-day cure period described above. Otherwise, any claim of such circumstances as Good Reason shall be deemed irrevocably waived by Executive.

(e) **WITHOUT CAUSE.** Immediately upon written notice by Cue to Executive of an involuntary termination without Cause (other than for death or Disability).

(f) **VOLUNTARY TERMINATION.** Upon 60 days' prior written notice by Executive to Cue of Executive's voluntary termination of employment without Good Reason (which Cue may, in its sole discretion, make effective earlier than any notice date).

9. CONSEQUENCES OF TERMINATION.

(a) **DEATH/DISABILITY.** In the event that Executive's employment ends on account of Executive's death or Disability, Executive or Executive's estate, as the case may be, shall be entitled to the following (with the amounts due under **Sections 9(a)(i)** through **9(a)(iv)** below to be paid within 60 days following termination of employment, or such earlier date as may be required by applicable law):

(i) any unpaid Base Salary through the date of termination;

(ii) any Annual Bonus earned but unpaid prior to the date of termination;

(iii) reimbursement for any unreimbursed business expenses incurred through the date of termination;

(iv) any accrued but unused vacation time in accordance with Cue policy, which shall be prorated for any year in which Executive's employment with Cue is terminated;

(v) all other payments, benefits or fringe benefits to which Executive shall be entitled under the terms of any applicable compensation arrangement or benefit, equity or fringe benefit plan or program or grant (collectively, **Sections 9(a)(i)** through **9(a)(v)** hereof shall be hereafter referred to as the "**Accrued Benefits**"); and

(vi) an Annual Bonus for the year in which such termination occurs, determined and payable pursuant to the terms and conditions of **Section 4** above as though no such termination had occurred.

(b) **TERMINATION FOR CAUSE OR WITHOUT GOOD REASON.** If Executive's employment is terminated (i) by Cue for Cause or (ii) by Executive without Good Reason, Cue shall pay to Executive the Accrued Benefits (other than the Annual Bonus described in **Section 9(a)(ii)** above).

(c) **TERMINATION WITHOUT CAUSE OR FOR GOOD REASON.** If Executive's employment by Cue is terminated by Cue other than for Cause, death or Disability or by Executive for Good Reason, Cue shall pay or provide Executive the following:

(i) the Accrued Benefits;

(ii) subject to Executive's compliance with **Section 10** below and Executive's continued compliance with **Section 11** below, and subject to **Section 21**, a lump sum cash severance payment in an amount equal to the sum of (A) the target Annual Bonus for the year of termination, prorated based on the number of days that Executive is employed in such year through the date of termination (provided, notwithstanding the foregoing if termination occurs on or prior to March 31, 2020 the amount so paid shall equal the full target Annual Bonus for 2019 which shall be in lieu of any Annual Bonus payment for 2019), plus (B) 12 months of Base Salary, with such lump sum payable on the first payroll date of Cue that occurs more than 60 days after Executive's termination (collectively, the "**Severance Amount**");

(iii) subject to Executive's compliance with **Section 10** below and Executive's continued compliance with **Section 11** below, if Executive elects COBRA coverage for health and/or dental insurance in a timely manner, the Company shall pay the monthly premium payments for such timely elected coverage (consistent with what was in place at termination) when each premium is due until the earliest of the following: (i) 18 months from termination; (ii) the date Executive obtains new employment that offers health and/or dental insurance that is reasonably comparable to that offered by the Company; or (iii) the date COBRA continuation coverage would otherwise terminate in accordance with the provisions of COBRA; and

(iv) The time vesting and exercisability of one hundred percent (100%) of Executive's stock options, stock appreciation rights, restricted stock units and restricted shares in each case that are issued and outstanding under a Company equity compensation plan ("**Equity Awards**") shall accelerate by a period of 12 months; and Executive shall be entitled to exercise such Equity Awards (if exercisable) in accordance with this paragraph. For purposes of Equity Awards with performance-based vesting conditions ("**Performance Awards**"), Executive shall be treated under this paragraph as having remained in service for an additional 12 months following actual termination/resignation, provided that Performance Awards shall not become vested or earned solely as a result of this paragraph, and such vesting and earning shall remain subject to the attainment of all applicable performance goals, and such Performance Awards, if and to the extent they become vested or earned, shall be payable at the same time as under the applicable award agreement. For purposes of determining the accelerated vesting of Equity Awards and the additional service credit for Performance Awards, Executive's Equity Awards and Performance Awards, as applicable, shall be presumed to vest ratably on a monthly basis over the number of calendar months of the time-based vesting or service-based vesting period established on the Grant Date of the Equity Award or Performance Award. Notwithstanding any provision of this Agreement or any applicable Equity Award agreement to the contrary, in the event of Executive's termination/resignation initiated by the Company without Cause or by Executive for Good Reason, Executive's vested and exercisable Equity Awards shall remain exercisable (if exercisable) until the date on which those Equity Awards expire, determined without regard to such termination/resignation.

Payments and benefits provided under this **Section 9(c)** shall be in lieu of any termination or severance payments or benefits to which Executive may be eligible under any of the plans, policies or programs of Cue or under the Worker Adjustment Retraining Notification Act of 1988, as amended, or any similar state statute or regulation. Should Executive die prior to the payment of the Severance Amount, the Severance Amount shall be paid to the heirs or estate of Executive in accordance with the schedule set forth herein.

(d) **OTHER OBLIGATIONS.** Upon any termination of Executive's employment with Cue, Executive shall automatically be deemed to have resigned from any and all other positions he then holds as an officer, director or fiduciary of Cue and any other entity that is part of the same consolidated group as Cue or in which capacity Executive serves at the direction of or as a result of his position with Cue; and Executive shall, within 10 days of such termination, take all actions as may be necessary under applicable law or requested by Cue to effect any such resignations.

(e) **EXCLUSIVE REMEDY.** The amounts payable to Executive following termination of employment hereunder pursuant to **Sections 9(a)**, **(b)** and **(c)** above shall be in full and complete satisfaction of Executive's rights under this Agreement and any other claims that Executive may have in respect of Executive's employment with Cue or any of its Affiliates, and Executive acknowledges that such amounts are fair and reasonable, and are Executive's sole and exclusive remedy, in lieu of all other remedies at law or in equity, with respect to the termination of Executive's employment hereunder or any breach of this Agreement.

(f) **NO MITIGATION OR OFFSET.** Executive shall not be required to seek or accept other employment or otherwise to mitigate damages as a condition to the receipt of benefits pursuant to this **Section 9**, and amounts payable pursuant to this **Section 9** shall not be offset or reduced by any amounts received by Executive from other sources.

