UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

OR

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

Commission File Number: 001-39856

CULLINAN ONCOLOGY, INC.
(Exact name of Registrant as specified in its Charter)

Delaware	**81-3879991**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
One Main Street Suite 520 Cambridge, MA	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 410-4650

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	CGEM	The Nasdaq Global Select Market

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting stock held by non-affiliates of the Registrant as of June 30, 2021 was $717,444,028 based on the closing price of the Registrant's shares of common stock on the Nasdaq Global Select Market on such date.

The number of shares of the Registrant's common stock outstanding as of March 1, 2022 was 44,608,613.

DOCUMENTS INCORPORATED BY REFERENCE

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

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements involve risks, uncertainties, and other factors that may cause actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. All statements, other than statements of historical facts, 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 and expected market growth are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- the success, cost and timing of our clinical development of our product candidates, including CLN-081, CLN-049 and CLN-619;
- the initiation, timing, progress, results and cost of our research and development programs and our current and future preclinical and clinical studies, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs;
- our ability to initiate, recruit and enroll patients in and conduct our clinical trials at the pace that we project;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations or warnings in the label of any of our product candidates, if approved;
- our ability to compete with companies currently marketing or engaged in the development of treatments that our product candidates are designed to target;
- our reliance on third parties to conduct our clinical trials and to manufacture drug substance for use in our clinical trials;
- the size and growth potential of the markets for oncology diseases and any of our current product candidates or other product candidates we may identify and pursue, and our ability to serve those markets;
- our ability to identify and advance through clinical development any additional product candidates;
- the commercialization of our current product candidates and any other product candidates we may identify and pursue, if approved, including our ability to successfully build a specialty sales force and commercial infrastructure to market our current product candidates and any other product candidates we may identify and pursue;
- the expected benefits of our hub-and-spoke business model, including our ability to identify research priorities and apply a risk-mitigated strategy to efficiently discover and develop product candidates;
- our ability to retain and recruit key personnel;
- our ability to obtain and maintain adequate intellectual property rights;
- our expectations regarding government and third-party payor coverage and reimbursement;
- our estimates of our expenses, ongoing losses, capital requirements and our needs for or ability to obtain additional financing;
- the potential benefits of strategic collaboration agreements, our ability to enter into strategic collaborations or arrangements, and our ability to attract collaborators with development, regulatory and commercialization expertise;
- our financial performance;
- developments and projections relating to our competitors or our industry;
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and future clinical trials; and
- other risks and uncertainties, including those listed under the section titled "Risk Factors."

You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under “Risk Factors” and elsewhere in this Annual Report on Form 10-K. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. Moreover, we operate in a very competitive and rapidly changing environment and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in or implied by any forward-looking statements we may make. No forward-looking statement is a guarantee of future performance.

You should read this Annual Report on Form 10-K and the documents that we reference herein and have filed or incorporated by reference as exhibits hereto completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this Annual Report on Form 10-K, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled “Risk Factors” and elsewhere in this Annual Report on Form 10-K.

Summary of the Material and Other Risks Associated with Our Business

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

- We are early in our development efforts and are substantially dependent on our lead product candidates, CLN-081, CLN-049 and CLN-619. If we are unable to advance these or any of our other product candidates through clinical development, or to obtain regulatory approval and ultimately commercialize any such product candidates, either by ourselves or with or by third parties or if we experience significant delays in doing so, our business will be materially harmed.
- Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates, and ultimately delay or prevent regulatory approval.
- Interim, "topline" and preliminary data from our clinical trials that we announce or publish may change as more patient data become available and are subject to confirmation, audit and verification procedures that could result in material changes in the final data.
- Our product candidates may cause undesirable side effects or have other properties that delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We have incurred significant losses since inception and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.
- We will require substantial additional funding to develop and commercialize our product candidates and identify and invest in new product candidates. If we are unable to raise capital when needed, we would be compelled to delay, reduce or eliminate our product development programs or other operations.
- We may not be successful in our efforts to use our differentiated hub-and-spoke business model to build a pipeline of product candidates with commercial value.
- Our subsidiaries are party to certain agreements that provide our licensors, collaborators or other shareholders in our subsidiaries with rights that could delay or impact the potential sale of our subsidiaries or could impact the ability of our subsidiaries to sell assets, or enter into strategic alliances, collaborations or licensing arrangements with other third parties.
- Our ability to realize value from our subsidiaries may be impacted if we reduce our ownership to a minority interest or otherwise cede control to other investors through contractual agreements or otherwise.
- A single or limited number of subsidiaries may comprise a large proportion of our value.
- Our reliance on a central team consisting of a limited number of employees presents operational challenges that may adversely affect our business.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- If we are unable to obtain and maintain patent and other intellectual property protection for our current and future product candidates and technology, or if the scope of intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize CLN-081, CLN-049 and CLN-619, or any other product candidates or technology may be adversely affected.
- We currently rely and expect to continue to rely on the outsourcing of the majority of our development functions to third parties to conduct our preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.
- COVID-19 has and may continue to adversely impact our business, including our preclinical studies and clinical trials and our ability to source drug supply.

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

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company focused on developing a diversified pipeline of targeted therapeutic candidates across multiple modalities in order to bring important medicines to cancer patients. Our strategy is to source innovation through both internal discovery efforts and external collaborations, focusing on advanced stage assets with novel technology platforms and differentiated mechanisms. Before we advance a product candidate into clinical development, we evaluate its potential for anti-tumor activity as a single agent as well as its ability to generate an immune system response or to inhibit oncogenic drivers. Using this strategy, we have efficiently developed or in-licensed a portfolio of product candidates that currently includes eight distinct programs.

Our pipeline currently includes three clinical-stage candidates and five preclinical programs. We are evaluating our lead candidate, CLN-081, in a Phase 1/2a trial in patients with non-small cell lung cancer, or NSCLC, harboring epidermal growth factor receptor, or EGFR, exon 20 insertion mutations who have previously received platinum-based chemotherapy. In December 2021, we presented efficacy and safety data from this trial that we believe supports CLN-081's differentiated clinical profile. In January 2022, we announced that the U.S. Food and Drug Administration, or the FDA, granted CLN-081 Breakthrough Therapy Designation, or BTD. Our two other clinical stage programs include CLN-049, a bispecific T cell-engaging antibody targeting FLT3 and CD3 that is in an ongoing clinical trial for patients with relapsed or refractory acute myeloid leukemia, or r/r AML; and CLN-619, a monoclonal antibody that stabilizes a unique tumor cell surface target, MICA/MICB, to promote an antitumor response via activation of both natural killer (NK) cells and certain T cells. CLN-619 is in an ongoing clinical trial for patients with advanced solid tumors. Both CLN-049 and CLN-619 demonstrated compelling antitumor activity preclinically in multiple in vivo models and we believe that both programs have first-in-class potential. Our preclinical pipeline includes two programs in investigational new drug application, or IND, enabling studies, CLN-617 and CLN-978, and three programs in research.

In order to advance and grow our portfolio, we adhere to our Cullinan Oncology approach, which is guided by the following core elements:

- Platform technology diversification to mitigate overall risk and maximize optionality
- Capital allocation strategy based on risk-adjusted potential, including staged funding to pre-specified scientific and clinical results
- Internal development capabilities complemented by external business development
- Disciplined asset evaluation and selection with emphasis on structural and mechanistic differentiation; and
- Focus on translational medicine and product candidates with in vivo single agent activity.

Our Pipeline

Our pipeline includes oncology product candidates and programs that are intentionally diversified by mechanism, technology platform, modality and stage of development. We rigorously assess each of our programs to justify continued investment and determine proper capital allocation. When certain programs do not meet our de-risking criteria for advancement, we terminate those programs and preserve our capital and resources to invest in programs with greater potential. As a result, our pipeline will continue to be dynamic.

We believe that each program candidate has differentiating design features or mechanisms of action, as well as first- and/or best-in-class potential. We currently hold worldwide development and commercialization rights to each of our product candidates, except for CLN-081, where Japan and Greater China rights have been partnered. Our current pipeline is summarized in the diagram below:

Our Strategy

We are advancing a broad and deep pipeline of targeted oncology product candidates, including multiple clinical stage programs, that span a range of cancer indications and diverse technology platforms. Our focused approach is to select and advance molecules with first- and/or best-in-class potential that activate the immune system or target key oncogenic drivers and have the promise of single agent efficacy. The key elements of our strategy are to:

- **Build a pipeline of differentiated oncology product candidates that are diversified by mechanism, therapeutic approach, modality and stage of development.** We seek to mitigate risk by maintaining a diversified portfolio of uncorrelated product candidates and programs, and by intentionally carrying a portfolio mix such that some programs are directed toward novel targets, while others focus on more validated pathways. For the latter programs, we seek drug candidates with mechanisms or formats that we believe will be responsible for differentiating tolerability, ease of administration, efficacy or a combination thereof. Importantly, before we advance a product candidate into clinical development, we evaluate its ability to generate an immune system response or to inhibit oncogenic drivers as a single agent in vivo.
- **Expand our pipeline through research collaborations, business development, and internally designed programs.** Our founders and management team are leaders in oncology drug discovery, clinical development and business development and commercial operations. Their proven track records and longstanding relationships in the life sciences industry provide us with access to ideas and assets from around the world. In addition, their experiences and deep understanding of molecular oncology and cancer immunotherapy also enable us to translate novel concepts into internally designed product candidates. We are actively evaluating external collaboration and in-licensing opportunities as well as internal development opportunities to continue to expand our pipeline.

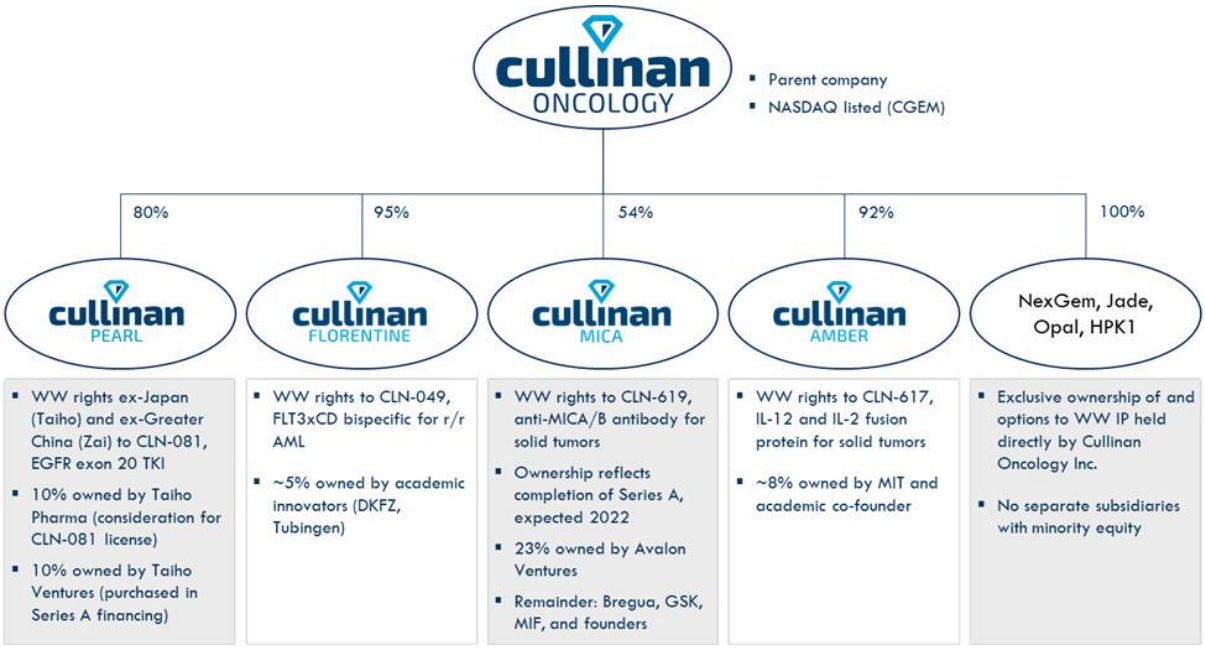
- **Advance our lead product candidate, CLN-081, toward potential regulatory approval for the targeted treatment of NSCLC patients with EGFRex20ins mutations.** As of December 2021, we had enrolled 73 patients across five dosing levels in our ongoing Phase 1/2a trial. We intend to leverage CLN-081's BTD to support our ongoing discussions with the FDA and to provide a CLN-081 regulatory update by the end of the first quarter of 2022.
- **Establish clinical proof-of-concept for CLN-049 and CLN-619 in patients with hematological malignancies and solid tumors, respectively.** Both CLN-049 and CLN-619 have strong potential for clinical differentiation. CLN-049's target, FLT3, is expressed frequently on AML cells and leukemic blasts but minimally on healthy blood cells, which differentiates FLT3 from other tumor surface antigens identified in AML, such as CD33 and CD123. Furthermore, by targeting extracellular FLT3, regardless of mutant or wild type status, we believe CLN-049 has the potential to reach a broader patient population than existing small molecule FLT3 kinase inhibitors acting on the intracellular domain, which are limited to a subset of approximately 25% of AML patients with FLT3 mutations. CLN-619's target, MICA/B, is expressed by a broad range of tumor types across both solid tumors and hematological malignancies. Furthermore, the MICA/B receptor, NKG2D, is expressed in both innate and adaptive effector cell populations. Finally, CLN-619 facilitates an antitumor immune response through multiple modes of action, including inhibition of MICA/B shedding, ADCC mediation, enhancement of NKG2D receptor binding, and prevention of decoy NKG2D by shed MICA/B. We intend to provide a clinical update on both programs by mid 2023.
- **Continue to advance and evolve our pipeline with a goal of advancing one product candidate into the clinic and one program into IND-enabling studies each year.** In addition to our three clinical stage product candidates, we have five additional preclinical programs that are designed with the goal of addressing limitations of approved oncology therapies. For example, we believe CLN-617 is the only single agent immunotherapy in development combining IL-2 and IL-12 with a collagen-binding domain to enhance retention of cytokines within the tumor microenvironment. Another of our research programs, CLN-978, is a half-life extended, humanized, single-chain T cell engaging antibody that we believe has the potential to improve on some of the shortcomings of the approved CD3/CD19 bispecific T cell engager, blinatumomab, and to compete with CD19-targeted CAR-T cell therapies. We expect to submit INDs for CLN-617 and CLN-978 by the end of the first half of 2023.
- **Evaluate strategic opportunities to accelerate development timelines and maximize the value of our portfolio.** We intend to maximize the value for each of our programs by opportunistically leveraging the existing infrastructure of other companies or internally pursuing later-stages of development and commercialization. Our subsidiaries hold the worldwide rights to our product candidates, except for CLN-081. Our licensor, Taiho Pharmaceutical Co., Ltd., or Taiho Pharma, retains rights in Japan and we sublicensed Greater China rights to Zai Lab (Shanghai) Co., Ltd., or Zai Lab. Our business model provides us with the flexibility to efficiently pursue various types of transactions and collaborations with third parties at the subsidiary level. It also enables us to preserve resources for continued internal investment upon successful achievements of development milestones. We have made and will continue to make decisions regarding each of our subsidiaries and programs with the overarching aim of maximizing both patient benefit and shareholder value.

Our Structure

We have historically established distinct subsidiaries for externally sourced programs to execute our strategy of building a diversified oncology company in a capital efficient manner. Our holding company, Cullinan Oncology, Inc., or Cullinan, provides all capital, human resources, and other services to each subsidiary via a shared services agreement. Each subsidiary holds the exclusive rights to intellectual property, or IP, for any of our product candidates and programs that was sourced externally. This structure enables us to keep licensors economically incentivized at the program level through our ability to offer equity and access to potential cash milestones and royalty payments. Further, because each subsidiary is a separate legal entity that holds all of the assets related to the development candidate, including the relevant intellectual property, and has no employees, fixed assets, or overhead costs, we have flexibility both to raise capital at either the parent or subsidiary level and to pursue subsidiary-level licenses or stock sales.

In the figure below, we have listed each subsidiary's product candidate as well as any relevant licensors or shareholders. Cullinan's ownership, as of December 31, 2021, as a percentage of fully-diluted shares outstanding is listed below
.

Our Structure



Note: The Company owned 45% of Cullinan MICA as of December 31, 2021.

The structure of our financing arrangements with each subsidiary enables us to increase our economic ownership when we provide additional capital. Further information about our subsidiaries, including ownership and governance, is included in the "Management's Discussion and Analysis" section of this Annual Report.

Our structure was designed to (i) enhance operational efficiency, (ii) maintain an optimal cost structure, (iii) attract leading collaborators and licensors and (iv) promote asset flexibility, as further described below.

- **Enhance operational efficiency**: We centralize all employees and services at our holding company and allocate resources to subsidiaries as needed. We empower managers to access these resources and make program-level decisions in order to increase productivity and speed. We believe this model enables a flexible organizational structure that can achieve scale through the addition of programs without increasing burdensome bureaucracy or redundant infrastructure.

- **Maintain an optimal cost structure**: We have a relatively small number of employees and have built a network of trusted external service providers, choosing to leverage their infrastructure and expertise as needed instead of embarking on capital-intensive lab, manufacturing and equipment expenditures. As of December 31, 2021, we had 31 full time employees and three consultants working on eight active programs. By reducing overhead costs, we believe we can increase the likelihood that we can generate a return on invested capital.

- **Attract leading collaborators and licensors**: Each of our subsidiaries has its own capitalization and governance, enabling us to keep collaborators and licensors economically incentivized at the program level. We believe that the experienced leadership team and shared services at our holding company differentiate us from other potential licensees.

- **Promote asset flexibility**: Each subsidiary holds the relevant intellectual property of its product candidates or programs and has none of its own employees, fixed assets, or overhead costs. This allows us to efficiently pursue various subsidiary-level transactions, such as stock or asset sales, licensing transactions, strategic partnerships, co-development arrangements, or spin-outs. It also provides us with the flexibility to terminate programs with minimal costs if results do not meet our de-risking criteria for advancement.