(g) **NO WAIVER OF ERISA-RELATED RIGHTS.** Nothing in this Agreement shall be construed to be a waiver by Executive of any benefits accrued for or due to Executive under any employee benefit plan (as such term is defined in the Employee Retirement Income Security Act of 1974, as amended) maintained by Cue, if any, except that Executive shall not be entitled to any severance benefits pursuant to any severance plan or program of Cue other than as provided herein.

(h) **CLAWBACK.** All awards, amounts or benefits received or outstanding under this Agreement shall be subject to clawback, cancellation, recoupment, rescission, payback, reduction or other similar action in accordance with the terms of any applicable law related to such actions, as may be in effect from time to time. Cue may take such actions as may be necessary to effectuate any provision of applicable law relating to clawback, cancellation, recoupment, rescission, payback or reduction of compensation, whether adopted before or after the Effective Date, without further consideration or action.

(i) **CHANGE IN CONTROL EQUITY AWARD ACCELERATION**. If Executive's employment by Cue is terminated by Cue other than for Cause or Executive's death or Disability, or is terminated by Executive for Good Reason, in any such case, 90 days prior to or upon or within 24 months following a Change in Control (as defined in the Plan), and notwithstanding anything in the Plan to the contrary, (a) one hundred percent (100%) of Executive's Equity Awards other than Performance Awards shall become fully vested as of the date of such termination/resignation, and such Equity Awards shall remain exercisable (if exercisable) until the earlier of one year from any termination/resignation or the latest date on which those Equity Awards expire or are eligible to be exercised under the applicable award agreements and (b) the service-based vesting condition of any Performance Award shall be deemed fully satisfied as of the date of such termination/resignation and such performance goals applicable to the Performance Awards shall be deemed to be achieved at the greater of target or actual performance as of the Change in Control, and such Performance Awards shall remain exercisable (if exercisable) until the earlier of one year from such termination/resignation or the latest date on which those Equity Awards expire or are eligible to be exercised under the applicable award agreements. Notwithstanding the foregoing, in no event shall Executive's Equity Awards receive less favorable treatment in connection with a Change in Control than is afforded to any other Plan participant's awards.

10. RELEASE. The Company's obligation to make the payments and provide the benefits to the Executive under Sections 9(c) and 9(i) is conditioned upon Executive signing and delivering to the Company a severance and release of claims agreement in a form to be provided by the Company (which will include, at a minimum, a release of all releasable claims, non-disparagement and cooperation obligations, reaffirmation of the Executive's continuing obligations under this Agreement or the Non-Competition Agreement, and an agreement not to compete with the Company for twelve (12) months after Executive's separation from employment). The Release Agreement shall be furnished to Executive within two business days after Executive's date of termination and must become irrevocable within 60 days following Executive's date of termination (or such shorter period as the Company may provide).

11. RESTRICTIVE COVENANTS.

(a) **CONFIDENTIALITY.**

(i) **COMPANY INFORMATION.** At all times during the Term and thereafter, Executive shall hold in strictest confidence, and shall not use, except in connection with the performance of Executive's duties, and shall not disclose to any person or entity, any Confidential Information of Cue. "**Confidential Information**" means any Cue proprietary or confidential information, technical data, trade secrets or know-how, including research, product plans, products, services, customer lists and customers, markets, software, developments, inventions, processes, formulas, technology, designs, drawings, engineering, marketing, distribution and sales methods and systems, sales and profit figures, finances and other business information disclosed to Executive by Cue, either directly or indirectly in writing, orally or by drawings or inspection of documents or other tangible property. However, Confidential Information does not include any of the foregoing items which has become publicly known and made generally available through no wrongful act of Executive.

(ii) **EXECUTIVE-RESTRICTED INFORMATION.** During the Term, Executive shall not improperly use or disclose any proprietary or confidential information or trade secrets of any person or entity with whom Executive has an agreement or duty to keep such information or secrets confidential.

(iii) **THIRD PARTY INFORMATION.** Executive recognizes that Cue has received and in the future will receive from third parties their confidential or proprietary information subject to a duty on Cue's part to maintain the confidentiality of such information and to use it only for certain limited purposes. At all times during the Term and thereafter, Executive shall hold in strictest confidence, and shall not use, except in connection with the performance of Executive's duties, and shall not disclose to any person or entity, such third party confidential or proprietary information, and shall not use it except as necessary in performing Executive's duties, consistent with Cue's agreement with such third party.

(b) **NONCOMPETITION.** Executive acknowledges that, in connection with his commencement of employment with the Company, he previously agreed to be bound by certain non-competition restrictions as set forth in the Original Agreement and the amended Agreement with the Company. To reaffirm such obligations, Executive agrees to execute a Non-Competition Agreement in the form attached hereto as **Attachment A** as a condition of his continued

employment. Executive acknowledges that his eligibility for a $5,000 cash bonus referenced therein is contingent upon his agreement to the non-competition provisions set forth in the Non-Competition Agreement. Executive further acknowledges that such consideration was mutually agreed upon by him and the Company and is fair and reasonable in exchange for his compliance with such non-competition obligations. For the avoidance of doubt, any reference elsewhere in the Agreement to Section 11(b) shall hereby incorporate by reference the attached Non-Competition Agreement and obligations referenced therein.

(c) **NONSOLICITATION; NONINTERFERENCE.**

(i) During Executive's employment with Cue and for a period of 24 months thereafter, Executive shall not, except in the furtherance of Executive's duties with Cue, directly or indirectly, individually or on behalf of any other person or entity, (i) solicit, aid or induce any customer of Cue or its Affiliates with whom Executive had meaningful business contact to purchase goods or services then sold by Cue or its Affiliates from another person or entity or assist or aid any other person or entity with whom Executive had meaningful business contact in identifying or soliciting any such customer, or (ii) interfere, or aid or induce any other person or entity with whom Executive had meaningful business contact in interfering, with the relationship between Cue or its Affiliates and any of their respective vendors, customers, joint venturers, licensees or licensors.

(ii) During Executive's employment with Cue and for a period of 24 months thereafter, Executive shall not, except in the furtherance of Executive's duties with Cue, directly or indirectly, individually or on behalf of any other person or entity, solicit, aid or induce any employee, consultant, representative or agent of Cue or its Affiliates (or any employee, consultant, representative or agent who has left the employment or retention of Cue or its Affiliates less than one year prior to the date that Executive solicits, aids or induces such person or entity (a "**Covered Person**")) to any other person or entity unaffiliated with Cue or hire or retain any such employee, consultant, representative or agent or any Covered Person, or take any action to materially assist or aid any other person or entity in identifying, hiring or soliciting any such employee, consultant, representative or agent or any Covered Person.

(d) **NONDISPARAGEMENT.** During the Term and for a period of 24 months thereafter, (A) Executive shall not make negative comments or otherwise disparage Cue or any company or other trade or business that "controls," is "controlled by" or is "under common control with," Cue within the meaning of Rule 405 of Regulation C under the Securities Act, including any "subsidiary corporation" of Cue within the meaning of Section 424(f) of the Internal Revenue Code of 1986 ("**Affiliates**") or any of their officers, directors, managers, employees, consultants, equityholders, agents or products, (B) in their interactions with Executive concerning the performance of his duties hereunder the members of the Board shall conduct themselves professionally and refrain from disparaging Executive and (C) Cue shall not and shall cause its directors officers and employees with titles of Senior Vice President or above not to make negative comments or otherwise disparage Executive. The foregoing shall not be violated by truthful statements (i) in response to legal process, required governmental testimony or filings or administrative or arbitral proceedings (including depositions in connection with such proceedings) or (ii) made in the course of Executive discharging his duties for Cue, (iii) made in response to any

statement made in breach of this paragraph or (iv) Executive making positive statements concerning another company or its technology, whether or not same competes with the Company, in Executive's reasonable good faith performance of Executive's duties after the Term to any new employer or entity to which Executive provides services (that are not in breach of any restrictive covenants to which Executive is subject pursuant to this Agreement).

(e) **COOPERATION.** Upon the receipt of reasonable notice from Cue, while employed by Cue and thereafter, Executive shall respond and provide information with regard to matters in which Executive has knowledge as a result of Executive's employment with Cue, and shall provide reasonable assistance to Cue, its Affiliates and their respective representatives in defense of any claims that may be made against Cue or its Affiliates, and shall assist Cue and its Affiliates in the prosecution of any claims that may be made by Cue or its Affiliates, to the extent that such claims may relate to the period of Executive's employment with Cue (collectively, the "**Claims**"). Executive shall promptly inform Cue if Executive becomes aware of any lawsuits involving Claims that may be filed or threatened against Cue or its Affiliates. Executive also shall promptly inform Cue (to the extent that Executive is legally permitted to do so) if Executive is asked to assist in any investigation of Cue or its Affiliates (or their actions) or another party attempts to obtain information or documents from Executive (other than in connection with any litigation or other proceeding in which Executive is a party-in-opposition) with respect to matters Executive believes in good faith to relate to any investigation of Cue or its Affiliates, in each case, regardless of whether a lawsuit or other proceeding has then been filed against Cue or its Affiliates with respect to such investigation, and shall not do so unless legally required. During the pendency of any litigation or other proceeding involving Claims, Executive shall not communicate with anyone (other than Executive's attorneys and tax and/or financial advisors and except to the extent that Executive determines in good faith is necessary in connection with the performance of Executive's duties hereunder) with respect to the facts or subject matter of any pending or potential litigation or regulatory or administrative proceeding involving Cue or any of its Affiliates without getting the prior written consent of Cue. Upon presentation of appropriate documentation, Cue shall pay or reimburse Executive for all reasonable out-of-pocket travel, duplicating or telephonic expenses incurred by Executive in accordance with Cue's applicable policies in complying with this **Section 11(e)**, and Executive shall be compensated by Cue at a reasonable hourly rate for assistance given after the end of the Term.

(f) **OWNERSHIP OF INFORMATION, IDEAS, CONCEPTS, IMPROVEMENTS, DISCOVERIES AND INVENTIONS, AND ALL ORIGINAL WORKS OF AUTHORSHIP.**

(i) As between the Parties, all information, ideas, concepts, improvements, discoveries and inventions, whether patentable or not, which are conceived, made, developed or acquired by Executive or which are disclosed or made known to Executive, individually or in conjunction with others, during the Term and which relate to Cue's business, products or services (including all such information relating to corporate opportunities, research, financial and sales data, pricing and trading terms, evaluations, opinions, interpretations, acquisition prospects, the identity of clients or customers or their requirements, the identity of key contacts within the client or customers' organizations or within the organization of acquisition prospects, or marketing and merchandising techniques, prospective names and marks) are and shall be the sole and exclusive

property of Cue. Moreover, all drawings, memoranda, notes, records, files, correspondence, manuals, models, specifications, computer programs, maps and all other writings or materials of any type embodying any of such information, ideas, concepts, improvements, discoveries and inventions are and shall be the sole and exclusive property of Cue.

(ii) In particular, Executive hereby specifically assigns and transfers to Cue all of Executive's worldwide right, title and interest in and to all such information, ideas, concepts, improvements, discoveries or inventions, and any United States or foreign applications for patents, inventor's certificates or other industrial rights that may be filed thereon, and applications for registration of such names and marks. During the Term and thereafter, Executive shall assist Cue and its nominee at all times in the protection of such information, ideas, concepts, improvements, discoveries or inventions, both in the United States and all foreign countries, including the execution of all lawful oaths and all assignment documents requested by Cue or its nominee in connection with the preparation, prosecution, issuance or enforcement of any applications for United States or foreign letters patent, and any application for the registration of such names and marks.

(iii) Moreover, if during the Term, Executive creates any original work of authorship fixed in any tangible medium of expression which is the subject matter of copyright (such as reports, videotapes, written presentations, computer programs, drawings, maps, architectural renditions, models, manuals, brochures or the like) relating to Cue's business, products or services, whether such work is created solely by Executive or jointly with others, Cue shall be deemed the author of such work if the work is prepared by Executive in the scope of Executive's employment; or, if the work is not prepared by Executive within the scope of Executive's employment but is specially ordered by Cue as a contribution to a collective work, as a part of any written or audiovisual work, as a translation, as a supplementary work, as a compilation or as an instructional text, then the work shall be considered to be work made for hire and Cue shall be the author of the work. In the event such work is neither prepared by Executive within the scope of Executive's employment or is not a work specially ordered and deemed to be a work made for hire, then Executive shall assign, and by these presents, does assign, to Cue all of Executive's worldwide right, title and interest in and to such work and all rights of copyright therein. Both during the Term and thereafter, Executive shall assist Cue and its nominee, at any time, in the protection of Cue's worldwide right, title and interest in and to the work and all rights of copyright therein, including the execution of all formal assignment documents requested by Cue or its nominee and the execution of all lawful oaths and applications for registration of copyright in the United States and foreign countries; *provided*, *however*, that Executive shall be compensated by Cue at a reasonable hourly rate for assistance given after the end of the Term.

(iv) Notwithstanding the foregoing provisions of this **Section 11(f)**, Cue hereby notifies Executive that the provisions of this **Section 11(f)** shall not apply to any inventions for which no equipment, supplies, facility or trade secret information of Cue was used and which were developed entirely on Executive's own time, unless (A) the invention relates (1) to the business of Cue, or (2) to actual or demonstrably anticipated research or development of Cue, or (B) the invention results from any work performed by Executive for Cue.