Our Programs

CLN-081

Our lead product candidate, CLN-081, is an orally available small molecule designed as a next generation, irreversible EGFR inhibitor in development for the treatment of NSCLC patients harboring EGFR exon 20 insertion mutations. In January 2022, we announced that the FDA granted Breakthrough Therapy Designation to CLN-081. The molecule was designed with a unique chemical scaffold to bind to the active site exon 20 insertion mutant EGFR, inhibiting mutant activity while sparing wild type EGFR activity. In preclinical studies, CLN-081 demonstrated high selectivity for cells with EGFR exon 20 insertion mutations, while relatively sparing cells expressing wild type EGFR. CLN-081 displayed potent antitumor activity in in vitro and in vivo models of exon 20 insertion mutant EGFR NSCLC.

We licensed worldwide rights, excluding Japan, to CLN-081 from Taiho Pharma in 2018 and initiated a Phase 1/2a dose escalation and expansion trial in previously treated, adult NSCLC patients with EGFRex20ins mutations. In December 2021, we provided a clinical update that included safety and efficacy data from 73 evaluable patients enrolled across five dose levels, ranging from 30 to 150mg BID. At the 100mg BID dose, we observed the following efficacy highlights:

- 14 of 36 (39%) response evaluable patients achieved a confirmed partial response.
- 35 of 36 (97%) response evaluable patients achieved a best response of partial response or stable disease.
- The estimated median duration of response was greater than 15 months and an estimated median progression free survival that was 12 months in the initial cohort of phase 1 patients (n=13); follow-up is ongoing for the patients enrolled in the Phase 2a cohort (n=23).

We also observed a favorable safety and tolerability profile at the 100mg BID dose level, as evidenced by the lack of Grade 3 or greater treatment-related adverse events, or TRAEs, of rash or diarrhea, which are associated with EGFR TKIs therapies. EGFR-associated TRAEs have been manageable with conventional supportive care, and the implementation of systematic GI prophylaxis has not been required. As seen with other EGFR TKIs, a case of Grade 3 treatment-related pneumonitis has been observed at the 100mg BID dose, although the patient had recently undergone treatment with checkpoint inhibitor therapy and had a concurrent presence of a significant hydropneumothorax, not related to treatment, in the contralateral lung. We believe that the totality of CLN-081's data at the 100mg BID dose reflects its differentiated clinical profile.

We sublicensed CLN-081 development rights in Greater China to Zai Lab in exchange for an upfront fee, milestones and royalties. The licensing agreement provided Zai Lab with an exclusive license to research, develop, commercialize and manufacture CLN-081 and products which contain CLN-081 in Greater China. See the section of this Annual Report titled "Business - License Agreements — Zai License Agreement" for more information.

Background on NSCLC and EGFR mutations

Lung cancer is by far the leading cause of cancer deaths among both men and women, comprising almost 25% of all cancer deaths. Each year, more people die of lung cancer than of colon, breast, and prostate cancers combined. The American Cancer Society estimated that, in 2022, there will be approximately 236,740 new cases of lung cancer and approximately 130,180 deaths from lung cancer in the United States. The most common subtype of lung cancer is NSCLC, which represents approximately 80% to 85% of all lung cancers.

EGFR is a receptor tyrosine kinase, or RTK, that normally functions to trigger cell division when growth factors bind to the receptor. Oncogenic mutations in the tyrosine kinase domain can induce growth factor independent activation of EGFR, resulting in uncontrolled cell growth and proliferation. Ultimately, these aberrant signals can contribute to the development of NSCLC. EGFR mutations are present in approximately 15% to 25% of U.S. and Western European NSCLC patients and approximately 30% to 50% of Asian NSCLC patients. Given its important role and prevalence in cancer, mutant EGFR is a critical target in lung cancer therapy. Exon 19 deletion and exon 21 L858R substitution mutations, collectively referred to as classical EGFR mutations, are the most common and account for over 75% of EGFR mutations in NSCLC. Multiple EGFR inhibitors, including gefitinib, erlotinib, afatinib, and osimertinib, target these common mutations and have been approved as first-line therapies, thus validating mutant EGFR as a target for the treatment of NSCLC.

Exon 20 insertions, which account for 7% to 13% of all EGFR mutations in NSCLC patients, are the most prevalent after the classical EGFR mutations. We estimate an incidence of approximately 2,000 to 5,000 NSCLC patients in the U.S. and approximately 1,000 to 3,000 patients in France, Germany, Italy, Spain, and the United Kingdom with EGFRex20ins mutations. Preclinical studies have shown that exon 20 insertions, as well as classical EGFR mutations, have the characteristics of oncogenic driver mutations, which are responsible for both tumorigenesis and the progression of cancer. However, in contrast to classical EGFR mutations, exon 20 insertions do not sensitize the kinase domain to treatment with approved EGFR inhibitors.

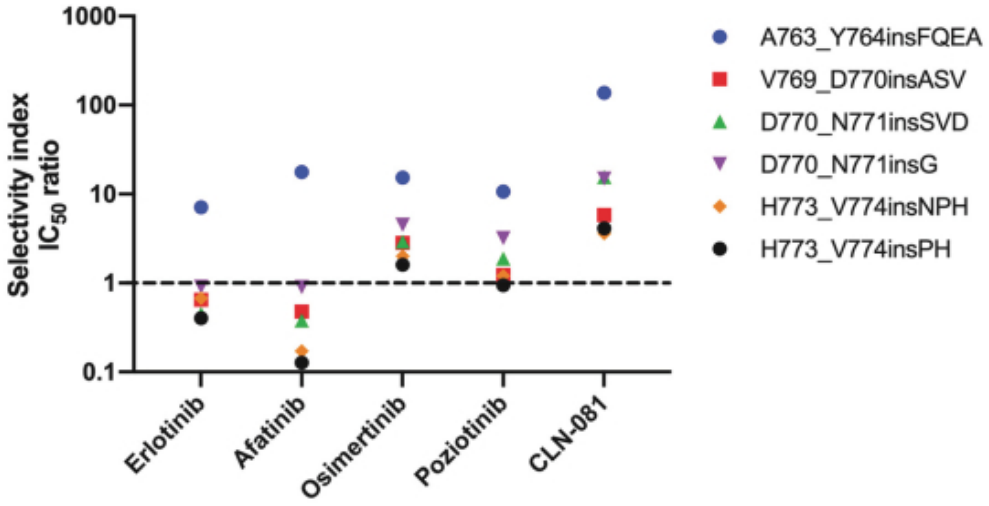
Currently, there are two targeted therapies with accelerated approval for NSCLC patients with EGFRex20ins mutations whose disease has progressed on or after platinum-based chemotherapy: amivantamab-vmjw (Rybrevant) and mobocertinib (Exkivity). Despite these accelerated approvals, we believe significant unmet need remains for NSCLC patients with EGFRex20ins mutations. Specifically, we believe there is an opportunity for an oral therapy with strong selectivity for mutant vs. wild type EGFR, which could potentially lead to an improved safety and tolerability profile, especially with respect to treatment related adverse events such as rash, diarrhea, and infusion site reactions, as well as cardiovascular events.

CLN-081

CLN-081 is a small molecule that was designed as an irreversible EGFR inhibitor with a novel pyrrolopyrimidine scaffold, which is unique among the therapies in development that are targeting EGFRex20ins mutations. CLN-081 is designed to fit into the ATP-binding site of EGFR where it covalently modifies C797, thereby forming a durable drug-protein linkage that irreversibly inhibits the mutant receptor. In preclinical studies, CLN-081 demonstrated high selectivity and inhibition of EGFR in cells expressing mutant EGFR proteins, with substantially less inhibition in cells expressing wild type EGFR.

The selectivity index of CLN-081 versus competing EGFR inhibitors was evaluated in vitro as measured by the ratio of the half-maximal growth inhibition, or IC50, value of cells expressing wild type EGFR versus cells expressing exon 20 insertion mutant EGFR. As shown below, CLN-081 demonstrated the highest selectivity index among a panel of EGFR targeted therapies, suggesting that CLN-081 may be capable of achieving clinically relevant inhibition of EGFR with exon 20 insertion mutations with relative sparing of wild type EGFR.

CLN-081 Demonstrated Superior Selectivity
Across Multiple EGFRex20ins Mutations

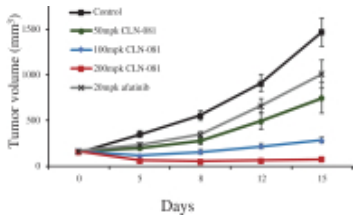


Preclinical Data

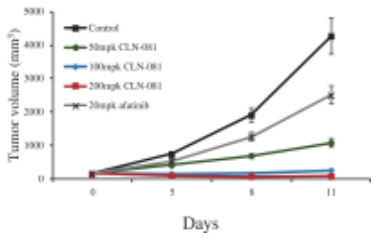
Multiple preclinical studies, including IND-enabling studies, of CLN-081 have been completed, which supported the submission and acceptance of our IND by the FDA in the second quarter of 2019. *In vivo* activity of CLN-081 was evaluated in multiple EGFRex20ins mutation-driven tumor models, including three of the most common insertion mutations as shown in the figure below. In all three mouse models, doses of 200 milligrams per kilogram, or mpk, of CLN-081 achieved persistent tumor regression with no body weight loss over five percent. In comparison, 20mpk of afatinib induced only modest tumor growth inhibition in these models. The results of these common insertion mutation models are summarized below.

Tumor Reduction Observed in Mice With CLN-081 Treatment vs. Afatinib or Vehicle in Multiple EGFRex20ins Mutant NSCLC Models

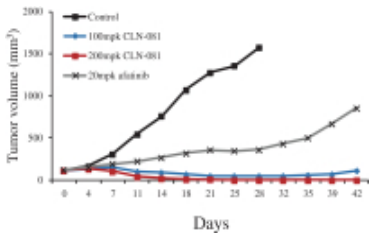
NCI-H1975 xenograft (EGFR D770 N771insSVD)



NIH/3T3 allografts (EGFR H773 V774insNPH)



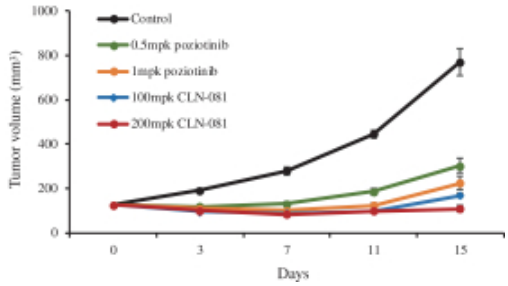
Lung cancer PDX (EGFR V769 D770insASV)



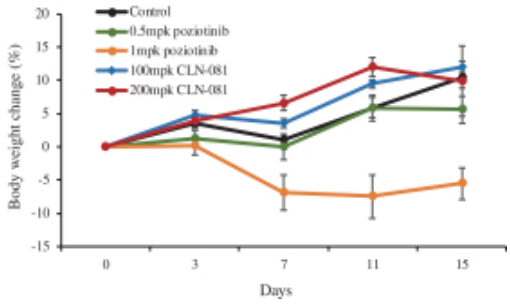
In another preclinical study, the antitumor activity and impact on body weight of CLN-081 was compared to that of poziotinib, which, at the time, was the most advanced EGFRex20ins inhibitor in clinical development. Antitumor activity and body weight change were measured in mice bearing a xenografts tumor as shown below. Comparable tumor growth suppression was observed in the mice treated with 1mpk of poziotinib as those treated with 100mpk of CLN-081. Notably, poziotinib treatment led to body weight loss in all mice. In contrast, mice treated with CLN-081 with doses up to 200mpk showed no significant body weight loss. We believe these results illustrate the potential selectivity and potential therapeutic window for CLN-081.

CLN-081 Inhibited Tumor Growth and Avoided Weight Loss in NSCLC with EGFRex20ins Mutations

NCI-H1975 xenograft (EGFR D770 N771insSVD)



Corresponding body-weight change in mice



Clinical Development

We initiated our ongoing Phase 1/2a trial of CLN-081 in the fourth quarter of 2019. This first-in-human, open-label, multi-center trial is designed to evaluate the safety and tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of CLN-081 in adult NSCLC patients with EGFRex20ins mutations. The trial included two major components: dose escalation and cohort expansion. Dose escalation began with a single patient accelerated titration design, and transitioned to 3+3 decision rules upon the first occurrence of a Grade 2 or greater TRAE, which occurred at the 100 mg BID dose level. This trial had a flexible, adaptive design that allowed for further expansion of any given cohort at the discretion of the Sponsor gated by acceptable safety and pre-specified efficacy criteria. Cohorts could be expanded to 6, then 13, then 36 patients gated by these criteria. We expanded cohorts at the 65, 100, and the 150 mg BID dose levels, including enrollment up to the maximum of 36 patients at the 100 mg BID dose level which has been completed. Although we expanded enrollment at 150 mg BID dose level, we subsequently discontinued enrollment after 11 patients had been enrolled, based on assessment of the overall clinical profile at this dose level. We have enrolled patients across sites in the U.S., the Netherlands, Singapore, Hong Kong, and Taiwan, and we plan to initiate additional sites, including in China.

As of December 2021, 73 patients across five dose escalation cohorts, including cohorts at 30, 45, 65, 100, and 150 mg BID dose levels, received at least one dose of CLN-081. The patient population in our trial is heavily pre-treated, with a median of two prior systemic therapies and 66% of patients having received two or more prior therapies at study entry (i.e. 3rd line of therapy or greater). Further, 37% of patients have received prior treatment with an EGFR inhibitor, including 5% that have received prior treatment with poziotinib or Exkivity, that target Exon20ins mutations. Over half (53%) of the patients received prior treatment with a checkpoint inhibitor.

Safety and Pharmacokinetic Data

The following table provides a summary of treatment related safety and tolerability events, including rash and diarrhea, which are toxicities related to inhibition of WT EGFR, as well as laboratory abnormalities including anemia and transaminase elevations across the 100 mg and 150 mg BID dose levels for comparison, as well as the overall safety population in our ongoing Phase 1/2a trial. We believe that this safety and tolerability profile compares favorably to other EGFR exon 20 inhibitors, in particular with respect to the incidence and severity of diarrhea.

Dose (BID)	100 mg	150 mg	Overall
Safety Population (n, %)	**39**	**11**	**73**
Grade 1 TRAE of interest			
Skin Rash	**21 (54)**	**4 (36)**	**38 (52)**
Diarrhea	**10 (26)**	**1 (9)**	**14 (19)**
Elevated ALT / AST	**2 (5)**	**1 (9)**	**6 (8)**
Anemia	**3 (8)**	**--**	**5 (7)**
Grade 2 TRAE of interest			
Skin Rash	**7 (18)**	**1 (9)**	**14 (19)**
Diarrhea	**3 (8)**	**1 (9)**	**4 (5)**
Elevated ALT / AST	**2 (5)**	**--**	**2 (3)**
Anemia	**1 (3)**	**--**	**2 (3)**
Grade 3 TRAE of interest			
Skin Rash	**--**	**1 (9)**	**1 (1)**
Diarrhea	**--**	**2 (18)**	**2 (3)**
Elevated ALT / AST	**2 (5)**	**2 (18)**	**6 (8)**
Anemia	**1 (3)**	**2 (18)**	**5 (7)**
Treatment Related Dose Reduction	**5 (13)**	**3 (27)**	**10 (14)**
Treatment Related Dose Discontinuation	**1 (3)**	**2 (18)**	**5 (7)**

In the 39 safety evaluable patients who have been treated at the dose of 100 mg BID, no patients have experienced Grade 3 or greater treatment related rash or diarrhea. At this dose level, 72% and 34% of patients have experienced treatment-related rash and diarrhea, respectively, of either Grade 1 or 2 severity; however, the ratio of patients who experience Grade 1 versus Grade 2 events is approximately 3:1 for both rash and diarrhea. Both events have been manageable with conventional supportive care, and implementation of systematic GI prophylaxis has not been required for diarrhea management. As has been seen with other EGFR TKI, a case of G3 treatment-related pneumonitis has been observed at this dose, although the patient had recent treatment with checkpoint inhibitor therapy and the concurrent presence of a significant hydropneumothorax, not related to treatment, in the contralateral lung.

Key observations in 11 safety evaluable patients at the 150 mg BID dose level included treatment-related Grade 3 diarrhea in two patients, Grade 3 rash in one patient, and two patients with Grade 3 and Grade 4 transaminitis. In addition, one patient who was off treatment with CLN-081 for more than three weeks because of progressive disease was reported as having G3 treatment-related pneumonitis; the patient had a concurrent Pneumocystis jiroveci infection. In addition, an increase in rates of dose reduction and dose discontinuation were observed among patients treated at the 150 mg BID compared to the 100 mg BID dose level. These observations informed our decision to discontinue further enrollment of patients at 150 mg BID, after 11 patients.

Preliminary pharmacokinetic, or PK, data demonstrated a near dose-dependent trend in exposure, as measured by unbound area under the curve, or AUC, and Cmax values. Furthermore, the target unbound AUC required to achieve tumor regression in preclinical studies was reached starting at the initial dose of 30 mg BID. Notable features of the CLN-081 PK profile include sustained PK exposure over GI50 for EGFRex20ins mutations for eight hours post dose, limited interpatient heterogeneity and limited exposure above the GI50 for WT EGFR at doses at or below 100 mg BID. Consistent with the clinical safety profile at 100 mg BID dose compared with the 150 mg BID dose, at the 150mg BID dose, we observed CLN-081 concentrations above WT EGFR GI50 ratios for approximately four hours.