(g) **RETURN OF COMPANY PROPERTY.** On the date of Executive's termination of employment with Cue for any reason (or at any time prior thereto at Cue's request), Executive shall return all property belonging to Cue or its Affiliates (including any Cue or Affiliate-provided laptops, computers, cell phones, wireless electronic mail devices or other equipment, or documents or property belonging to Cue or an Affiliate).

(h) **EFFECT OF EXECUTIVE BECOMING A BAD LEAVER.** Notwithstanding any provision of this Agreement to the contrary, if (i) Executive materially breaches any of the covenants set forth in Section 11(a)(i), 11(a)(ii), 11(a)(iii), 11(b), 11(c), 11(d) or 11(f) hereof at any time during the period commencing on the Effective Date and ending 18 months after Executive's termination of employment with Cue for any reason and (ii) Executive fails to cure such breach within 10 days of the effective date of written notice of such breach given by Cue, then Executive shall be deemed a "**Bad Leaver**." If Executive is or becomes a Bad Leaver, then (i) any severance being paid to Executive pursuant to this Agreement or otherwise shall immediately cease upon commencement of such action and (ii) Executive shall be liable to repay to Cue any severance previously paid to him by Cue, less $100 to serve as consideration for the release described in **Section 10** above.

(i) **TOLLING.** If Executive violates any of the terms of the restrictive covenant obligations articulated herein, the obligation at issue will run from the first date on which Executive ceases to be in violation of such obligation.

12. EQUITABLE RELIEF AND OTHER REMEDIES. Executive acknowledges that Cue's remedies at law for a breach or threatened breach of any of the provisions of **Section 11** above would be inadequate and in the event of such a breach or threatened breach, in addition to any remedies at law, Cue, without posting any bond, shall be entitled to seek to obtain equitable relief in the form of specific performance, a temporary restraining order, a temporary or permanent injunction or any other equitable remedy that may then be available, without the necessity of showing actual monetary damages or the posting of a bond or other security.

13. NO ASSIGNMENTS. This Agreement is personal to each of the Parties. Except as provided in this **Section 13**, neither Party may assign or delegate any rights or obligations hereunder without first obtaining the written consent of the other Party. Cue may assign this Agreement to any of its Affiliates or to any successor to all or substantially all of the business and/or assets of Cue, *provided* that Cue shall require such Affiliate or successor to expressly assume and agree to perform this Agreement in the same manner and to the same extent that Cue would be required to perform it if no such succession had taken place. As used in this Agreement, "Cue" shall mean Cue and any Affiliate or successor to its business and/or assets that assumes and agrees to perform the duties and obligations of Cue under this Agreement by operation of law or otherwise.

14. NOTICE. Any notice that either Party may be required or permitted to give to the other shall be in writing and may be delivered personally, by electronic mail or via a postal service, postage prepaid, to such electronic mail or postal address and directed to such person as Cue may notify Executive from time to time; and to Executive at his electronic mail or postal address as

shown on the records of Cue from time to time, or at such other electronic mail or postal address as Executive, by notice to Cue, may designate in writing from time to time.

15. SECTION HEADINGS; INCONSISTENCY. The section headings used in this Agreement are included solely for convenience and shall not affect, or be used in connection with, the interpretation of this Agreement. In the event of any inconsistency between the terms of this Agreement and any form, award, plan or policy of Cue, the terms of this Agreement shall govern and control.

16. SEVERABILITY. Whenever possible, each provision of this Agreement shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be invalid, illegal or unenforceable in any respect under any applicable law or rule in any jurisdiction, such invalidity, illegality or unenforceability shall not affect any other provision of this Agreement or any action in any other jurisdiction, but this Agreement shall be reformed, construed and enforced in such jurisdiction.

17. COUNTERPARTS. This Agreement may be executed in several counterparts, each of which shall be deemed to be an original but all of which together shall constitute one and the same instrument.

18. APPLICABLE LAW; CHOICE OF VENUE AND CONSENT TO JURISDICTION; SERVICE OF PROCESS; WAIVER OF JURY TRIAL.

(a) All questions concerning the construction, validity and interpretation of this Agreement and the performance of the obligations imposed by this Agreement shall be governed by the internal laws of the State of Delaware applicable to agreements made and wholly to be performed in such state without regard to conflicts of law provisions of any jurisdiction.

(b) For purposes of resolving any dispute that arises directly or indirectly from the relationship of the Parties evidenced by this Agreement, the Parties hereby submit to and consent to the exclusive jurisdiction of the Commonwealth of Massachusetts and further agree that any related litigation shall be conducted solely in the courts of Middlesex County, Massachusetts or the federal courts for the United States for the District of Massachusetts, where this Agreement is made and/or to be performed, and no other courts.

(c) Each Party may be served with process in any manner permitted under State of Delaware law, or by United States registered or certified mail, return receipt requested.

(d) BY EXECUTION OF THIS AGREEMENT, THE PARTIES ARE WAIVING ANY RIGHT TO TRIAL BY JURY IN CONNECTION WITH ANY SUIT, ACTION OR PROCEEDING ARISING OUT OF OR BASED ON THIS AGREEMENT.

19. MISCELLANEOUS. No provision of this Agreement may be modified, waived or discharged unless such waiver, modification or discharge is agreed to in writing and signed by Executive and such officer or director as may be designated by Cue. No waiver by either Party at any time of any breach by the other Party of, or compliance with, any condition or provision of this Agreement to be performed by such other Party shall be deemed a waiver of similar or

dissimilar provisions or conditions at the same or at any prior or subsequent time. This Agreement together with all exhibits hereto sets forth the entire agreement of the Parties in respect of the subject matter contained herein and supersedes any and all prior agreements or understandings between Executive and Cue or its Affiliates with respect to the subject matter hereof, including without limitation the Original Agreement. No agreements or representations, oral or otherwise, express or implied, with respect to the subject matter hereof, have been made by either Party that are not expressly set forth in this Agreement.

20. REPRESENTATIONS. Executive represents and warrants to Cue that (a) Executive has the legal right to enter into this Agreement and to perform all of the obligations on Executive's part to be performed hereunder in accordance with its terms, and (b) Executive is not a party to any agreement or understanding, written or oral, and is not subject to any restriction, which, in either case, could prevent Executive from entering into this Agreement or performing all of Executive's duties and obligations hereunder.

21. TAX MATTERS.

(a) **WITHHOLDING.** Any and all amounts payable under this Agreement or otherwise shall be subject to, and Cue may withhold from such amounts, any federal, state, local or other taxes as may be required to be withheld pursuant to any applicable law or regulation.

(b) SECTION 409A COMPLIANCE.

(i) The intent of the Parties is that payments and benefits under this Agreement be exempt from (to the extent possible) or compliant with Section 409A ("**Section 409A**") of the Internal Revenue Code of 1986 and the regulations and guidance promulgated thereunder, as amended (collectively, the "**Code**") and, accordingly, to the maximum extent permitted, this Agreement shall be interpreted accordingly. To the extent that any provision hereof is modified in order to comply with Section 409A, such modification shall be made in good faith and shall, to the maximum extent reasonably possible, maintain the original intent and economic benefit to the Parties of the applicable provision without violating the provisions of Section 409A. In no event shall Cue be liable for any additional tax, interest or penalty that may be imposed on Executive by Section 409A or damages for failing to comply with Section 409A.

(ii) A termination of employment shall not be deemed to have occurred for purposes of any provision of this Agreement providing for the payment of any amounts or benefits that constitute "nonqualified deferred compensation" under Section 409A upon or following a termination of employment unless such termination is also a "separation from service" within the meaning of Section 409A and, for purposes of any such provision of this Agreement, references to a "termination," "termination of employment" or like terms shall mean "separation from service." Notwithstanding anything to the contrary in this Agreement, if Executive is deemed on the date of termination to be a "specified employee" under Section 409A, then with regard to any payment or the provision of any benefit that is considered "nonqualified deferred compensation" under Section 409A payable on account of a "separation from service," such payment or benefit shall not be made or provided until the earlier of (A) the expiration of the six-month period measured from the date of such "separation from service" of Executive, and (B) the date of Executive's death, to the extent required under Section 409A. Upon the expiration of the foregoing

delay period, all payments and benefits delayed pursuant to this **Section 21(b)(ii)** (whether they would have otherwise been payable in a single sum or in installments in the absence of such delay) shall be paid or reimbursed to Executive in a lump sum on the first business day following the six-month period, and any remaining payments and benefits due under this Agreement shall be paid or provided in accordance with the normal payment dates specified for them herein.

(iii) To the extent that reimbursements or other in-kind benefits under this Agreement constitute "nonqualified deferred compensation" for purposes of Section 409A, (A) all expenses or other reimbursements hereunder shall be made on or prior to the last day of the taxable year following the taxable year in which such expenses were incurred by Executive, (B) any right to reimbursement or in-kind benefits shall not be subject to liquidation or exchange for another benefit and (C) no such reimbursement, expenses eligible for reimbursement or in-kind benefits provided in any taxable year shall in any way affect the expenses eligible for reimbursement, or in-kind benefits to be provided, in any other taxable year.

(iv) For purposes of Section 409A, Executive's right to receive any installment payments pursuant to this Agreement shall be treated as a right to receive a series of separate and distinct payments. Whenever a payment under this Agreement specifies a payment period with reference to a number of days, the actual date of payment within the specified period shall be at the sole discretion of the Board.

(v) Notwithstanding any other provision of this Agreement to the contrary, in no event shall any payment under this Agreement that constitutes "nonqualified deferred compensation" for purposes of Section 409A be subject to offset by any other amount unless otherwise permitted by Section 409A.

(c) **MODIFICATION OF PAYMENTS.** In the event it shall be determined that any payment, right or distribution by Cue or any other person or entity to or for the benefit of Executive pursuant to the terms of this Agreement or otherwise, in connection with, or arising out of, Executive's employment with Cue or a change in ownership or effective control of Cue or a substantial portion of its assets (a "**Payment**") is a "parachute payment" within the meaning of Code Section 280G on account of the aggregate value of the Payments due to Executive being equal to or greater than three times the "base amount," as defined in Code Section 280G (the "**Parachute Threshold**"), so that Executive would be subject to the excise tax imposed by Code Section 4999 (the "**Excise Tax**") and the net after-tax benefit that Executive would receive by reducing the Payments to the Parachute Threshold is greater than the net after-tax benefit Executive would receive if the full amount of the Payments were paid to Executive, then the Payments payable to Executive shall be reduced (but not below zero) so that the Payments due to Executive do not exceed the amount of the Parachute Threshold, reducing first any Payments under **Section 9** above.

BY SIGNING THIS AGREEMENT BELOW, EXECUTIVE ACKNOWLEDGES THAT EXECUTIVE:

(1) HAS READ AND UNDERSTOOD THE ENTIRE AGREEMENT;

(2) HAS HAD THE OPPORTUNITY TO ASK QUESTIONS AND CONSULT COUNSEL OR OTHER ADVISORS ABOUT ITS TERMS; AND

(3) AGREES TO BE BOUND BY IT.

IN WITNESS WHEREOF, Cue has caused this Agreement to be executed in its name and on its behalf, and Executive acknowledges understanding and acceptance of, and agrees to, the terms of this Agreement, all as of the Effective Date.

CUE BIOPHARMA, INC.	**DANIEL R. PASSERI**
/s/ Frank Morich	/s/ Daniel R. Passeri
Print Name: Frank Morich	
Title: Chairman of the Board	

ATTACHMENT A

NON-COMPETITION AGREEMENT

This Non-Competition (the "Agreement") is made by and between Cue Biopharma, Inc., a Delaware corporation (hereinafter referred to collectively with its subsidiaries as the "Company"), and the undersigned employee (the "Employee").

For good consideration, including, without limitation, the continued employment of the Employee by the Company and, with respect to the non-competition restrictions, the additional consideration set forth in Section 1(c), the Employee and the Company agree as follows:

1. Non-Competition.

a) During the Restricted Period (as defined below), the Employee will not, in the Applicable Territory (as defined below), directly or indirectly, whether as an owner, partner, officer, director, employee, consultant, investor, lender or otherwise, except as the passive holder of not more than 1% of the outstanding stock of a publicly-held company, engage or assist others in engaging in any business or enterprise that is competitive with the Company's business, including but not limited to any business or enterprise that researches, develops, manufactures, markets, licenses, sells or provides any product or service that competes with any product or service researched, developed, manufactured, marketed, licensed, sold or provided, or planned to be researched, developed, manufactured, marketed, licensed, sold or provided by the Company (a "Competitive Company"), if the Employee would be performing job duties or services for the Competitive Company that are of a similar type that the Employee performed for the Company at any time during the last two (2) years of the Employee's employment. As a senior leader for the Company, the Employee acknowledges and agrees that, in the performance of the Employee's duties for the Company (including without limitation, assisting the Company with its overall business strategy), the Employee will be involved in all aspects of the Company's business and operations. Accordingly, the Employee acknowledges and agrees that undertaking any leadership role in a Competitive Company would constitute performing job duties or services of a similar type that the Employee performed for the Company.

b) Certain Definitions. Solely for purposes of this Section 1:

i. the "Restricted Period" shall include the duration of the Employee's employment with the Company and the twelve (12) month period thereafter; provided, however, that the Restricted Period shall automatically be extended to two (2) years following the cessation of the Employee's employment if the Employee breaches a fiduciary duty to the Company or the Employee unlawfully takes, physically or electronically, any property belonging to the Company. Notwithstanding the foregoing, the Restricted Period shall end immediately upon the Employee's last day of employment with the Company if: (x) the Company terminates the Employee's employment other than for Cause (as defined below); or (y) the Company notifies the Employee in writing that it is waiving the post-employment restrictions set forth in this Section 1 (such notice to be provided no later than the Employee's last day of employment or by the seventh (7th) business day following an Employee's notice of resignation, if later).