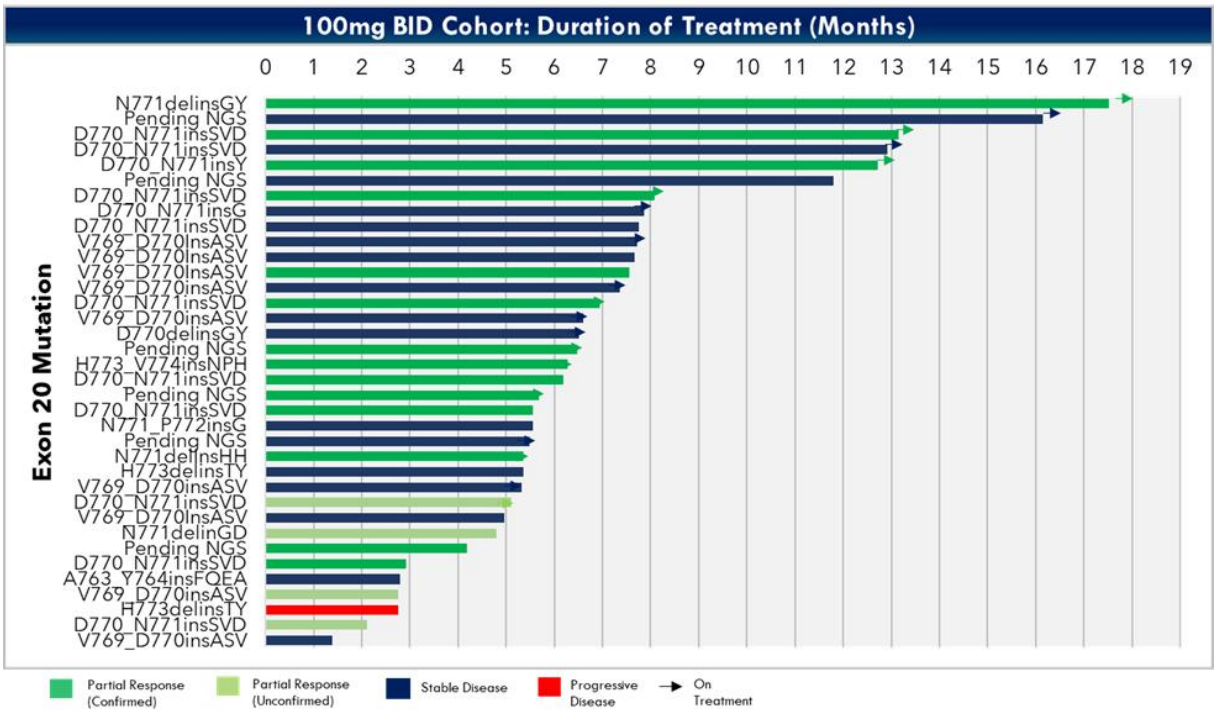
Efficacy Data

The following table summarizes best response characteristics for response-evaluable patients treated at the 100 mg BID (N=36) and 150 mg BID (N=11) BID dose levels as well as the overall population across dose levels in aggregate (N=70) as of a December 13, 2021 data cutoff. Among patients treated at 100 mg BID at the data cutoff, 14 patients achieved a confirmed response, indicating a 39% confirmed overall response rate (cORR). This cORR was higher than the 27% cORR among 11 patients at the 150mg BID dose cohort. At the 100mg BID dose cohort, 35 of 36 (97%) patients experienced a best response of stable disease or partial response, including confirmed or unconfirmed responses.

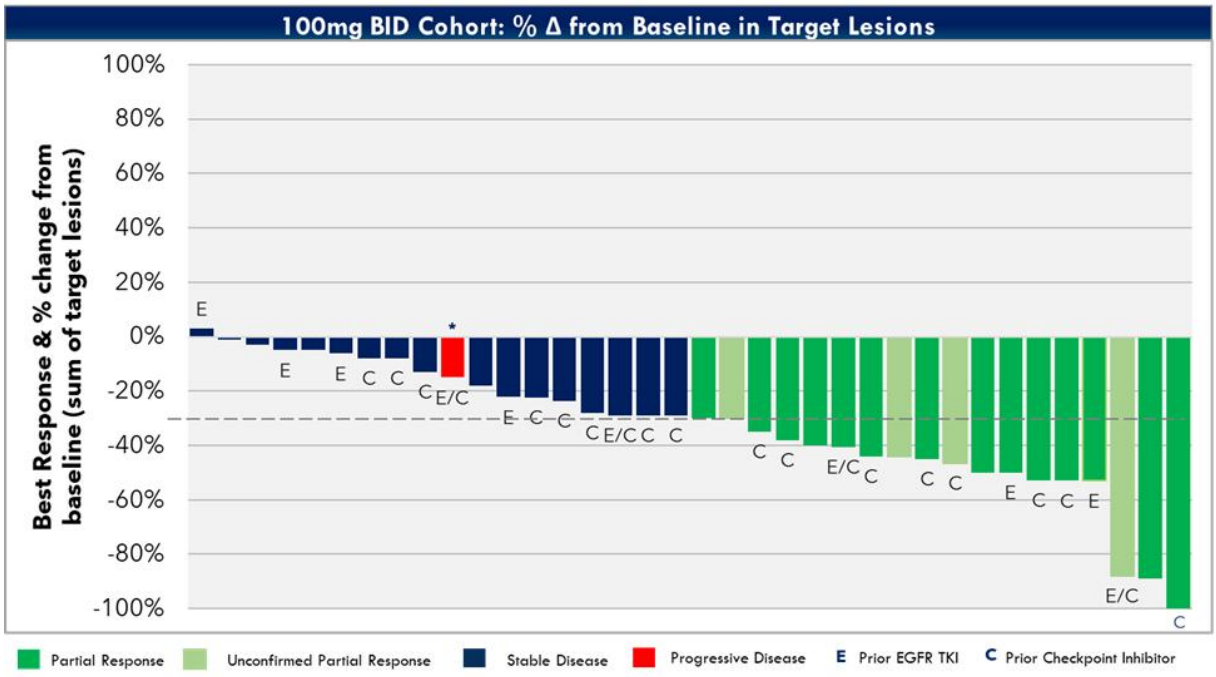
Response	100 mg BID (n=36)	150 mg BID (n=11)	Overall (n=70)
Best Response, n (%)			
PR (Confirmed)	14 (39)	3 (27)	25 (36)
PR (Pending)	1 (3)	--	1 (1)
PR (Unconfirmed)	3 (8)	2 (18)	7 (10)
Stable Disease (SD)	17 (47)	5 (45)	34 (49)
Progressive Disease (PD)	1 (3)	1 (9)	3 (4)

Below are additional efficacy analyses for the 36 patients treated at the 100mg BID dose cohort, including a swimmer's chart (A), a waterfall chart with percentage best change from baseline (B), and a spider plot with percentage change in target lesions over time (C). We have also included estimated response duration and progression free survival from patients treated in the Phase 1 cohort (n=13) at 100mg BID (D). Patients in the trial have their initial tumor imaging performed after approximately six weeks of treatment, and then every nine weeks thereafter. Based on these analyses, we believe that CLN-081 has shown substantial antitumor activity with broad EGFR exon 20 variant coverage; a rapid onset of action; and encouraging response quality as measured by duration of response and progression-free survival.

(A) Preliminary Efficacy Results from Ongoing Phase 1/2a Trial of CLN-081

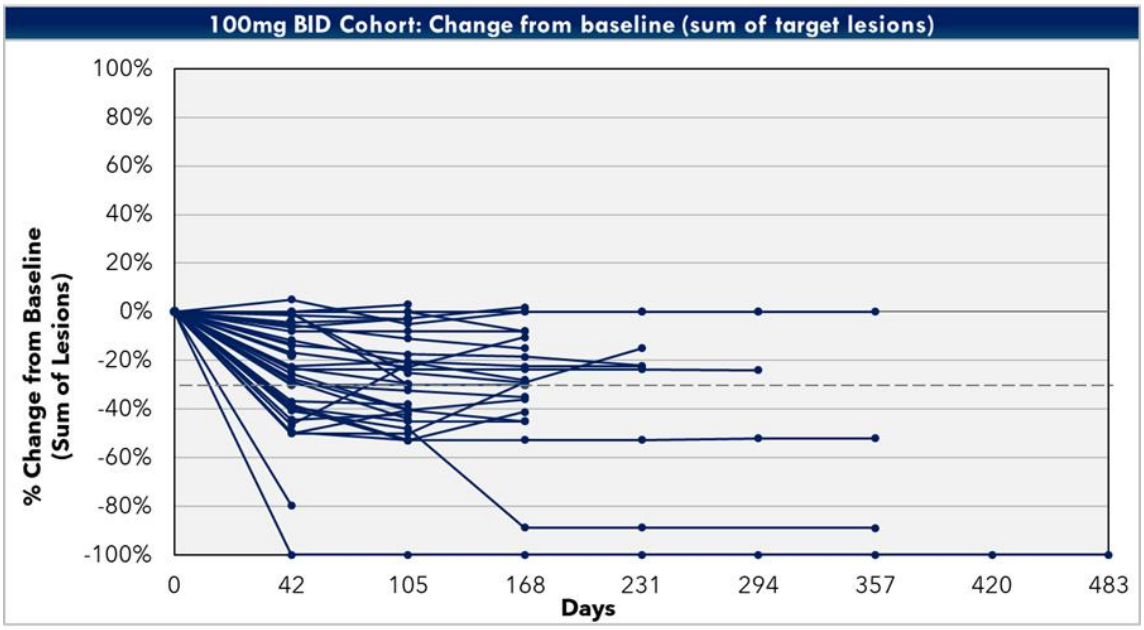


(B) Best Response % Change from Baseline (target lesion)



** Progressive disease due to progression of non-target lesions.*

(C) Percentage Change in Sum of Target Lesions from Baseline



(D) Estimated Median Duration of Response, Median Progression Free Survival, and Disease Control Rate from the Phase 1 100mg BID Cohort

Phase 1 Patients at 100 mg BID (n = 13)	
*Duration of Response, Median	>15 months
*Progression Free Survival, Median	12 months
**Disease Control Rate	92%

* Based upon Kaplan-Meier estimates
** Disease control rate (DCR): % of patients with stable disease ≥6 months or any PR

CLN-049

Our second clinical-stage oncology product candidate, CLN-049, is a humanized bispecific antibody that we are developing for the treatment of AML. We are currently evaluating CLN-049 in a clinical trial in adult patients with r/r AML. CLN-049 is designed to simultaneously bind to FLT3 on the extracellular domain of target leukemic cells and to CD3 on T cells, triggering the T cells to kill the target cancer cells. FLT3 is a validated proto-oncogene and several kinase inhibitors targeting mutant FLT3 are approved for the treatment of r/r AML, but are limited to approximately 25% of the AML population with FLT3 mutations. By targeting FLT3 on the extracellular domain, CLN-049 has the potential to address up to approximately 80% of AML patients. Preclinically, we have observed that CLN-049 led to highly potent FLT3-dependent killing of leukemic cells in vitro at a wide range of FLT3 expression levels on AML cells regardless of FLT3 mutational status. In preclinical studies, treatment with CLN-049, even at low doses, led to survival benefit in an AML xenograft model and complete elimination of leukemic blasts in mouse models implanted with AML cell lines or primary patient leukemic cells.

Background on Acute Myeloid Leukemia and FLT3

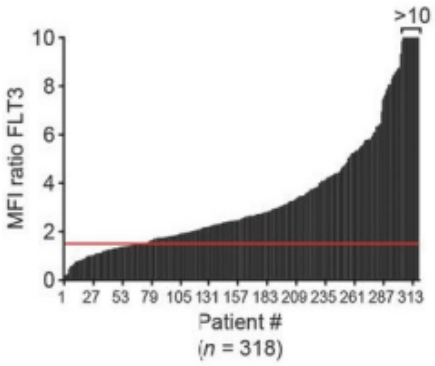
The American Cancer Society estimates that, in 2022, there will be approximately 20,000 newly diagnosed patients with AML and approximately 11,500 deaths from AML in the U.S. AML is a complex hematologic malignancy characterized by uncontrolled proliferation of malignant immature myeloid blast cell populations. These blasts may completely infiltrate and replace the bone marrow, resulting in major disruption of normal hematopoiesis and pancytopenia, very high numbers of circulating blasts in the peripheral blood, and infiltration of visceral organs as well as the skin. In addition, patients with AML may be susceptible to bleeding complications due to thrombocytopenia and experience complications from treatment with cytotoxic chemotherapy. These patients may also be severely immuno-compromised secondary to their disease and experience prolonged periods of neutropenia and lymphopenia. As a result, these patients are often susceptible to life-threatening infections that also contribute to severe morbidity and mortality.

Despite advancements in the treatment of AML, there continues to be a high unmet need in these patients. Eligible newly diagnosed patients are typically treated with intensive induction chemotherapy, which may include continuous infusion of cytarabine with an anthracycline, in an attempt to achieve a complete remission. The majority of patients that experience complete remission undergo hematopoietic stem cell transplantation, or HSCT. Despite aggressive first-line combination chemotherapy, the recent approvals of multiple targeted small molecules for molecularly defined AML patient subsets, and the use of HSCT in patients with a suitable matched donor, the prognosis of patients with AML remains extremely poor. Although 60% to 85% of younger adult patients achieve complete remissions, patients older than 60 years of age have inferior complete response rates of 40% to 60%. In addition, approximately 40% of all patients relapse following HSCT.

FLT3, or FMS-like tyrosine kinase 3, is a Class III RTK with a well-recognized and essential role in hematopoiesis. In healthy individuals, expression of FLT3 is restricted to a subpopulation of hematopoietic stem and progenitor cells, or HSPCs, inducing their proliferation and differentiation into monocytes, dendritic cells, B cells, and T cells. FLT3 has been identified as a proto-oncogene and plays a key role in promoting leukemic cell proliferation and survival. Several small molecule kinase inhibitors targeting FLT3 mutations are in development or have been approved for the treatment of AML. However, these product candidates and approved therapies only address approximately 25% of AML patients who have intracellular FLT3 genetic mutations but do not address the larger subset of patients with extracellular expression of FLT3 on the surface of cancer cells.

Studies have shown that FLT3 is expressed by FACS staining on AML blasts in approximately 80% of AML patients, regardless of an oncogenic driver mutation. In one study, leukemic bulk cells from 318 newly diagnosed or relapsed AML patients were evaluated for cell surface FLT3 protein expression, and 78% were found positive for FLT3, as shown in the figure below. This broad expression of FLT3 in AML patients suggests that targeting FLT3 with a biologic agent, namely a T cell engaging bispecific antibody that recruits T cells to kill tumor cells expressing FLT3 on the cell surface, could address a larger AML patient population than the targeted small molecule inhibitors targeting mutated version of the intracellular signaling domain of FLT3 that are approved or in development. Compared to other tumor surface antigens identified in AML, such as CD33 and CD123, FLT3 expression is generally restricted to a subpopulation of bone marrow HSPCs and circulating dendritic cells. FLT3 plays a key role in driving leukemogenesis and malignant progression of AML, promoting leukemic cell proliferation and survival. We believe that the expression of FLT3 on the surface of leukemic blasts in most AML patients and its role as a known oncogenic driver make it an attractive therapeutic target for a T cell engager approach.

Approximately 80% of AML Patients Show Positive Cell Surface FLT3 Protein Expression



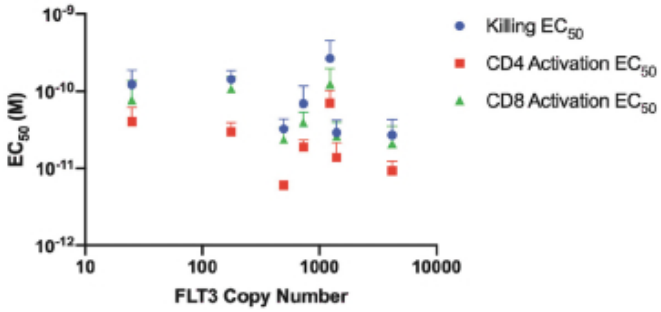
CLN-049

CLN-049 is a humanized bispecific antibody construct comprised of two FLT3-binding domains, an Fc-silenced humanized IgG1 backbone, and CD3-binding single-chain Fv domains, or scFvs, fused to the C-terminus of the antibody's heavy chain. In multiple preclinical studies, CLN-049 has demonstrated the ability to redirect T cells to lyse FLT3-expressing AML cells *in vitro* and potent antitumor activity *in vivo*. By targeting extracellular FLT3, regardless of mutant or wild type status, we believe CLN-049 has the potential to address up to approximately 80% of AML patients, a broader patient population than existing small molecule FLT3 kinase inhibitors acting on the intracellular domain, which are limited to a subset of approximately 25% of AML patients with FLT3 mutations.

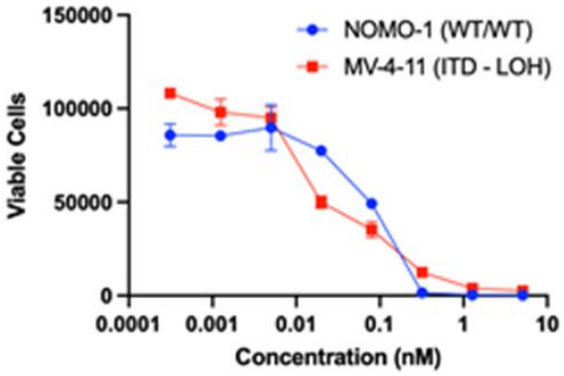
Preclinical Data

Given the observed variability in FLT3 expression levels among patients, we characterized the killing potential of CLN-049 across multiple cell lines expressing differing levels of FLT3 on the cell surface. As shown in the figures below, CLN-049 was observed to mediate robust target-dependent cell killing in vitro across all AML cell lines tested. Importantly, we observed that the EC50 value, i.e., the drug concentration at which 50% of target cells are killed, was in the sub-nM range and did not seem to be dependent on the number of FLT3 receptor molecules found on AML target cells. In particular, we observed potent target cell killing even when those cells expressed fewer than 100 copies of the FLT3 receptor per cell. We also observed potent redirected lysis of AML cell lines with WT or mutant FLT3 expression. Based on these results, we believe CLN-049 may effectively kill AML target cells with even low levels of FLT3 expression, regardless of WT or mutant origin, which could potentially translate into deeper and more durable responses in the clinic and may allow us to treat a larger subset of AML patients.

CLN-049 Demonstrated Killing of Target Cells Expressing a Range of FLT3, *in vitro*

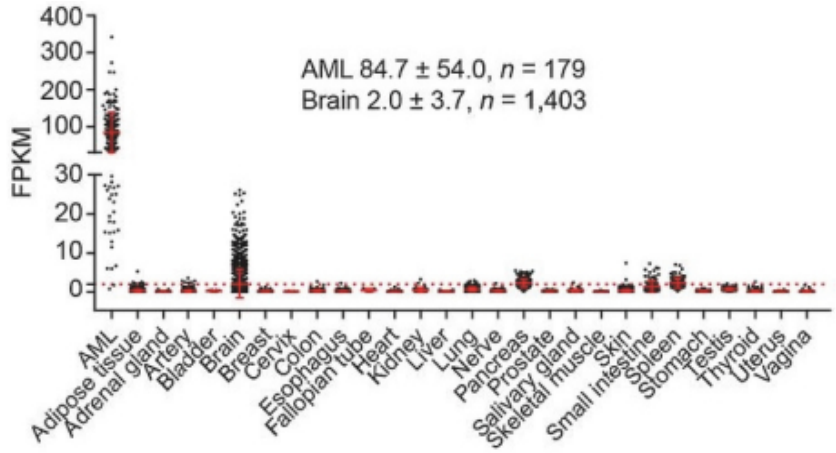


CLN-049 Demonstrated Killing of Target Cells Expressing WT and Mutant FLT3, *in vitro*



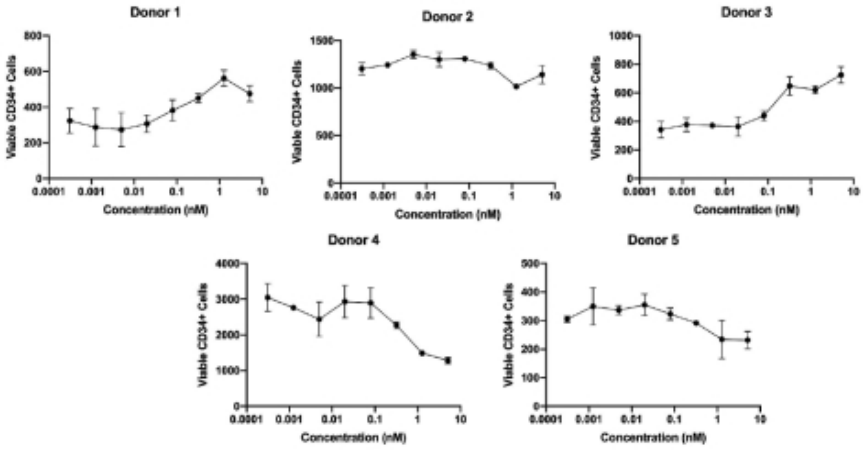
FLT3 is not widely expressed on normal immune cells, but rather is restricted to certain hematopoietic stem cell precursors in the bone marrow and dendritic cell subsets in the periphery. As shown in the figure below, a recent study found that the expression level of FLT3 transcript was significantly higher on AML cells compared to normal tissues.

FLT3 Transcript Level is Higher on AML Cells Than on Normal Human Solid Tissues



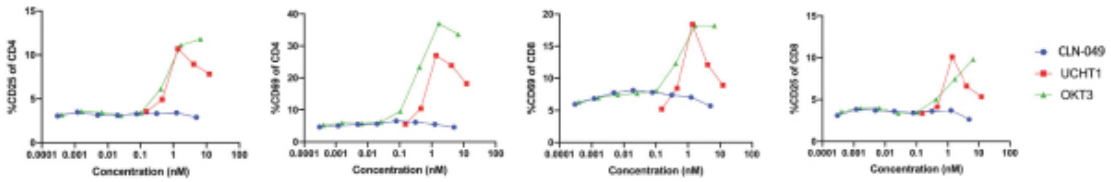
Importantly, we observed that CLN-049 treatment *in vitro* did not lead to a significant reduction in CD34+ bone marrow cells, as shown in the figure below, supporting our hypothesis that CLN-049 preferentially kills FLT3-expressing leukemic cells while sparing normal cells.

CLN-049 Treatment Did Not Result in Significant Killing of Normal CD34+ Bone Marrow Cells *In Vitro*



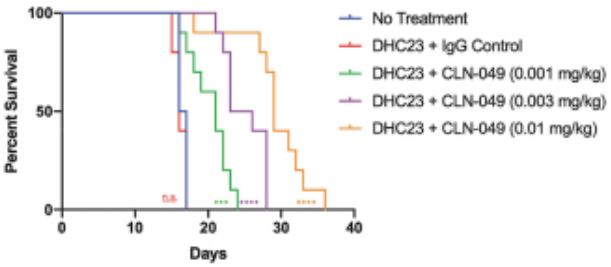
CLN-049 has two CD3-binding arms that can potentially crosslink CD3 on T cells, which may result in target cell-independent T cell activation and systemic cytokine-related toxicities. In preclinical studies, we examined whether CLN-049 can lead to spurious T cell activation in the absence of target cells. As shown below, incubation of purified human T cells with CLN-049 in the absence of target-expressing cells did not induce T cell activation markers CD25 and CD69 on either CD4+ or CD8+ T cells as opposed to positive control anti-CD3 antibodies OKT3 and UCHT1 (CLN-049 parental anti-CD3 antibody) that induced T cell activation.

CLN-049 Did Not Trigger the Upregulation of Activation Marker CD69 On Purified Human CD4+ or CD8+ T Cells in the Absence of FLT3 Expressing Target Cells



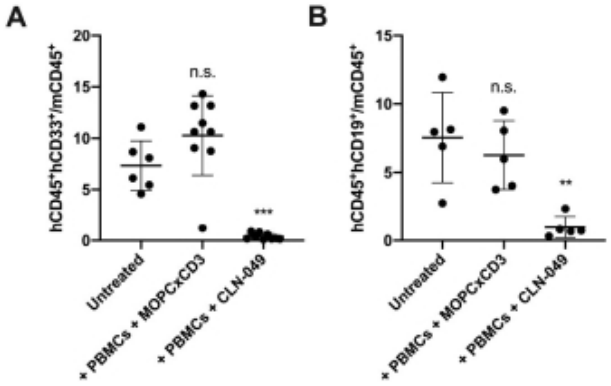
The potential efficacy of CLN-049 was evaluated in a humanized mouse model where a human AML cell line was implanted systemically. As shown in the figure below, CLN-049 controlled AML leukemic burden in the engrafted human PBMC (DHC23) mice and led to the extension of the animals' survival in a dose-dependent manner. We believe CLN-049 effected this result by redirecting the T cells in the human PBMC population to kill the target AML cells.

Dose-dependent Effect of CLN-049 on the Survival of Mice with Disseminated Leukemic AML Cells



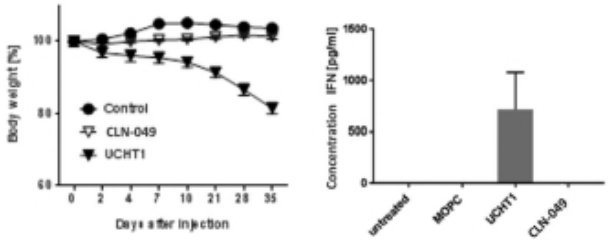
The anti-leukemic activity of CLN-049 was also evaluated using patient-derived AML blasts and PBMCs in a disseminated humanized mouse model. As shown in the figure below, treatment with CLN-049 resulted in a significant reduction in the overall leukemic burden in the bone marrow of both the primary AML blast (left panel) and ALL blast model (right panel). In contrast, a control T cell engaging bispecific antibody having the same format as CLN-049 but containing a non-specific target-binding domain did not impact the leukemic burden as compared to untreated control.

CLN-049 Demonstrated Anti-Leukemic Activity in Humanized Mouse Models with Primary AML and ALL Cells



To further evaluate the safety of CLN-049 *in vivo*, CLN-049 was administered in a humanized mouse model inoculated with human PBMC. This study was specifically designed to test possible off-target effects of CLN-049. As shown in the figure below, the administration of CLN-049 did not cause meaningful body weight loss in the treated mice, with the overall body weight profiles being comparable to those of the control group. In contrast, administration of a bivalent cross-linking anti-CD3 antibody, the parental CD3 antibody UCHT1 from which the scFv domains of CLN-049 were derived, led to significant body weight loss (left panel) and the release of the cytokine interferon gamma in serum (right panel), as shown below.

Effect of CLN-049 on Body Weight and Cytokine Release in Humanized Mice



This result further supports our hypothesis that, *in vivo*, the two CD3 binding domains in CLN-049 cannot cross-link CD3 and therefore CLN-049 does not activate T cells in the absence of human FLT3-expressing target cells.

In December 2021, we initiated a Phase 1 clinical trial evaluating a single ascending dose of CLN-049 in r/r AML patients. The study is designed to primarily evaluate the PK and safety of the intravenous administration of CLN-049.

CLN-619

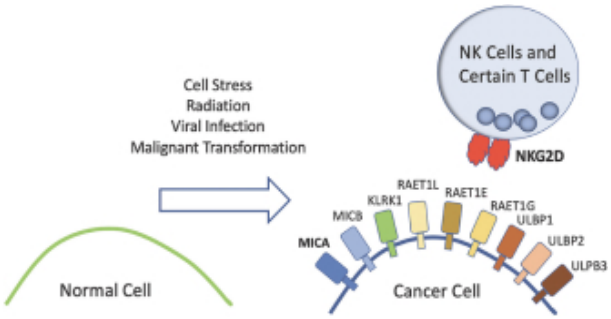
Our third clinical stage product candidate, CLN-619, is a MICA/B-targeted, humanized IgG1 monoclonal antibody that we intend to initially develop for the treatment of solid tumors. CLN-619 was designed to promote an antitumor response through multiple mechanisms of action, including inhibition of MICA/B shedding, ADCC mediation, enhancement of NKG2D receptor binding, and prevention of decoy NKG2D by shed MICA/B. The MICA/B receptor, NKG2D, is expressed in both innate and adaptive immune cell populations. Although several companies have disclosed preclinical MICA/B targeting programs, we are unaware of any clinical stage, antibody-based programs engaging this target, implying CLN-619 has first-in-class potential. In multiple *in vivo* preclinical tumor models, CLN-619 administration as a single agent was associated with antitumor activity and reduced levels of serum MICA/B.

We believe CLN-619 has the potential to become a novel backbone agent for immuno-oncology therapy given the broad expression of MICA/B across tumor types and the biological rationale for combining CLN-619 with other agents. We are currently evaluating CLN-619 in an ongoing clinical trial for patients with advanced solid tumors. The trial design includes parallel evaluation of CLN-619 as a monotherapy and in combination with checkpoint inhibitor therapy modules.

Background on NKG2D and MICA/B

NKG2D is a key activating receptor on NK cells responsible for cytolysis upon binding to ligands expressed on target cells. NKG2D is also expressed on other types of immune cells, including $CD8^+$ αβ T cells, natural killer T, or NKT, cells, and γδ T cells, and can prime such cells for activation and enhance their antitumor activity as a co-activating receptor. Healthy cells do not normally express ligands of NKG2D, but will do so in response to cellular stress, such as oxygen or nutrient deprivation, radiation, viral infection, or oncogenic transformation. As illustrated below, there are eight NKG2D ligands in humans: MICA and MICB; UL16 binding protein, or ULBP 1, 2, and 3; and Retinoic Acid Early Transcript, or RAET, 1E, 1G, and 1L (also known as ULBP 4, 5, and 6). All NKG2D ligands comprise an α1α2 extracellular major histocompatibility complex, or MHC, Class I-like superdomain that functionally interacts with the homo-dimeric NKG2D receptor.

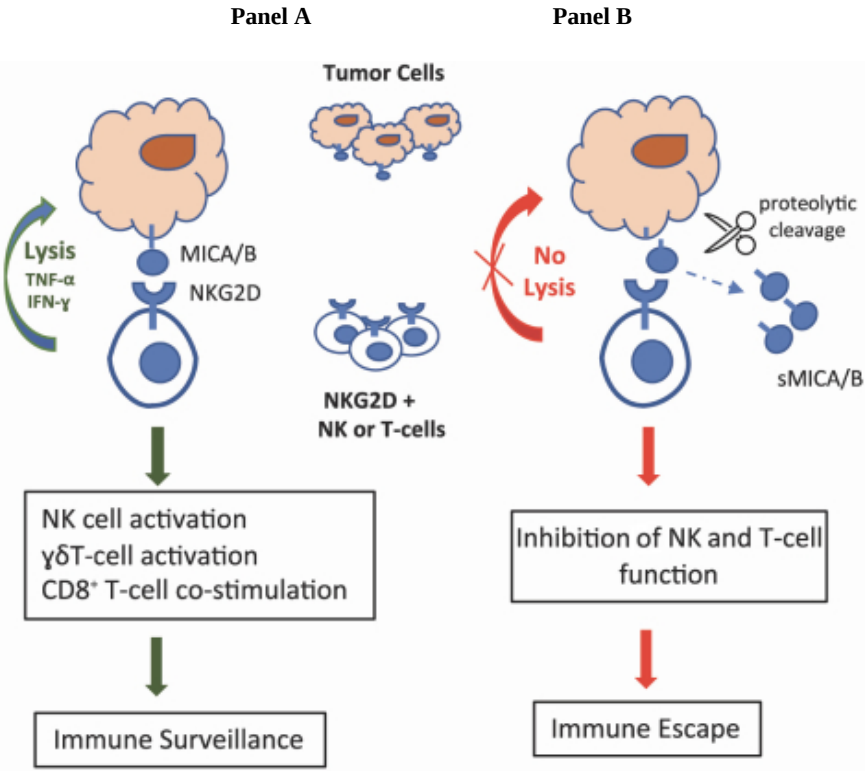
Overview of NKG2D Ligands



MICA/B proteins are broadly recognized by NK cells, □□ T cells, and CD8+ □ß T cells via the NKG2D receptor. The engagement between the NKG2D receptor and MICA/B proteins triggers the effector cytolytic responses of NK cells and □□ T cells against tumor cells expressing MICA/B. In the case of CD8+ □ß T cells, effector responses mediated by the T cell receptor are enhanced by NKG2D-MICA/B interactions. NKG2D-mediated stimulation also results in the induction of cytokines, which further promotes the recruitment and the proliferation of immune cells and bolsters the immune response.

To evade potential cytotoxic destruction by NK cells and T cells, tumor cells expressing MICA/B have adopted shedding of MICA/B from their cell surface as a key evasion mechanism. The MICA/B alpha-3 domain contains a stretch of amino acids that allows for protease cleavage of an extracellular portion of MICA/B and subsequent release from the cell surface, thereby reducing the ability of MICA/B to interact with NKG2D and resulting in decreased NKG2D-mediated killing of tumor cells. This mechanism also concomitantly increases the amount of circulating serum MICA/B, or sMICA/B. Soluble NKG2D ligands have also been shown to contribute to an immunosuppressive microenvironment. The mechanisms underlying this biology are illustrated below. Below, Panel A shows the normal mechanism by which tumor-associated ligands of NKG2D, such as MICA/B, can induce tumor cell killing. Panel B shows how tumor cells, through the proteolytic cleavage of MICA/B, can escape immune surveillance and immune cell-mediated killing.

Role of NKG2D Ligands, MICA/B, in Immune Cell-Mediated Killing of Tumor Cells



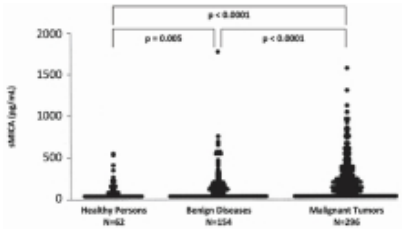
Given that proteolytic shedding of NKG2D ligands is an important immune escape mechanism, soluble levels of NKG2D ligands, such as sMICA, in a patient's serum may serve as an important indicator of prognosis. Several studies have shown that cancer patients with high levels of sMICA have a significantly worse prognosis than those patients with low levels of sMICA. The prognostic role of sMICA has been observed across patients with multiple distinct tumor types, including melanoma, NSCLC, pancreatic cancer, colorectal cancer, hepatocellular carcinoma, and multiple myeloma. Across 19 studies that included more than 2,500 patients, a meta-analysis showed that high sMICA levels were associated with poor prognosis of patients with high statistical significance.

Conversely, multiple studies have shown that the levels of sMICA in healthy individuals are low, usually less than 100 pg/mL, as compared to cancer patients who have high levels of sMICA that can exceed 1,000 pg/mL. However, in the majority of cancer patients, sMICA levels are usually between 100 to 1,000 pg/mL, as shown in the figure below. This data suggests that levels of sMICA/B in a patient's serum may have the potential to be used as a biomarker to evaluate the therapeutic effectiveness of antibodies designed to block proteolytic cleavage of MICA/B from the tumor cell surface.

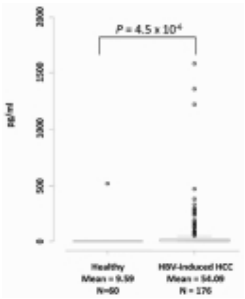
In the figure below, Panel A compares the levels of sMICA in normal healthy individuals to those with benign disease and those with cancer. Panel B shows sMICA levels in patients with hepatocellular carcinoma, or HCC, induced by hepatitis B virus, or HBV, relative to healthy controls. Panel C shows sMICA levels in healthy controls, or HC, compared to patients with chronic hepatitis, or CH, liver cirrhosis, or LC, or HCC.

Three Independent Studies Demonstrate Elevated Levels of sMICA in Cancer Patients

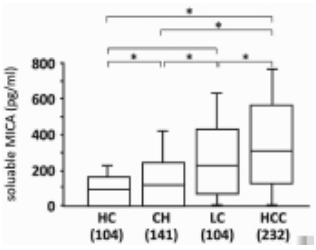
Panel A



Panel B

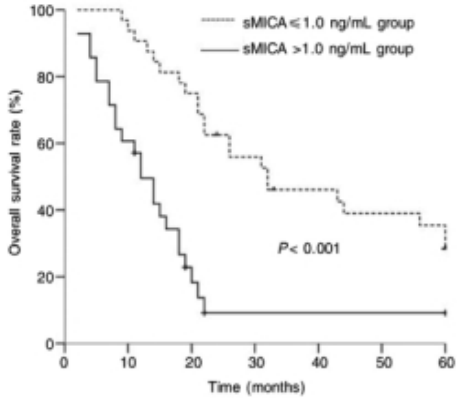


Panel C



In a study of 60 patients with advanced hepatocellular carcinoma and different serum levels of MICA, patients in the high serum MICA level group (>1 ng/ml) exhibited poorer survival than patients in the low serum MICA group (1 ng/ml). The results suggest that higher serum MICA levels relate to poor prognosis in advanced hepatocellular carcinoma.