ii. "Applicable Territory" shall mean the geographic areas in which the Employee provided services or had a material presence or influence at any time during his/her last two (2) years of employment. As a senior leader for the Company, the Employee acknowledges that the Employee's duties and responsibilities require the Employee to have a material presence and/or influence anywhere that the Company does business.

iii. "Cause" shall mean any of: (a) the Employee's conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude, or any felony; or (b) a good faith finding by the Company in its sole discretion that the Employee has (i) engaged in dishonesty, misconduct or gross negligence; (ii) committed an act that injures or would reasonably be expected to injure the reputation, business or business relationships of the Company; (iii) breached the terms of this Agreement or any other restrictive covenant or confidentiality agreement with or policy of the Company; (iv) failed or refused to comply with any of the Company's policies or procedures; or (v) failed to perform the Employee's duties and/or responsibilities to the Company's satisfaction.

c) Additional Consideration for Non-Competition Restrictions. In exchange for the Employee's compliance with the restrictions set forth in this Section 1, and as referenced in the Employee's Employment Agreement to which this Agreement is attached, the Company, subject to approval of its Board of Directors where applicable, will pay the Employee a $5,000 non-competition bonus, less applicable taxes and withholdings, which will be paid to the Employee in the first payroll cycle following the Employee's execution of this Agreement (and in any event during the 2021 calendar year). The Employee understands and agrees that the above-stated consideration has been mutually agreed upon by the Company and the Employee, is fair and reasonable, and is sufficient consideration in exchange for the restrictions set forth in this Section 1.

2. Notice of New Business Activities. The Employee agrees that during any period of time when the Employee is subject to restrictions pursuant to Section 1, the Employee will notify any prospective employer or business associate of the terms and existence of this Agreement and the Employee's continuing obligations to the Company hereunder. The Employee further agrees, during such period, to give notice to the Company of each new business activity the Employee plans to undertake, at least (10) business days prior to beginning any such activity. The notice shall state the name and address of the individual, corporation, association or other entity or organization ("Entity") for whom such activity is undertaken and the name of the Employee's business relationship or position with the Entity. The Employee also agrees to provide the Company with other pertinent information concerning such business activity as the Company may reasonably request in order to determine the Employee's continued compliance with his/her obligations under this Agreement. The Employee hereby authorizes the Company to notify others, including but not limited to customers of the Company and any of the Employee's future employers or prospective business associates, of the terms and existence of this Agreement and the Employee's continuing obligations to the Company hereunder.

3. Miscellaneous.

a) Equitable Remedies. The Employee acknowledges that the restrictions contained in this Agreement are necessary for the protection of the business and goodwill of the Company and are considered by the Employee to be reasonable for such purpose. The Employee agrees that any breach or threatened breach of this Agreement is likely to cause the Company substantial and irrevocable damage which is difficult to measure. Therefore, in the event of any such breach or threatened breach, the Employee agrees that the Company, in addition to such other remedies which may be available, shall have the right to obtain an injunction from a court restraining such a breach or threatened breach without posting a bond and the right to specific performance of the provisions of this Agreement and the Employee hereby waives the adequacy of a remedy at law as a defense to such relief. Additionally, the Employee acknowledges and agrees that, while any non-solicitation obligations the Employee may have are essential to the protection of the Company's legitimate business interests, such interests cannot be adequately protected without the non-competition obligations set forth in Section 1.

b) Obligations to Third Parties. The Employee represents that, except as the Employee has disclosed in writing to the Company, the Employee is not bound by the terms of any agreement with any previous employer or other party to refrain from using or disclosing any trade secret or confidential or proprietary information in the course of his/her employment with the Company, to refrain from competing, directly or indirectly, with the business of such previous employer or any other party, or to refrain from soliciting employees, customers or suppliers of such previous employer or other party. The Employee further represents that his/her performance of all the terms of this Agreement and the performance of his/her duties as an employee of the Company does not and will not conflict with or breach any agreement with any prior employer or other party (including, without limitation, any nondisclosure or non-competition agreement), and that the Employee will not disclose to the Company or induce the Company to use any confidential or proprietary information or material belonging to any previous employer or others.

c) Not Employment Contract. The Employee acknowledges that this Agreement does not constitute a contract of employment, does not imply that the Company will continue his/her employment for any period of time, and does not change the at-will nature of his/her employment.

d) Acknowledgments.

The Employee acknowledges that he or she has the right to consult with counsel prior to signing this Agreement. The Employee further acknowledges that he or she was provided at least ten (10) business days to review this Agreement and that the Agreement is supported by fair and reasonable consideration independent from the Employee's continuation of employment.

e) Successors and Assigns. The Employee's obligations under this Agreement are personal and shall not be assigned by the Employee. This Agreement shall, however, be binding upon and inure to the benefit of the Company and its successors and assigns, including any corporation or entity with which or into which the Company may be merged or that may succeed to all or substantially all of its assets or business. The Employee expressly consents to be bound by the provisions of this Agreement for the benefit of any successor or assign of the Company without the necessity that this Agreement be re-signed, in which event "Company" shall be interpreted to include any successor or assign of the Company.

f) Interpretation. If any restriction or definition set forth in Section 1 is found by any court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of conduct, activities, or geographic area, it shall be interpreted to extend only over the maximum period of time, range of conduct, activities or geographic area as to which it may be enforceable.

g) Severability. In case any provision of this Agreement shall be invalid, illegal or otherwise unenforceable, the validity, legality and enforceability of the remaining provisions shall in no way be affected or impaired thereby.

h) Waivers. No delay or omission by the Company in exercising any right under this Agreement will operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion is effective only in that instance and will not be construed as a bar to or waiver of any right on any other occasion.

i) Governing Law and Consent To Jurisdiction. Notwithstanding anything to the contrary in the Employment Agreement to which this Agreement is appended, this Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to the conflicts of laws provisions thereof). Any action, suit, or other legal proceeding which is commenced to resolve any matter arising under or relating to any provision of this Agreement shall be commenced only in a court in Suffolk County, Massachusetts (or, if appropriate, a federal court located within Massachusetts), and the Company and the Employee each consents to the jurisdiction of such courts. The Company and the Employee each hereby irrevocably waives any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this Agreement.

j) Entire Agreement; Amendment. This Agreement supersedes all prior agreements, written or oral, between the Employee and the Company relating to the subject matter of this Agreement; provided, however, that for the avoidance of doubt, nothing herein supersedes the Employee's continuing obligations set forth in Section 11(a)-(b), (d)-(i) of the Employment Agreement by and between him and the Company, as amended. Further, notwithstanding anything to the contrary, if there is a conflict between this Agreement and any provision in the Employment Agreement, such conflict shall be resolved in the manner most protective of the Company. This Agreement may not be modified, changed or discharged in whole or in part, except by an agreement in writing signed by the Employee and the Company. The Employee agrees that any change or changes in his/her duties, authority, title, reporting relationship, territory, salary or

compensation after the signing of this Agreement shall not affect the validity or scope of this Agreement.

k) Captions. The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

[*Remainder of Page Intentionally Left Blank*]

THE EMPLOYEE ACKNOWLEDGES THAT HE/SHE HAS CAREFULLY READ THIS AGREEMENT AND UNDERSTANDS AND AGREES TO ALL OF THE PROVISIONS IN THIS AGREEMENT.