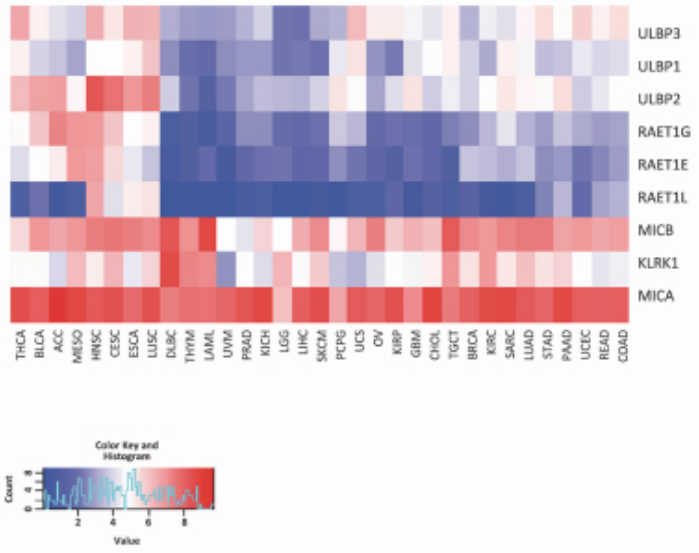
Kaplan Meier Curve of Hepatocellular Carcinoma Patients with Different Serum Levels of MICA



An analysis of the expression of the NKG2D ligands in The Cancer Genome Atlas, or TCGA, shows that MICA and MICB are the two ligands for NKG2D that are most frequently expressed across a wide range of tumor types. In the results of the TCGA analysis shown below, the red shading indicates high expression levels of NKG2D ligands and blue shading indicates low expression levels. We believe the positive expression profile of MICA/B in many tumor types provides attractive development opportunities across a wide range of indications.

Expression of NKG2D Ligands Across Multiple Tumor Types

Disease Name	Cohort
Adrenocortical carcinoma	ACC
Bladder urothelial carcinoma	BLCA
Breast invasive carcinoma	BRCA
Cervical and endocervical cancers	CESC
Cholangiocarcinoma	CHOL
Colon adenocarcinoma	COAD
Lymphoid Neoplasm Diffuse Large B-cell Lymphoma	DLBC
Esophageal carcinoma	ESCA
FFPE Pilot Phase II	FPPP
Glioblastoma multiforme	GBM
Head and Neck squamous cell carcinoma	HNSC
Kidney Chromophobe	KICH
Kidney renal clear cell carcinoma	KIRC
Kidney renal papillary cell carcinoma	KIRP
Acute Myeloid Leukemia	LAML
Brain Lower Grade Glioma	LGG
Liver hepatocellular carcinoma	LIHC
Lung adenocarcinoma	LUAD
Lung squamous cell carcinoma	LUSC
Mesothelioma	MESO
Ovarian serous cystadenocarcinoma	OV
Pancreatic adenolcarcinoma	PAAD
Pheochromocytoma and Paraganglioma	PCPG
Prostate adenocarcinoma	PRAD
Rectum adenocarcinoma	READ
Sarcoma	SARC
Skin Cutaneous Melanoma	SKCM
Stomach adenocarcinoma	STAD
Stomach and Esophageal carcinoma	STES
Testicular Germ Cell Tumors	TGCT
Thyroid carcinoma	THCA
Thymoma	THYM
Uterine Corpus Endometrial Carcinoma	UCEC
Uterine Carcinosarcoma	UCS
Uveal Melanoma	UVM



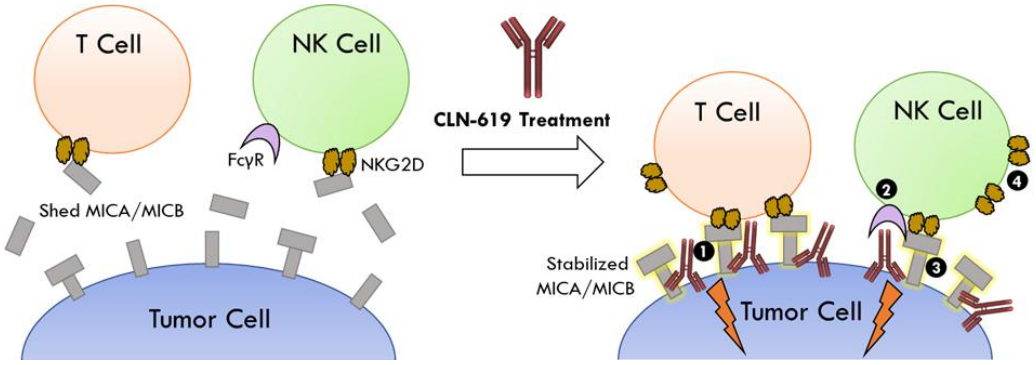
Data generated via analysis of TCGA database by Monoceros Biosystems.

CLN-619

CLN-619 is a MICA/B-targeted humanized IgG1 antibody with an antibody-dependent cell-mediated cytotoxicity-, or ADCC-, competent Fc gamma 1 domain capable of mediating effector cell functions through binding to Fc gamma receptors on cytotoxic innate immune cells.

We believe CLN-619 may affect antitumor activity through a multi-pronged mechanism of action. First, we believe that CLN-619 may shield the proteolytic cleavage sites of MICA and MICB on cancer cells from proteases commonly found in the tumor microenvironment (noted as “1” in the figure below). This mechanism would enable the accumulation of MICA/B on the surface of cancer cells and the reduction of shed soluble MICA/B circulating in the serum. In preclinical studies, treatment with parental CLN-619 clones resulted in increased cell surface expression and reduced serum levels of MICA/B in various tumor cell lines, while CLN-619 treatment *in vivo* led to reduced serum levels of MICA/B. Elevated expression of MICA/B on the surface of cancer cells is expected to enhance killing of cancer cells by NK cells via binding of their NKG2D to MICA/B. MICA/B also interacts with NKG2D expressed on gamma delta T cells and NKT cells, where NKG2D can play the role of a co-activating receptor, lowering the threshold for T cell-mediated cancer cell lysis. Second, CLN-619 has a human IgG1 backbone with a wild-type Fc gamma domain, which allows it to engage NK cells by binding to their Fc gamma receptor III/CD16/A, leading to ADCC (noted as “2” in the figure below). In preclinical studies, treatment with CLN-049 was shown to induce ADCC *in vitro*. Third, our preliminary preclinical data suggests that CLN-619 may have the potential to enhance the binding of MICA/B to NKG2D receptors on NK cells or other immune cells to provide for improved cancer cell lysis (noted as “3” in the figure below). Finally, by preventing the shedding of MICA/B, CLN-619 can potentially prevent the decoy of NKG2D by shed MICA/B circulating in serum (noted as “4” in the figure below). We believe that all of these mechanisms may be acting in a coordinated and unique manner to engage NK cells, which could result in the cancer cell lysis observed in the preclinical studies described below.

Three CLN-619 Modes of Action

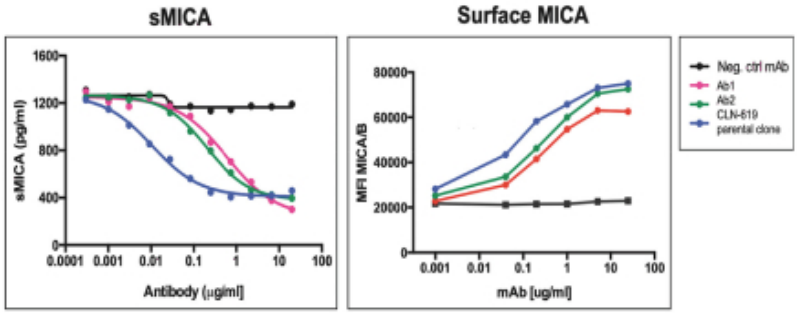


Preclinical Data

The key mechanistic underpinning of CLN-619's antitumor activity is its ability to stabilize and prevent the shedding of MICA/B expressed on the surface of cancer cells. In preclinical studies, CLN-619 prevented shedding across a variety of cancer cell lines. In a representative hepatoma PLC/PRF/5 cell line, soluble MICA in the supernatant decreased, and correspondingly, surface MICA levels increased, in a dose-dependent manner, following treatment with CLN-619. CLN-619 was more potent than other antibody candidates (Ab1 and Ab2) in preventing MICA shedding as shown in the figure below.

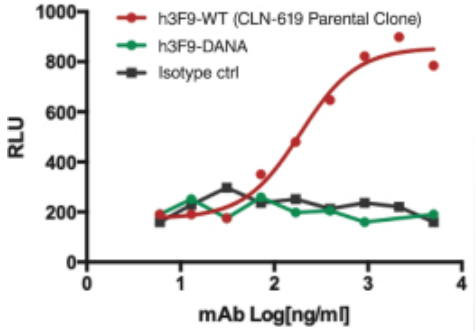
Parental Clone of CLN-619 Reduced Serum MICA and Increased Surface MICA Levels in Hepatoma

PLC/PRF/5 Cell Lines



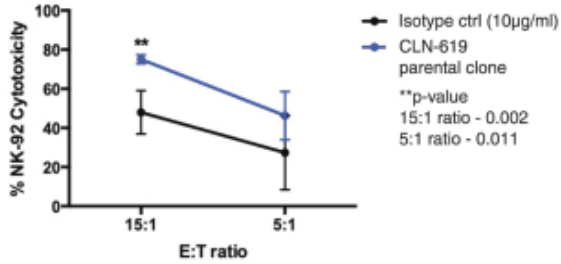
CLN-619 also demonstrated the ability to enhance NK cell-mediated killing of MICA/B expressing cancer cells *in vitro*. In an ADCC reporter bioassay, the parental clone of CLN-619, which has antibody variable region sequences from a mouse hybridoma from which CLN-619 was derived, induced ADCC in a dose-dependent and MICA/B binding-dependent manner, as shown in the figure below, where killing activity was measured by the relative luminescence units, or RLU. Such ADCC activity was abrogated when mutations in the Fc region were introduced into h3F9-DANA, which eliminated the binding to Fc□RIIIa on NK cells that is key to mediating ADCC. An isotype control also failed to trigger ADCC, demonstrating the requirement of MICA/B target engagement.

Parental Clone of CLN-619 Induced ADCC *In Vitro*



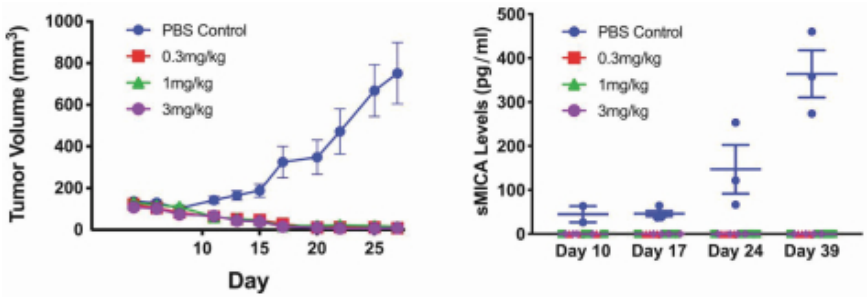
In an *in vitro* assay using human NK-92 cells and PLC/PRF/5 cancer cells, the parental clone of CLN-619 enhanced the killing of MICA/B-specific cancer cells by NK cells. As shown in the figure below, the parental clone of CLN-619, at both low and high effector to target, or E:T, ratios, significantly enhanced the extent of target cell killing compared to a control antibody.

***In Vitro* Assay Using Human NK-92 Cells and PLC/PRF/5 Cancer Cells**



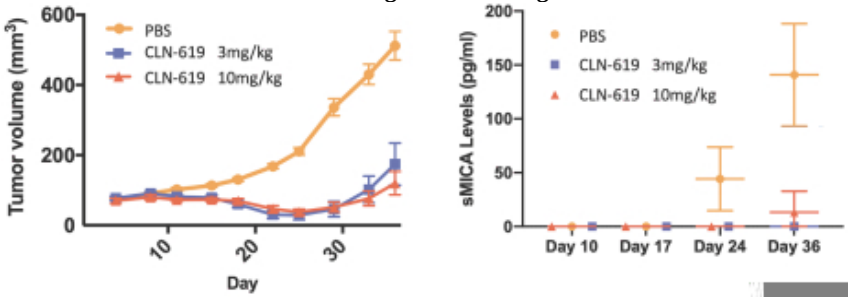
The antitumor activity of CLN-619 was further evaluated in multiple mouse tumor models. In a representative PLC/PRF/5 liver cancer xenograft model, CLN-619 treatment as a single agent resulted in tumor regression at all doses tested, as shown in the left panel of the figure below. In addition, the body weight profiles of treatment groups were comparable to the control group. Importantly, near complete suppression of MICA shedding as measured by soluble MICA levels in the serum was observed, as shown in the right panel of the figure below.

CLN-619 Demonstrated Tumor Regression and Reduced Serum MICA Levels in a PLC/PRF/5 Liver Cancer Xenograft Model



Similarly, in a representative lung cancer xenograft model, CLN-619 treatment as a single agent resulted in tumor growth inhibition at all doses tested, as shown in the left panel of the figure below. We also observed near complete suppression of MICA shedding at all doses tested as measured by soluble MICA serum levels, as shown in the right panel of the figure below.

CLN-619 Demonstrated Tumor Growth Inhibition and Reduced Serum MICA Levels in a HCC1534 Lung Cancer Xenograft Model



Clinical Development Plan

We are currently evaluating CLN-619 in a clinical trial in patients with advanced solid tumors. The trial design includes initial evaluation of CLN-619 as a monotherapy and in combination with checkpoint inhibitor therapy in dose escalation cohorts. Upon establishing a recommended phase 2 dose, or RP2D, the trial design includes several expansion cohorts to evaluate the preliminary efficacy of CLN-619 as both a monotherapy and in combination with checkpoint inhibitor therapy in patients with multiple solid tumor types. In addition, we will collect and analyze biomarkers, including sMICA, to inform the future development of CLN-619.

CLN-617

CLN-617 is a fusion protein uniquely combining, in a single agent, two potent antitumor cytokines, IL-2 and IL-12, with a collagen-binding domain for the treatment of solid tumors. The combination of IL-2 and IL-12 therapeutic administration has previously been shown to synergistically enhance T and NK cell functions *in vitro* and mediated pronounced therapeutic activity in preclinical tumor models, even in well-established mouse models with primary and/or metastatic tumors. For nearly five decades, clinical researchers have studied the powerful role cytokines play in stimulating an immune response to cancer. However, severe toxicities associated with systemic cytokine administration and a short serum half-life have hindered their clinical development and broader commercial uptake. Despite numerous advancements in protein engineering, delivery and targeting mechanisms, there are currently only two FDA-approved cytokine-based cancer therapies, with the most recent approval occurring over twenty years ago.

We have included multiple differentiating features in CLN-617's design in order to address the historical limitations of cytokine-based therapy. First, the structure of CLN-617 contains a collagen-binding domain that is designed to enable the retention of cytokines in the local tumor microenvironment following intratumoral administration. Collagen binding may help minimize the systemic dissemination and associated toxicities of IL-2 and IL-12 and prolong their immunostimulatory antitumor activity. Second, we believe that CLN-617 is the only product candidate to our knowledge that co-delivers IL-2 and IL-12 proteins, functionally enabling synergistic T and NK cell activation. Third, CLN-617's construct uses wild type cytokines, which potentially reduces immunogenicity risk associated with engineered cytokines. Finally, unlike other intratumoral cytokine-based therapies, CLN-617 does not rely on viral or nucleic acid for in situ expression and activity.

In preclinical studies, murine surrogates of CLN-617 demonstrated robust single agent antitumor activity in both injected and non-injected contralateral tumors without inducing systemic toxicity, as measured by reduction in body weight. Given the broad expression of collagen across multiple tumor types and the well-validated antitumor activity of cytokine-based therapies, we believe CLN-617 may have utility across a broad range of solid tumors. We believe that CLN-617 is a first-in-class opportunity given it is the only anti-cancer product candidate we are aware of that is designed to co-deliver IL-2 and IL-12 cytokines and retain them in the tumor microenvironment. We are currently advancing CLN-617 through IND-enabling studies and expect to submit an IND by the end of the first half of 2023.

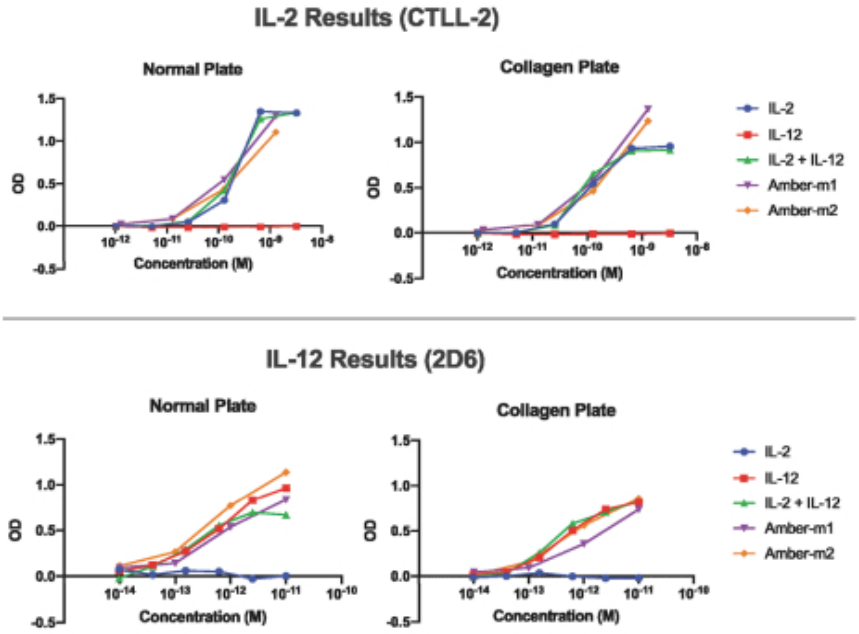
The collagen-binding retention technology used in CLN-617 is based on technology that originated in the laboratory of Professor Dane Wittrup at the Massachusetts Institute of Technology, or MIT. We have further developed and refined this technology to create our AMBER platform, which we believe represents a novel platform with the potential to broaden the therapeutic window of cytokines and other immunostimulatory agents, with substantially reduced systemic toxicity.

Preclinical Data

We have generated a variety of multifunctional AMBER-based constructs containing both IL-2 and IL-12 fused to various collagen-binding domains, and we refer to the murine surrogates of these constructs as AMBER-m1, AMBER-m2, AMBER-m3, AMBER-m4, etc. While Professor Wittrup's foundational study focused on lumican, we evaluated collagen-binding domains with different affinities including other proteins that bind to collagen in the tumor microenvironment to enhance retention of the cytokines.

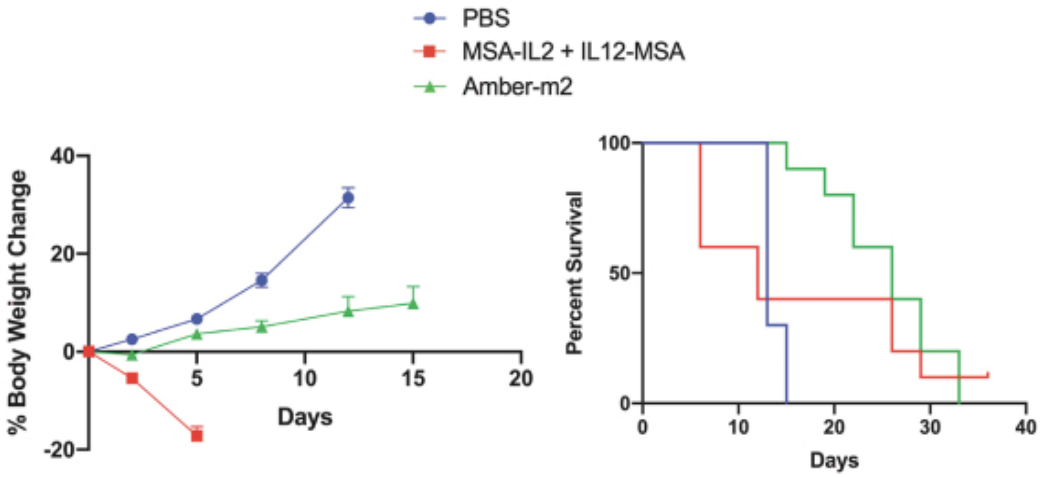
Our murine surrogate AMBER constructs have been assessed for productivity, product quality, and bioactivity. We tested the bioactivity of both IL-2 and IL-12 cytokines by measuring proliferation of respective cell lines in response to IL-2 and IL-12. We compared our constructs with collagen-binding domains to native cytokines in the presence and absence of collagen. As shown below, cytokine activity, measured by optical density, or OD, is maintained in the multifunctional AMBER-m1 and AMBER-m2 constructs and activity is comparable in both the absence and presence of collagen.

In AMBER Constructs, Cytokine Activity Was Fully Retained after Fusion to Collagen-Binding Domain



Based on these results, we further assessed the antitumor activity and tolerability of AMBER-m2 *in vivo* in C57BL/6 mice bearing B16F10 tumors. We compared intratumoral administration of AMBER-m2 to a combination of MSA-IL2 and IL12-MSA, which lack collagen-binding domains. As expected, treatment with MSA-IL2 and IL12-MSA led to systemic toxicity, as measured by reduction in body weight (left panel of figure below). In contrast, AMBER-m2 exhibited single-agent antitumor activity without inducing systemic toxicity, as measured by survival (right panel of figure below). Based on these results, we believe that AMBER-m2, which is presumably retained in the tumor microenvironment, may have the potential to mitigate the systemic toxicity associated with IL-2 and IL-12 therapy, thus potentially improving the therapeutic index while delivering antitumor activity.

Antitumor Activity and Tolerability of MSA-IL2 + IL12-MSA or AMBER

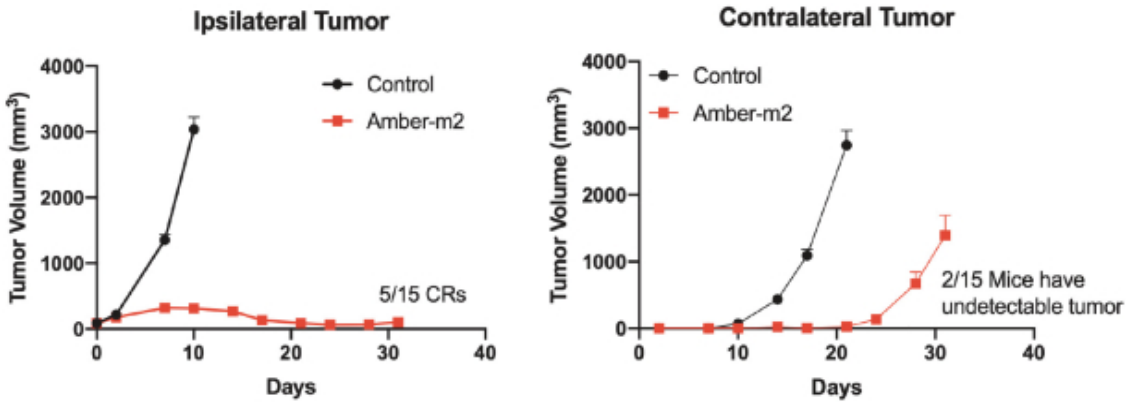


In the experiments above, body weight changes are no longer recorded following animal death, accounting for the difference in days duration between the left and right figures for the MSA-IL2 + IL12-MSA treated animals.

We hypothesized that in addition to mediating local antitumor activity, AMBER-m2 may be capable of generating responses against non-injected contralateral tumors due to the induction of systemic immunity, also known as an abscopal effect. To test our hypothesis, we utilized C57BL/6 mice bearing two B16F10 tumors: an ipsilateral tumor that was directly injected with AMBER-m2 and a contralateral tumor that was implanted 10 days later and never treated with AMBER-m2. Tumor control was observed in both the treated and untreated distal tumors, thus demonstrating an abscopal effect.

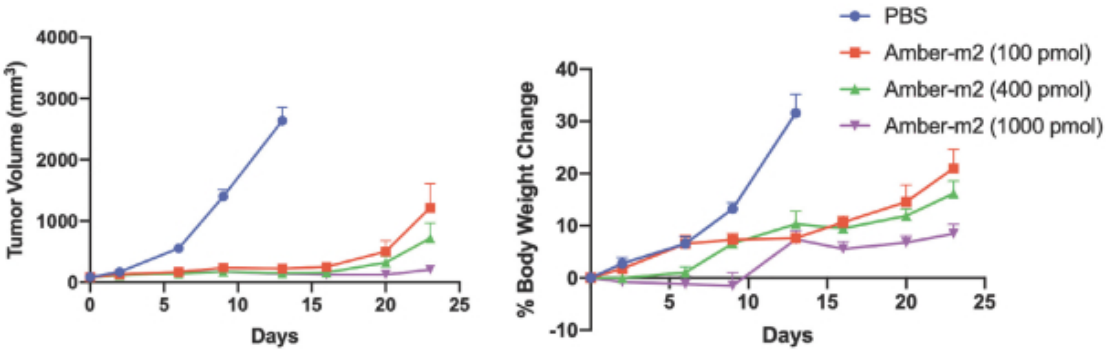
AMBER-m2 Inhibits Tumor Growth in Both Injected (Ipsilateral) and Uninjected (Contralateral)

B16F10 Tumors, Providing Evidence for an Abscopal Effect



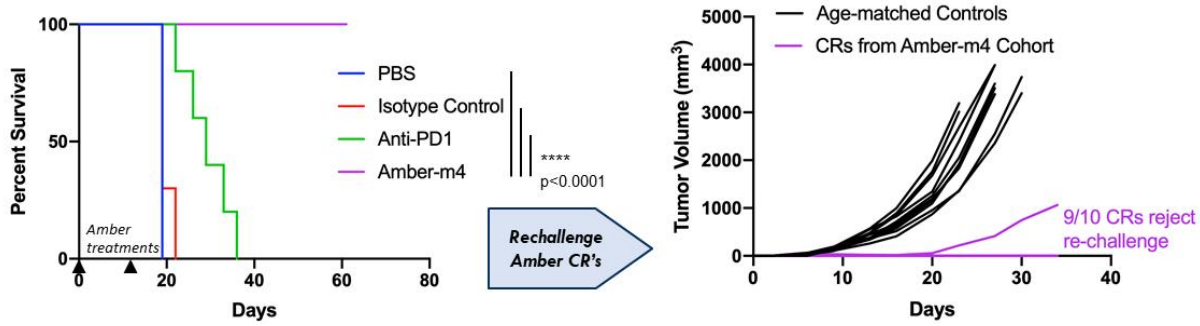
We have also evaluated the dose responsiveness of AMBER-m2 in the B16F10 model. Increasing dose levels of AMBER-m2 led to increased tumor growth control (left panel of figure below), and all doses did so without inducing significant body weight loss (right panel of figure below). Notably, the highest tested dose of 1,000 pmol is an equivalent dose of 6.4 mpk of body weight, which translates to 0.7 mpk of IL-2 and 2.3 mpk of IL-12. In comparison, only 100 pmol of MSA-IL2 and IL12-MSA led to lethal body weight loss.

Impact of AMBER-m2 on Tumor Growth and Body Weight in the B16F10 Model



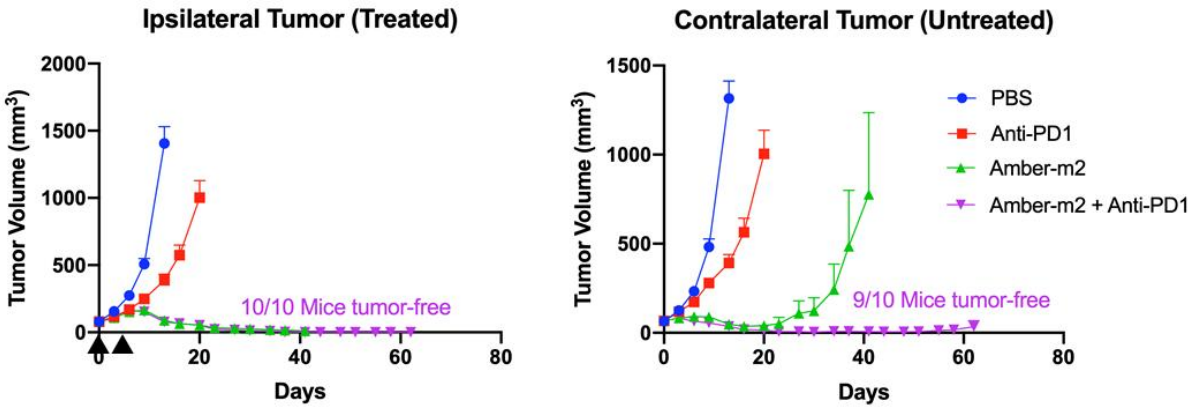
We have also evaluated our AMBER murine constructs in the CT26 and MC38 syngeneic mouse models. As shown in the left panel below, treatment with AMBER-m4 led to statistically significant survival increases relative to control and anti-PD1 arms in the MC38 model. Subsequently, we re-injected tumors into animals that achieved a complete response following treatment with AMBER-m4. As shown in the right panel below, nine out of ten mice previously treated with AMBER-m4 rejected the newly injected tumors. Similar results were achieved in the CT26 syngeneic model.

Impact of AMBER-m4 on Survival and Tumor Re-Challenge in the MC38 Model



In addition, preclinical results show the synergistic effect of combining a checkpoint inhibitor with AMBER murine constructs. Below is an example of combination treatment with anti-PD1 and one of our AMBER constructs in the MC38 model.

Impact of AMBER-m2 as Monotherapy or in Combination with Anti-PD1 on Tumor Growth in the MC38 Model



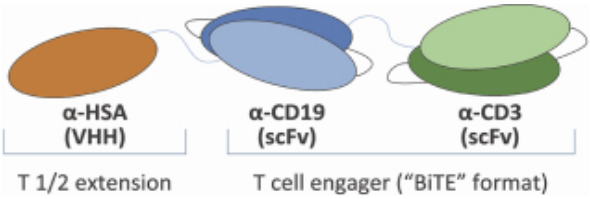
Based on the results of our preclinical studies, we believe that the inclusion of a collagen-binding domain by our AMBER platform has the potential to allow for the safe retention of high levels of cytokines in the tumor microenvironment. While remarkable progress has been made in the treatment of cancer with the adoption of checkpoint inhibitors, including pembrolizumab, ipilimumab, and nivolumab, only a fraction of patients with solid tumors respond to these therapies. We believe a well-tolerated agent that can deliver the functional synergies of IL-2 and IL-12 has the potential to treat a broad range of solid tumors, including those that are not responsive to checkpoint inhibitors.

CLN-978

CLN-978 is a half-life extended, humanized, single-chain bispecific antibody designed to simultaneously engage CD19 on cancer cells and CD3 on T cells, triggering redirected T cells to lyse the target cancer cells. In addition, CLN-978 has a human serum albumin, or HSA, binding domain designed to prolong its serum half-life. CLN-978, referred to as NexGem in the figures below, mediated CD19-dependent target cell lysis *in vitro* on target cell lines with a range of CD19 target expression levels. In preclinical *in vivo* studies, treatment with NexGem, at extremely low and infrequent doses, led to inhibition of tumor growth and tumor regression in a human CD3 transgenic syngeneic lymphoma mouse model. We intend to initially evaluate CLN-978 as a novel treatment for B-cell malignancies, and are currently undertaking IND-enabling pharmacology, pharmacokinetic, and safety studies.

We designed CLN-978 based on a BiTE-like format using tandemly arranged scFvs for CD19 and CD3, similar to blinatumomab. In addition, we incorporated a third domain in the form of a single-domain antibody, or VHH, for binding to HSA. We believe that binding of CLN-978 to albumin has the potential to extend its serum half-life, potentially addressing limitations related to blinatumomab's dosing regimen. An illustration of the CLN-978 structure is shown in the following figure.

Design of CLN-978, a CD19/CD3-bispecific T Cell Engager with Extended Serum Half-life



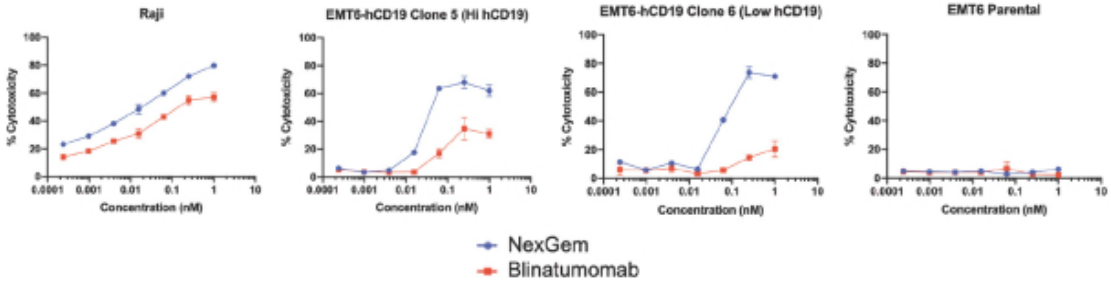
We have collaborated with Adimab LLC to generate antibody-derived binding domains specific for CD19, CD3, and HSA with optimized biophysical and biochemical properties, tailored binding affinities as well as other parameters that are key to developability, manufacturability and preclinical testing of drug candidates. In multiple head-to-head preclinical comparison studies, NexGem has demonstrated improved activity compared to blinatumomab both in terms of redirecting of T cells to lyse CD19-expressing cells *in vitro* and enhanced tumor growth inhibition *in vivo*. Although comparative data from preclinical studies must be interpreted with caution and we may not observe the same differential effect in clinical trials, we believe these preclinical results support further evaluation of CLN-978 for its potential to improve upon the clinical efficacy observed with blinatumomab and for its potential to offer a more convenient dosing profile. In addition to convenience, we believe the ability to target cells with low CD19 expression would potentially enable us to address patients that are not yet adequately addressed by blinatumomab, such as those with CD19-low non-Hodgkin's lymphoma or those patients that progress following CAR-T therapy.

We expect the properties of CLN-978 may facilitate our efforts on manufacturing processes and IND-enabling studies, as we believe they will enable us to leverage standard cell line development and purification technologies for GMP manufacturing and conventional non-human primate models for GLP toxicology assessment. We are currently advancing CLN-978 through IND-enabling studies and expect to submit an IND by the end of the first half of 2023.

Preclinical Data

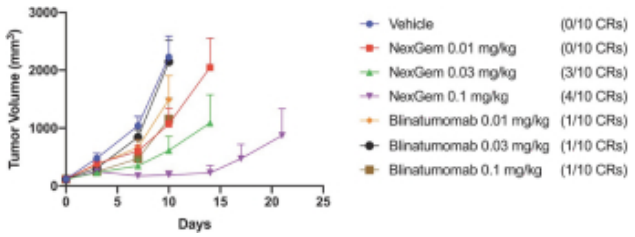
Our NexGem candidates incorporate a CD19 binding domain that was engineered to achieve 100x enhanced binding affinity to CD19 compared to blinatumomab as measured using plasmon resonance, which we believe may contribute to improved cytolytic potency in an *in vitro* model. As shown in the figure below, NexGem outperformed blinatumomab in the cell lines evaluated as measured by both the EC50 value of redirected cell lysis and the maximum percentage of lysis. Notably, the relative improvement in cytolytic potency of CLN-978 as compared to blinatumomab was the highest in target cells expressing relatively low levels of CD19. We believe this observation supports our hypothesis that CLN-978 may have the potential to more adequately address the patient population with lower levels of CD19 expression and/or patients in which CD19 expression is downregulated as a resistance mechanism to CD19-targeted therapies. It was also shown that the robust lysis of target cells was dependent on CD19 expression, as the EMT6 parental cell line, which lacks CD19 expression, was not susceptible to lysis at any of the drug concentrations tested.