EMPLOYEE

Date: _____

/s/ Daniel R. Passeri
Name: Daniel R. Passeri

CUE BIOPHARMA, INC

Date: _____

By: /s/ Frank Morich
Name: Frank Morich
Title: Chairman of the Board

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXHIBIT 10.28

FIRST AMENDMENT TO THE EXCLUSIVE PATENT LICENSE AND RESEARCH COLLABORATION AGREEMENT

This Amendment to the Exclusive Patent License And Research Collaboration Agreement (this "**Amendment**") is entered into as of November 9, 2020 (the "**First Amendment Effective Date**"), by and between CUE BIOPHARMA, INC., a corporation organized and existing under the laws of Delaware (**"Company" or "Cue"**) and MERCK SHARP & DOHME CORP., a corporation organized and existing under the laws of New Jersey (**"Merck"**). Cue and Merck may be referred to herein individually as a "**Party**" or collectively as the "**Parties**".

WHEREAS, the Parties entered into that certain Exclusive Patent License And Research Collaboration Agreement as of November 14, 2017 (the "**Agreement**");

WHEREAS, pursuant to Section 2.10.1 of the Agreement, Merck at its sole discretion may extend the Research Program specified in the Agreement for a total of up to [**] additional years on a year-by-year basis;

WHEREAS, following discussions between the Parties, Merck has decided to extend the Research Program for an additional year in order to accomplish further research pursuant to the Agreement;

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Cue and Merck hereby agree as follows:

1. All capitalized terms not defined in this Amendment shall have the respective meanings ascribed to them in the Agreement.

2. Pursuant to Section 2.10.1 of the Agreement, and subject to the remaining terms and conditions set forth in this Amendment, Merck hereby extends the Research Program and the Research Program Term for a first additional year (the "**First Extension Year**"); *provided*, *however*, such First Extension Year shall begin on [**] and end on December 31, 2021.

3. Section 5.2.1 of the Agreement is hereby amended by deleting the first milestone event listed in the table and replacing it with the following two milestone events and corresponding payment amounts:

1. Upon Cue's advancement of a Cue Biologic toward achieving an optimized lead candidate	US$ 300,000
[**]	[**]

Merck acknowledges that the first milestone listed above has been achieved and will pay the associated milestone payment in accordance with the terms of the Agreement.

4. Schedule 2.1 of the Agreement is hereby modified to add the provisions, commitments, goals and activities set forth in Appendix A to this Amendment as the Research Program for the First Extension Year (the "**First Research Program Extension Plan**"). For clarity, the First Research Program Extension Plan as set forth in Appendix A states the entire Research Program to be carried out by Company during the First Extension Year.

5. In addition to the License Fee, milestone payments and royalties, if any, payable by Merck to Company during the Term, and subject to the maximum amounts set forth on Appendix B, Merck will reimburse Company for [**]. Notwithstanding that Merck's obligation to reimburse Company is subject to the maximum amounts set forth in Appendix B, Company will [**], regardless of whether such FTE costs or expenses exceed the amount required to be reimbursed by Merck.

6. Merck hereby acknowledges that the Agreement was required to be filed by Company with the U.S. Securities and Exchange Commission ("SEC"). If Company determines that this Amendment is also required to be filed with the SEC, the Parties will consult and cooperate with each other as set forth in Section 4.4 of the Agreement.

7. Except as expressly amended by this Amendment, all other terms and conditions of the Agreement shall remain in full force and effect, and are unmodified by this Amendment. The Agreement, as modified by this Amendment, contains the entire understanding of the Parties with respect to the subject matter thereof. Any other express or implied agreements and understandings, negotiations, writings and commitments, either oral or written, with respect to the subject matter thereof are superseded by the terms of the Agreement as amended hereby. The Schedules and Exhibits to this Amendment are incorporated herein by reference and shall be deemed a part of this Amendment.

8. This Amendment may be signed in any number of counterparts (including by facsimile or electronic transmission), each of which shall be deemed an original, but all of which shall constitute one and the same instrument. After facsimile or electronic transmission, the Parties agree to execute and exchange documents with original signatures.

9. This Amendment shall be governed by and construed in accordance with the laws of the State of New York without reference to any rules of conflict of laws or renvoi.

[Signature Page Follows]

IN WITNESS WHEREOF, the Parties have executed this Amendment as of the First Amendment Effective Date.

MERCK SHARP & DOHME CORP.	**CUE BIOPHARMA, INC.**
BY: /s/ Ben Thorner Ben Thorner	BY: /s/ Daniel R. Passeri Daniel R. Passeri
TITLE: Senior Vice President and Head of Business Development	TITLE: CEO

Appendix B

First Research Program Extension Funding

1. **Definitions.** the following terms, whether used in the singular or plural, shall have the respective meanings set forth below.

   1.1 "FTE" shall mean [**] hours of a full-time scientist's work time over twelve (12) consecutive calendar months (including normal vacations, sick days and holidays).

   1.2 "FTE Rate" shall mean an amount equal to [**] U.S. dollars (US$[**]) for one (1) full FTE, which represents the fully burdened annual rate for each such FTE and includes related salary, benefits, administration, facilities costs and overhead.

2. **Merck Research Program Funding.** During the First Extension Year. Merck will provide Company with certain research funding as set forth in this Appendix B, including Attachment 1. Company shall apply the research funding it receives from Merck solely to carry out its Research Program activities in accordance with the terms and conditions of the Agreement, including this Amendment, and the First Research Program Extension Plan.

3. **FTE Payments.** During the First Extension Year Merck shall pay Company the FTE Rate [**]. Payments will be calculated and made for each Calendar Quarter equal to [**].

4. **Maximum FTE Commitment.** In no event shall Merck's aggregate payments for FTEs exceed [**] U.S. dollars (US$[**]) for the First Updated Research Program term.