Comparison of NexGem Versus Blinatumomab *in vitro* Cytotoxicity Assays



NexGem has also demonstrated antitumor activity *in vivo* compared to blinatumomab in a human CD3 transgenic model, where the mice were implanted with a syngeneic tumor engineered to express human CD19. As shown in the figure below, NexGem outperformed blinatumomab in tumor growth inhibition at every dose level tested. Furthermore, at the 0.1 mg/kg dose level, NexGem treatment resulted in a complete response in 40% of mice compared to only 10% of mice treated with blinatumomab.

Antitumor Activity of NexGem Versus Blinatumomab In a Human CD3 Transgenic Mouse Model Bearing Human CD19 Expressing Syngeneic Tumors



Our Other Preclinical Programs

In addition to the programs described above, we are actively developing three additional preclinical oncology programs: Jade, Opal and a discovery collaboration with Mt Sinai to develop HPK1 degraders.

We are developing our Jade program as part of an ongoing collaboration with the Fred Hutchinson Cancer Research Center, a world leader in finding self-reactive, human T cells of high affinity. Our goal is to develop a TCR-T cell therapy targeting a novel senescence and cancer-related protein. We are collaborating with Fred Hutchinson Cancer Research Center to search for and optimize naturally occurring TCRs against this target.

For our Opal program, we are exploring a construct that combines checkpoint inhibition and immune co-stimulatory receptor activation in a single protein. We are evaluating various single-chain fusion protein formats using an affinity optimized PD-1 extracellular domain and a single-chain 4-1BBL designed to preferentially activate the 4-IBB/CD137 pathway on T cells inside tumors. We believe that the combination of these natural binding elements could potentially drive synergistic antitumor immune mobilization while reducing the toxicity often associated with untargeted co-stimulatory immune agonists. We are designing our lead construct such that the activation of the co-stimulatory receptor is dependent on the binding to immune checkpoint ligands, which have generally higher expression levels in tumor tissues compared to normal tissues. We also believe that our approach has the potential to demonstrate advantages over antibody-based bispecific constructs that typically require selection of format specific epitopes and appropriate affinities for target binding.

HPK1 (MAP4K1) is a T cell specific kinase that negatively regulates T cell activation and TCR signaling. HPK1-/- T cells produce elevated levels of pro-inflammatory TH1 cytokines, including IFNg, TNFa and CCL3. We are collaborating with Mt. Sinai to optimize and develop HPK1 protein degraders with best- and/or first-in-class potential. We believe that a degrader approach may control tumor growth more effectively compared to inhibiting HPK1 kinase activity. The Mt. Sinai team includes, Dr. Steven Burakoff, who validated HPK1 as an immuno-oncology target and Dr. Jian Jin, an expert in degrader chemistry. We have an exclusive option for any intellectual property that arises from this collaboration.

Competition

The biotechnology and pharmaceutical industries are characterized by the rapid evolution of technologies and understanding of disease etiology, intense competition and a strong emphasis on intellectual property. We believe that our differentiated business model, approach, scientific capabilities, know-how and experience provide us with competitive advantages. However, we face, and will continue to face, competition from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. We expect substantial competition from multiple sources, including major pharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions, governmental agencies and public and private research institutions worldwide. Many of our competitors, either alone or through collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and recruiting patients in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

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

With respect to our lead product candidate, CLN-081, we are aware of other EGFR inhibitors that have accelerated approval or are in clinical development for the treatment of NSCLC patients harboring EGFRex20ins mutations. In May 2021, Rybrevant (amivantimab), an EGFR/cMET bispecific antibody that was developed and is now marketed by Johnson & Johnson obtained accelerated approval from the FDA for adult patients with locally advanced or metastatic NSCLC with EGFRex20ins mutations whose disease has progressed on or after platinum-based chemotherapy. Additionally, in September 2021, Exkivity (mobocertinib), which was developed and is now marketed by Takeda Pharmaceuticals, Inc., obtained accelerated approval from the FDA for adult patients with locally advanced or metastatic NSCLC with EGFRex20ins mutations whose disease has progressed on or after platinum-based chemotherapy. We believe that the most advanced clinical stage program is DZD9008 from Dizal Pharmaceutical Co., Ltd. Other clinical-stage EGFR ex20ins TKI programs include poziotinib from Spectrum Pharmaceuticals, Inc., Black Diamond's Therapeautics, Inc., BDTX-189, Oric Pharmaceuticals, Inc.'s ORIC-114 (Voronoi, Inc., in People's Republic of China, Hong Kong, Macau and Taiwan) and Blueprint Medicine Corporation's LNG-451.

With respect to CLN-049, we are aware of several companies that are developing bispecifics for the treatment of AML, including those targeting CD3 and CD33 (Amgen Inc., or Amgen and Amphivena Therapeutics, Inc.), CD123 (Macrogenics, Inc. and Xencor, Inc.), and CCL1/CLEC12A (Merus N.V. and Genentech, Inc.). These agents are limited to a subset of AML blasts that express CD33, CD123, and CCL1, whereas multiple published studies have demonstrated that FLT3 is expressed in approximately 80% of AML blasts. Amgen is developing a bispecific T cell engager targeting FLT3 for AML. There are also several targeted small molecule therapies approved for the treatment of r/r or first-line AML, including for AML with FLT3 mutations, such as Astellas Pharma Inc.'s XOSPATA (gilteritinib) and Novartis International AG's RYDAPT (midostaurin). We are also aware of other small molecules that are approved or in development for AML patients with FLT3 mutations, including IDH inhibitors, such as TIBSOVO (ivosidenib) by Servier Pharmaceuticals and IDHIFA (enasidenib) by Agios Pharmaceuticals, BCL2 inhibitors, such as VENCLEXTA (ventoclax) by AbbVie, and hedgehog pathway inhibitors, such as DAURISMO (glasdegib) by Pfizer.

With respect to CLN-619, we are aware of several companies that are developing cancer therapies targeting MICA/B as a monotherapy and/or in combination with other agents, including: Fate Therapeutics, Inc., Innate Pharma, Inc. (in collaboration with AstraZeneca Inc.), CanCure LLC, Genentech Inc., Novartis International AG, or Novartis, and Bristol-Myers Squibb Company, or Bristol-Myers Squibb. To our knowledge, none of them has entered clinical development.

With respect to CLN-617, we are not aware of any other drug candidates currently under development that integrate both IL-2 and IL-12 into a single multi-functional construct and stimulate the immune system in a tumor-specific manner. We are aware of several companies actively developing clinical-stage programs as either individual IL-2 or IL-12 therapies, including: Nektar Therapeutics, Inc., Alkermes plc, Sanofi, Philogen S.p.A., Roche AG, Apeiron Biologics AG and Dragonfly Therapeutics Inc.

With respect to our CLN-978 program, we are aware of a number of companies developing product candidates that target CD19 or other tumor antigens relevant to B-cell ALL and NHL using immune cells or other cytotoxic modalities. These mainly include immune cell redirecting therapeutics (e.g., T cell engagers), adoptive cellular therapies (e.g., CAR-Ts) and antibody drug conjugates. Companies developing cell therapies or antibodies targeting CD19 include Morphosys AG, Novartis, Gilead Sciences Inc., Bristol-Myers Squibb, Allogene Therapeutics Inc., Nkarta Inc. and Amgen.

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

License Agreements

Taiho License Agreement

In February 2019, our partially-owned subsidiary Cullinan Pearl Corp., or Cullinan Pearl, entered into a License and Collaboration Agreement, or the Taiho License Agreement, with Taiho Pharma. Pursuant to the Taiho License Agreement, Cullinan Pearl obtained an exclusive, royalty-bearing worldwide license (excluding Japan) to develop, manufacture, commercialize and, subject to certain limitations, sublicense CLN-081 and products containing CLN-081, for use worldwide outside Japan, under the licensed patent rights and know-how.

Under the Taiho License Agreement, Cullinan Pearl agreed to conduct all development activities in accordance with a target product profile and a development plan intended to generate data to seek regulatory approval of CLN-081 from the FDA and European Medicines Agency, or EMA, and make such data available to Taiho Pharma for use to seek regulatory approval in Japan. Certain of these development activities require using commercially reasonable efforts. Cullinan Pearl must disclose experimental data, results or similar know-how to Taiho Pharma and grant a non-exclusive, royalty free, worldwide license, with the right to sublicense, to Taiho Pharma to develop, manufacture and commercialize CLN-081 and its products in Japan. Cullinan Pearl, and in certain cases Taiho Pharma, are obligated to provide progress reports to each other on development efforts before and, for so long as such party is developing a licensed product, after the first commercial sale of CLN-081. Taiho Pharma also has right of negotiation with Cullinan Pearl in the event Cullinan Pearl decides to commence negotiations with or if Cullinan Pearl receives a bona fide term sheet from a third-party regarding the license, sale, assignment, transfer or material disposition of rights with respect to the licensed product.

As partial consideration for the license, Cullinan Pearl paid an initial, non-refundable, non-creditable license fee of $2.5 million and issued Taiho Pharma 1,860,000 shares of Cullinan Pearl common stock. In addition, Cullinan Pearl is obligated to pay non-refundable, non-creditable research and development, regulatory and sales milestone payments upon the occurrence of certain milestone events in an aggregate amount of up to $154.5 million for development, regulatory and sales milestones. Each milestone is payable only once. No milestones have been achieved to date under the Taiho License Agreement.

Furthermore, on a country-by-country and product-by-product basis, Cullinan Pearl is required to pay running mid-single digit to low tens digits royalty percentages of annual aggregate net sales worldwide outside Japan, during the royalty term (such royalty term determined on a product-by-product and country-by-country basis), subject to certain offsets, deductions or reductions related to loss or impairment of exclusivity in the territory. Such royalty obligations will expire on a country-by-country and product-by-product basis upon the latest of (a) the expiration of the last patent which covers a product in such country, (b) the expiration of the applicable exclusivity granted by a regulatory authority and (c) ten years following the first commercial sale of the product in such country.

In the event (i) Taiho Pharma does not exercise its right of negotiation with respect to a licensed product or (ii) Taiho Pharma does exercise its right of negotiation, but the parties do not consummate a transaction, then at the time Cullinan Pearl enters into a subsequent transaction with a third-party for (a) less than all or less than substantially all of Cullinan Pearl's rights in a licensed product, Cullinan Pearl is obligated to pay Taiho Pharma a mid-single digit percentage of revenue from such transactions or (b) all or substantially all of Cullinan Pearl's rights in a licensed product, Cullinan Pearl is obligated to pay Taiho Pharma a low single digit percentage of revenue from such transactions, provided, however, that such payment under (b) shall not be required following the consummation of an initial public offering of Cullinan Pearl meeting certain requirements.

In December 2020, Cullinan Pearl entered into a license agreement, or the Zai License Agreement, with Zai Lab. Pursuant to the terms of the Taiho License Agreement, we are obligated to pay Taiho a mid-teen percentage of the $20.0 million upfront payment received from Zai Lab, as well as a mid-teen percentage of potential future milestone revenue received from Zai Lab under the Zai License Agreement. In the first quarter of 2021, Zai Lab paid the upfront fee to Cullinan Pearl and Cullinan Pearl recorded the corresponding transaction payment due to Taiho Pharma within research and development expenses.

Either party may terminate the Taiho License Agreement upon a material breach by the other party or bankruptcy of the other party. Cullinan Pearl may terminate the Taiho License Agreement at any time and for any commercially reasonable justification. Unless earlier terminated, the Taiho License Agreement continues in effect on a product-by-product basis until it expires upon the expiration of all applicable royalty terms with respect to all products in all countries worldwide.

Zai License Agreement

In December 2020, Cullinan Pearl entered into the Zai License Agreement with Zai Lab. Pursuant to the Zai License Agreement, Cullinan Pearl granted Zai Lab an exclusive, royalty-bearing license to research, develop, commercialize and manufacture CLN-081 and products containing CLN-081 in the field in China, Hong Kong, Macau and Taiwan, or collectively, the Territory. Cullinan Pearl has also granted Zai Lab the right to grant sublicenses in multiple tiers in accordance with the Zai License Agreement, under the licensed technology and any improvements discovered or created during the term, to exploit the products in the field in the Territory.

Cullinan Pearl retained (i) all rights under the licensed technology to fulfill its obligations under the Zai License Agreement, (ii) the exclusive rights to exploit the licensed compound and products outside the Territory, (iii) the non-exclusive rights under the licensed technology to conduct global studies in accordance with the Zai License Agreement and (iv) the non-exclusive rights to manufacture or have manufactured the licensed compound or product in the Territory, solely to support (x) the manufacture, development and commercialization of the licensed compound and products outside of the Territory and (y) the manufacture, development and commercialization of the product by Zai Lab in the Territory.

Pursuant to the terms of the Zai License Agreement, Zai Lab shall use commercially reasonable efforts to develop the products in the field in the Territory, including the conduct of all development activities of the products in the field in the Territory in accordance with the development plan.

As partial consideration for the license and rights, Zai Lab paid will pay Cullinan Pearl an upfront, one-time, irrevocable, non-refundable, non-creditable license fee of $20.0 million within 40 days of the execution of the Zai License Agreement. In addition, Zai Lab is obligated to pay Cullinan Pearl non-refundable, non-creditable research and development, regulatory and sales milestone payments upon the occurrence of certain milestone events in an aggregate amount of up to $211.0 million. Each milestone is payable only once. No milestones have been achieved to date under the Zai License Agreement.

Furthermore, on a region-by-region and product-by-product basis, Zai Lab is required to pay tiered royalties from high single digit to low teen digit royalty percentages on annual aggregate net sales of all future products in the Territory in a calendar year, during the royalty term (such royalty term determined on a product-by-product and region-by-region basis), subject to certain offsets, deductions or reductions related to the expiration of the last-to-expire valid claim in such region, such time as generic competition with respect to such product occurs in such region or in connection with obtaining a license for any patents owned or controlled by a third-party in order to commercialize the licensed product; provided, however, that the royalties due to Cullinan Pearl shall not be reduced by more than fifty percent (50%). Such royalty obligations will be payable on a region-by-region and product-by-product basis from the first commercial sale of the applicable product in such region until the latest of (a) the date the last-to-expire valid claim in such region expires and (b) the tenth anniversary following the first commercial sale of such product in such region. Upon the expiration of the royalty terms, the licenses granted by Cullinan Pearl to Zai Lab in such region with respect to such product in the field shall become fully paid-up, perpetual, irrevocable and sublicensable in multiple tiers.

Either party may terminate the agreement on a region-by-region basis or in its entirety upon a material breach by the other party or bankruptcy of the other party. Zai Lab may terminate the Zai License Agreement in its entirety or on a product-by-product basis at any time and for any or no reason, provided, however, that Zai Lab will terminate the Zai License Agreement upon prior written notice to Cullinan Pearl if it determines that it shall discontinue all development and commercialization activities with respect to the products. Furthermore, Cullinan Pearl may terminate the Zai License Agreement in its entirety, if Zai Lab or its affiliates commence a legal, administrative or other action challenging the validity, enforceability or scope of any licensed patent or patent (other than the licensed patent) owned or controlled by Cullinan Pearl and its affiliates. In addition, if no active development activities have been conducted by Zai Lab and its affiliates or a permitted sublicensee within 10 months of the execution of the Zai License Agreement and such inactivity is not caused by a serious adverse event or serious adverse drug reaction, a force majeure event or Cullinan Pearl's failure to supply sufficient quantities of clinical supply product, then Zai Lab will be deemed to have abandoned development for the product and Cullinan Pearl shall have the right to terminate the Zai License Agreement upon written notice, unless Zai Lab has cured such abandonment within 60 days of such written notice. The agreement may also be terminated by mutual written agreement. Unless earlier terminated, the Zai License Agreement continues in effect on a product-by-product basis until the expiration of all applicable royalty terms with respect to all products in any region in the territory.

DKFZ/Tübingen License Agreement

In August 2020, our partially owned subsidiary Cullinan Florentine Corp., or Cullinan Florentine, entered into an Exclusive License Agreement, or the DKFZ/Tübingen License Agreement, with Deutsches Krebsforschungszentrum, or DKFZ, Eberhard Karls University of Tübingen, Faculty of Medicine, or University of Tübingen, and Universitätsmedizin Gesellschaft für Forschung und Entwicklung mbH, Tübingen, or UFE. Pursuant to the DKFZ/Tübingen License Agreement, DKFZ and University of Tübingen, collectively referred to as the Licensor, granted to Cullinan Florentine an exclusive (even as to Licensor, UFE and its and their affiliates), worldwide, milestone- and royalty-bearing, license under certain licensed patent rights, applications, technical information and know-how, with the right to grant sublicenses through multiple tiers to research, develop, commercialize or otherwise exploit licensed products, itself and through its affiliates and third parties, within the field. Cullinan Florentine has the sole right, but not the obligation, to prosecute and maintain all licensed patent rights worldwide, provided that Licensor may take over or continue such prosecution and maintenance if Cullinan Florentine elects to cease the prosecution or maintenance of a licensed patent right.

Under the DKFZ/Tübingen License Agreement, Cullinan Florentine is obligated to achieve certain regulatory and research and development performance benchmarks, or collectively, the Performance Benchmarks, by certain specified dates, or collectively, the Performance Dates. If a Performance Benchmark is not achievable by the applicable Performance Date, Cullinan Florentine may extend the Performance Date for any single Performance Benchmark by a mid-single digit amount of months by providing written notice to Licensor and paying a non-refundable, non-creditable extension fee per each such extension. Cullinan Florentine may extend the Performance Date for any single Performance Benchmark up to a low single digit amount of times, provided that Cullinan Florentine may only request an extension a mid-single digit amount of times. If Cullinan Florentine is unable to seek a further extension per the preceding sentence, then Cullinan Florentine may seek a further extension by providing written notice to Licensor and any such extension shall be subject to the prior written approval of the Licensor, such approval not to be unreasonably withheld or delayed. As of December 31, 2021, Cullinan Florentine has met the first performance benchmark to create a master cell bank.