5. **Reimbursement of Certain Expenses.** Merck shall reimburse Company for the actual out-of-pocket costs incurred by Company, without mark-up or any administrative fees, in performing the First Updated Research Program to the extent such out-of-pocket costs are expressly set forth in the budget attached hereto as Attachment 1 (the **"Expense Budget"**) and to the extent Company provides appropriate documentation (including original receipts); provided that consumable expenses shall be invoiced at flat cost of $[**] per Calendar Quarter regardless of the actual costs incurred; provided further, however, that in no event shall Company be entitled to receive payment for (and Company shall be solely responsible for) any and all out-of-pocket costs that are in excess of the total out-of-pocket costs set forth in the Expense Budget. Company shall issue invoices to Merck for such out-of-pockets costs on a Calendar Quarter basis with no mark-up on cost. All such invoices shall be issued in U.S. dollars. Merck shall pay the undisputed amount of such invoices within [**] after receipt thereof.

6. **Maximum Expense Commitment.** In no event shall Merck's aggregate reimbursement for out-of-pocket expenses hereunder exceed [**] U.S. dollars (US$[**]) for the First Extension Year and the performance by Company of the First Research Program Extension Plan. If Merck elects to request Company to [**] as contemplated by the First Research Program Extension Plan, the Parties will agree in writing on the out-of-pocket costs to be reimbursed by Merck prior to any [**] being initiated.

7. **Invoices and Payments.** After the end of the relevant Calendar Quarter, Company will submit to Merck an invoice showing the amounts owed, including the number of FTEs which actually performed services in furtherance of the First Research Program Extension Plan and the calculation of the FTE charges payables and supporting documentation showing the out-of-pocket expenses incurred. All such invoices shall be calculated and stated in U.S. dollars. Merck shall pay the undisputed amount of each invoice within [**] after its receipt thereof,

Appendix B – Attachment 1

Expense Budget

[**]

Exhibit 10.30

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

FIRST AMENDMENT TO THE AMENDED AND RESTATED LICENSE AGREEMENT

This First Amendment to the Amended and Restated License Agreement ("First Amendment") is by and between Albert Einstein College of Medicine, Inc., a corporation organized and existing under the laws of the State of New York, having an office and place of business at 1300 Morris Park Avenue, Bronx, New York 10461 ("Licensor") and Cue Biopharma, Inc., a corporation organized and existing under the laws of the State of Delaware, having an office and place of business at c/o MDB Capital Group LLC, 401 Wilshire Blvd, Suite 1020, Santa Monica, California 90401 ("Licensee"). The effective date of this First Amendment is October 30, 2018 ("First Amendment Effective Date").

WHEREAS, Licensor and Licensee are parties to that certain Amended and Restated License Agreement entered into July 31, 2017 (the "Amended and Restated License Agreement");

WHEREAS, Section 12.15 of the Amended and Restated License Agreement sets forth certain diligence obligations, including Licensee's obligation to submit an investigational new drug application ("IND Application") to the FDA for a Licensed Product within [**] of the Original Effective Date, i.e., by [**]; and

WHEREAS, Licensor has determined that Licensee has been diligent in its efforts to submit an IND Application to the FDA for a Licensed Product, and whereas Licensee has informed Licensor that Licensee intends to submit an IND Application to the FDA for a Licensed Product in [**];

NOW, THEREFORE, in consideration of the mutual covenants contained in the Amended and Restated License Agreement and in this First Amendment and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, Licensor and Licensee hereby agree as follows:

1. Section 12.15(b) of the Amended and Restated License Agreement is hereby amended to read as follows:

    (b) Submit an investigational new drug application to the FDA for a Licensed Product by [**]; and

2. Except as expressly amended hereby, all terms and conditions of the Amended and Restated License Agreement shall remain unchanged and in full force and effect. In the event of any conflict between the terms of this First Amendment and the terms of the Amended and Restated License Agreement, the terms of this First Amendment shall govern. The amendments made herein shall be effective as of the First Amendment Effective Date. All capitalized terms used in this First Amendment that are not otherwise defined herein shall have the same meanings as such terms are given in the Amended and Restated License Agreement. This First Amendment may be executed in any number of counterparts, each of which shall be an original and all of which together shall constitute one and the same document. The Amended and Restated

License Agreement shall, together with this First Amendment, be read and construed as a single instrument.

IN WITNESS WHEREOF, the Parties hereto have executed this First Amendment as of the First Amendment Effective Date.

ALBERT EINSTEIN COLLEGE OF MEDICINE, INC.

By: /s/ Janis Paradiso

Name: Janis Paradiso, MBA

Title: Director, Office of Biotechnology & Business Development

CUE BIOPHARMA INC.

By: /s/ Colin G. Sandercock

Name: Colin G. Sandercock

Title: Sr. VP and General Counsel

EXHIBIT 21

SUBSIDIARIES OF CUE BIOPHARMA, INC.

Registrant's consolidated subsidiaries are shown below, together with the state or jurisdiction of organization of each subsidiary and the percentage of voting securities that Registrant owns in each subsidiary.

Name of Subsidiary	Jurisdiction of Incorporation or Organization	Percent of Outstanding Voting Securities Owned
Cue Biopharma Securities Corp.	Massachusetts	100%

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statements (Nos. 333-229140 and 333-23957) on Form S-3 and Registration Statements (Nos. 333-224018, 333-230282 and 333-237140) on Form S-8 of Cue Biopharma, Inc. of our report dated March 9, 2021, relating to the consolidated financial statements of Cue Biopharma, Inc. and Subsidiary appearing in this Annual Report on Form 10-K of Cue Biopharma, Inc. for the year ended December 31, 2020.

/s/ RSM US LLP

Boston, Massachusetts
March 9, 2021

EXHIBIT 31.1

CERTIFICATION OF THE PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Daniel R. Passeri, certify that:

1. I have reviewed this Annual Report on Form 10-K of Cue Biopharma, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 9, 2021

/s/ Daniel R. Passeri
Name: Daniel R. Passeri
Title: Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION OF THE PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Kerri-Ann Millar, certify that:

1. I have reviewed this Annual Report on Form 10-K of Cue Biopharma, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 9, 2021

/s/ Kerri-Ann Millar
Name: Kerri-Ann Millar
Title: Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

EXHIBIT 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Cue Biopharma, Inc. (the "Company") for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), we, Daniel R. Passeri, Chief Executive Officer of the Company, and Kerri-Ann Millar, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, to our knowledge that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

A signed original of this written statement required by Section 906 has been provided to Cue Biopharma, Inc. and will be retained by Cue Biopharma, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

/s/ Daniel R. Passeri
Name: Daniel R. Passeri
Title: Chief Executive Officer
(Principal Executive Officer)

Date: March 9, 2021

/s/ Kerri-Ann Millar
Name: Kerri-Ann Millar
Title: Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Date: March 9, 2021