Cullinan Florentine paid to Licensor an upfront non-refundable, non-creditable option exercise fee of $600,000 and, as partial consideration for the licenses, has issued 758,246 and 348,682 shares of its common stock to DKFZ and University of Tübingen, respectively, who together own 5.19% of Cullinan Florentine's fully diluted shares outstanding as of December 31, 2021. DKFZ and UFE were also granted the right to appoint one representative to the board of directors of Cullinan Florentine for so long as DFKZ and UFE in aggregate hold a mid-double digit percentage of shares of Cullinan Florentine common stock issued pursuant to the DFKZ/Tubingen License Agreement or until a financing threshold representing the aggregate investment in Cullinan Florentine is reached.

Additionally, Cullinan Florentine shall pay certain non-refundable, non-creditable milestone payments to Licensor upon the occurrence of certain clinical and regulatory events by a licensed product, whether triggered by Cullinan Florentine, its affiliates or sublicensees. Each milestone payment is paid one time only up to an aggregate of $28.0 million. No milestones have been achieved to date under the DKFZ/Tübingen License Agreement.

Furthermore, Cullinan Florentine is required to pay running low to mid-single digit royalty percentage on net sales of each licensed product on a country-by-country and product-by-product basis during the royalty term, subject to certain offsets or reductions. The aggregate, worldwide royalties due to Licensor for net sales of any licensed product in a calendar year shall not be reduced to an amount less than low to mid-single digit percentages. Such royalty obligations will expire on a country-by-country and product-by-product basis upon the later of (a) the expiration of the last valid claim of a patent which covers a product in such country and (b) a low double digit anniversary following the first commercial sale of a product in such country. Under certain conditions upon a first change in control, Cullinan Florentine shall pay a non-refundable, non-creditable mid-single digit percent of sale proceeds, provided, however, that such payment shall not be required following consummation of an initial public offering of Cullinan Florentine.

Either party may terminate the agreement upon a material breach by the other party or insolvency of the other party. Cullinan Florentine may terminate the DKFZ/Tübingen License Agreement for any or no reason after the first filing of an investigational new drug application or clinical trial agreement, or CTA, by providing prior written notice. Licensor may terminate the agreement by providing prior written notice, if Cullinan Florentine or any of its affiliates challenges the validity of certain patent rights. Unless earlier terminated, the DKFZ/Tübingen License Agreement continues on a perpetual basis.

MIT Exclusive Patent License Agreement

In December 2019, our partially-owned subsidiary Cullinan Amber Corp., or Cullinan Amber, entered into an Exclusive Patent License Agreement, or the MIT License Agreement, with the Massachusetts Institute of Technology, or MIT. Pursuant to the MIT License Agreement, MIT granted to Cullinan Amber an exclusive, worldwide, milestone-, equity- and royalty-bearing license under certain licensed patent rights and applications, with the right to grant sublicenses through three tiers (so long as Cullinan Amber remains an exclusive licensee of the patent rights in the field worldwide) to develop, make, have made, use, sell, have sold, offer to sell, lease, and import licensed products containing specific fusion proteins in the field of diagnosis, prognosis, prophylaxis or treatment of cancer in humans or other animals. MIT shall prepare, file, prosecute and maintain all of the patent rights, and Cullinan Amber shall cooperate with the prosecution, provide comments on patent prosecution documents, and pay all fees and costs relating to such prosecution and maintenance.

Cullinan Amber paid MIT an upfront license issue fee of $50,000 and shall reimburse MIT for certain documented, out-of-pocket expenses incurred by MIT in connection with the preparation, filing, prosecution, maintenance and defense of the patent rights. As of December 31, 2021, Cullinan Amber has reimbursed MIT for $0.1 million in connection with out-of-pocket expenses incurred by MIT in connection with the preparation, filing, prosecution, maintenance and defense of patent rights. In addition, as partial consideration, Cullinan Amber has issued 200,066 shares of common stock of Cullinan Amber to MIT, which owns five percent (5%) of Cullinan Amber's fully diluted shares outstanding as of December 31, 2021. The MIT License Agreement also provides for anti-dilution adjustments, requiring Cullinan Amber to issue MIT additional shares to ensure the shares issued to MIT do not equal less than the mid-single digit percentage amount until a financing threshold representing the aggregate investment in Cullinan Amber is reached. MIT was also granted participation rights, up to a low double-digit percentage of the securities issued, in any proposed financings of Cullinan Amber. Cullinan Amber is also responsible for paying non-refundable, creditable annual license maintenance fees in an increasing amount over a certain number of years of the license and a fixed amount subsequent to this period of time. In addition, MIT granted to Cullinan Amber an exclusive option to amend the definition of field to include expansion fields, and each such amendment would trigger the payment to MIT of an amendment fee and cause an amendment, to be negotiated upon exercise of the option, to Cullinan Amber's financial obligations with respect to the licensed products to reflect the additional rights and value being added.

Additionally, Cullinan Amber shall pay certain non-refundable, non-creditable milestone payments to MIT upon the achievement by itself or its sublicensees of certain clinical and regulatory milestones in an aggregate amount up to $7.0 million for each distinct licensed product. Each milestone payment is paid one time only up to a certain payment amount, except there are separate milestone payments payable for a second and third indication of a licensed product in an aggregate amount up to $5.5 million per product. Cullinan Amber shall also pay to MIT certain one-time milestone payments for the achievement of certain commercial milestones based on the calculation of net sales across all licensed products in all indications in an aggregate amount up to $12.5 million. No milestones have been achieved to date under the MIT License Agreement.

Under certain conditions upon a change in control, Cullinan Amber is required to pay a specified change in control fee and Cullinan Amber's clinical and regulatory milestone payments shall be increased by a certain low three-digit percentage amount.

Furthermore, Cullinan Amber is required to pay a running mid-single digit royalty percentage on net sales of all licensed products for each reporting period, subject to certain offsets or reductions. The royalties due to MIT for net sales of all licensed products shall not be reduced by more than fifty percent (50%). Cullinan Amber is also required to share any income from sublicensing the licensed products, with the percentage to be determined by the clinical phase of the licensed product, no greater than low-to-mid double-digit percentages. Such royalty obligations will expire on a country-by-country and product-by-product basis upon the expiration or abandonment of all issued patents and filed patent applications within the patent rights.

Under the MIT License Agreement, MIT must notify Cullinan Amber of certain patentable inventions conceived and reduced to practice during a certain period of time, or Improvements, and Cullinan Amber has the option to acquire rights to those improvements upon MIT's approval of a business and development plan, not to be unreasonably withheld, for a specified fee. In addition to this specified fee, Cullinan Amber's financial obligations with respect to the Improvements may be amended to reflect the value being added, such as by adding an upfront fee, maintenance fees, and milestone payments.

Cullinan Amber may voluntarily terminate the MIT License Agreement for any reason after providing written notice within a specified period of time in advance, provided that all amounts due to MIT have been paid. MIT has the right to terminate the MIT License Agreement upon written notice to Cullinan Amber if Cullinan Amber ceases to carry out its business related to the MIT License Agreement. Either party may terminate the MIT License Agreement upon a material breach by the other party. Unless earlier terminated, the MIT License Agreement shall remain in effect until the expiration or abandonment of all issued patents and the filed patent application within the patent rights.

Adimab Collaboration Agreement

In November 2018, we entered into a Collaboration Agreement, or the Adimab Collaboration Agreement, with Adimab, LLC, or Adimab. Pursuant to the Adimab Collaboration Agreement, we selected a single-digit number of biological targets against which Adimab used its proprietary platform technology to discover and/or optimize antibodies based upon mutually agreed upon research plans. Under the Adimab Collaboration Agreement, we have the ability to select a specified low single-digit number of additional biological targets against which Adimab will provide additional antibody discovery and optimization services.

During the research term and evaluation term for a given research program with Adimab, we have a non-exclusive worldwide license under Adimab's technology to perform certain research activities and to evaluate the program antibodies to determine whether we want to exercise its option to obtain a royalty-free, fully paid, non-exclusive license under Adimab's background patent rights to exploit such antibodies sublicensable through multiple tiers, or the Adimab Option. In the event we exercise the Adimab Option, we will pay an option fee for each target subject to certain adjustments.

Under the Adimab Collaboration Agreement, we paid a one-time, non-creditable, non-refundable technology access fee. We are also required to pay an annual access fee and research funding fees in connection with Adimab's full-time employees' compensation for performance of Adimab's obligations under the Adimab Collaboration Agreement. We are also obligated to make certain research delivery, clinical and sales milestone payments to Adimab in an aggregate amount of up to $15.8 million for each product, on a product-by-product basis, subject to certain reductions and discounts.

Furthermore, we are obligated to pay certain royalty payments on a product-by-product basis at a low single-digit percentage of annual aggregate worldwide net sales. Such royalty obligations will expire on a country-by-country and product-by-product basis upon the later of (a) a certain low double-digit number of years after the first commercial sale of such product in such country and (b) the expiration of the last issued and not expired, permanently revoked, or invalid claim within a program patent covering such product as defined in the agreement.

We may terminate the Adimab Collaboration Agreement at any time, for any reason, upon a specified period advance written notice. The term of the Adimab Collaboration Agreement expires upon the last research program's evaluation term in the event no Adimab Option is exercised or, in the event an Adimab Option is exercised, after the royalty term thereof expires at the later of a specified period or invalid patent coverage of the relevant product.

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by obtaining, maintaining, defending, and enforcing patents and other intellectual property, in the United States and internationally, for our proprietary therapeutic molecules, technology, improvements, platforms, product candidates and components thereof, novel biological discoveries, new therapeutic approaches and potential indications, and other inventions that are important to our business. For our product candidates, generally we initially pursue patent protection covering compositions of matter, methods of use, and methods of production. Throughout the development of our product candidates, we will seek to identify additional means of obtaining patent protection that would potentially enhance commercial success, including improvement to pharmaceutical formulations, methods of use and production.

As of December 31, 2021, our patent portfolio includes 10 patent families, including both patent applications we own, and issued patents and patent applications exclusively in-licensed from external technology originators in a respective field. Specifically, we have exclusively in-licensed at least 2 issued US patents, 38 patents issued in foreign jurisdictions, and 129 patent applications pending worldwide. Our earliest issued patents are expected to expire in 2034. Later patents, that may issue from our pending patent applications, are expected to expire between 2037 and 2041, excluding any patent term adjustments or extensions, if applicable, that may be available. As to the patent term extension to restore patent term effectively lost following patent grant but during the FDA regulatory review process, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval.

Our portfolio related to our CLN-081 product candidate includes five patent families directed to compositions, and methods of using such compositions therapeutically. The first family, which is in-licensed from Taiho Pharma, covers compositions with claims directed to our CLN-081 product candidate. This patent family includes issued patents in the U.S., major European countries and China, and such patents are expected to expire in 2034, excluding any patent term adjustments or extensions, if applicable. Within this family, patent application were filed in Australia, Brazil, Canada, China, Hong Kong, Macau, European Patent Office, Austria, Belgium, Switzerland, Czech Republic, Germany, Denmark, Spain, Finland, France, United Kingdom, Greece, Hungry, Ireland, Italy, Netherlands, Norway, Poland, Portugal, Romania, Sweden, Turkey, Indonesia, India, Japan, Korea, Mexico, Malaysia, Philippines, Russian Federation, Singapore, Thailand, Taiwan, United States of America, and Vietnam. Three families, also in-licensed from Taiho Pharma, include both issued patents and pending patent applications with claims directed to methods of using the CLN-081 product candidate in treating additional diseases where we believe CLN-081 has potential to be active. The first of these three families, titled “Selective Inhibitor of Exon20 Insertion Mutant EGFR”, is expected to expire in 2037, excluding any patent term adjustments or extensions, if applicable, that may be available. Within this family, patent applications have so far been filed in Australia, Brazil, Canada, China, European Patent Office, Indonesia, Israel, Japan, Jordan, Korea, Malaysia, Mexico, New Zealand, Philippines, Russian Federation, Singapore, Thailand, United States of America, Vietnam, South Africa, and Taiwan. The second of these three families, titled “Selective Inhibitor of Exon 18 and Exon 21 Mutant EGFR”, is expected to expire in 2038, excluding any patent term adjustments or extensions, if applicable, that may be available. Within this family, patent applications have so far been filed in Australia, Canada, China, European Patent Office, Israel, Korea, Taiwan, Singapore, and United States of America. The third of these three families, titled “L718 and/or L792 mutant type treating resistance EGFR inhibitor”, is expected to expire in 2039, excluding any patent term adjustments or extensions, if applicable, that may be available. An international application has been filed under this family. We own a fifth application, which is directed to certain methods of use and dosing protocols. This family is expected to expire in 2041, excluding any patent term adjustments or extensions, if applicable, that may be available. A PCT application and an application in Taiwan have been filed under this family.

We, through our subsidiary Cullinan MICA, own three patent families related to our CLN-619 product candidate, including patent families directed to compositions, and methods of using such compositions therapeutically. The family of patent applications with claims directed to CLN-619 compositions, if issued, are expected to expire in 2039, excluding any patent term adjustments or extensions, if applicable. For the first of these patent families, patent applications have so far been filed in Australia, Brazil, Canada, China, European Patent Office, India, Indonesia, Israel, Japan, Korea, Malaysia, Mexico, New Zealand, Philippines, Russian Federation, Singapore, Thailand, United States of America, Vietnam and South Africa. A family of patent applications with claims directed to additional anti-MICA antibody compositions, if issued, are expected to expire in 2039, excluding any patent term adjustments or extensions, if applicable. Patent applications have so far been filed for this family in Australia, Brazil, Canada, China, European Patent Office, India, Israel, Japan, Korea, Mexico, New Zealand, Russian Federation, United States of America, South Africa and Hong Kong. A patent family with claims directed to additional anti-MICA antibody compositions and methods of use, if issued, is expected to expire in 2043, excluding any patent term adjustments or extensions, if applicable. A United States provisional application has been filed under this family.

Our portfolio related to our CLN-049 product candidate includes one patent family, in-licensed from the University of Tubingen, directed to compositions, and methods of using such compositions therapeutically. This family of patent applications contain claims directed to CLN-049 compositions, which, if issued, are expected to expire in 2039, excluding any patent term adjustments or extensions, if applicable. Patent applications have so far been filed for this family in the United States, Europe, China, Australia, Brazil, Canada, Indonesia, Israel, India, Mexico, New Zealand, Philippines, Singapore, Thailand, South Korea, Vietnam, South Africa, Russia, Japan, Malaysia and Hong Kong.

Our portfolio related to our CLN-617 product candidate and Cullinan Amber program includes two patent families. The first family was in-licensed from MIT, directed to compositions, and methods of using such compositions therapeutically. This family of patent applications contain claims covering Cullinan Amber related compositions, which, if issued, are expected to expire in 2039, excluding any patent term adjustments or extensions, if applicable. An international application has been filed under this family. The second family is a PCT application owned by Cullinan Amber, which is directed to certain compositions, and methods of using such compositions therapeutically. This family contains claims covering additional Cullinan Amber related compositions, which, if issued, are expected to expire in 2041, excluding any patent term adjustments or extensions, if applicable.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office, or the USPTO, review period in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period.

Manufacturing

We do not own or operate, and currently have no plans to establish, any Good Manufacturing Practice, or GMP, manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates obtain marketing approval. We also rely, and expect to continue to rely, on third parties to package, label, store and distribute our investigational product candidates and, if marketing approval is obtained, our commercial products. We believe this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment and personnel while also enabling us to focus our expertise and resources on the development of new product candidates.

We receive material from our contract manufacturing organizations, or CMOs, for preclinical testing. We receive clinical supply material manufactured in compliance with current Good Manufacturing Practice requirements, or cGMPs, and we conduct audits before and during the trial, in cooperation with a CMO, to ensure compliance with the mutually agreed process descriptions and cGMP regulations.

Our lead product candidate, CLN-081, is a small molecule that is manufactured in synthetic processes from available starting materials. The chemistry appears amenable to scale-up and does not currently require unusual equipment in the manufacturing process. We generally expect to rely on third parties for the manufacture of companion diagnostics, which are assays or tests that identify an appropriate patient population for CLN-081. Depending on the technology solutions we choose, we may rely on multiple third parties to manufacture and sell a single test.

To date, we have obtained drug substance, or DS, for CLN-049 and CLN-619, our most advanced biologic candidates, from single-source third-party contract manufacturers, WuXi Biologics, WuXi, and Abzena, respectively. While any reduction or halt in supply of DS from these contract manufacturers could limit our ability to develop our product candidates until we find a qualified replacement contract manufacturer, we have procured sufficient DS to initiate our planned clinical studies for both CLN-049 and CLN-619. WuXi has also supplied CLN-049 drug product, or DP, and we have procured sufficient CLN-049 DP for our planned clinical studies. We have engaged a separate contract manufacturer to produce CLN-619 DP, Vetter, which has manufactured sufficient DP to initiate our planned clinical studies. We intend to put in place agreements under which our third-party contract manufacturers will generally provide us with necessary quantities of DS and DP on a project-by-project basis, based on our projected development and commercial supply needs.

Our CLN-049 and CLN-619 product candidates are manufactured from a vial of a master cell bank, or MCB, from the respective production cell lines. We have one MCB for each program that was produced and tested in accordance with cGMPs and applicable regulations. For CLN-049, the MCB is stored in one location, and we are making plans to store at a second location. The research cell bank, or RCB, for CLN-049 is stored at a different location from the MCB. For CLN-619, the MCB is stored at two independent sites, and the RCB is stored at a separate location from the RCB locations. We intend to produce working cell banks for each product candidate later in product development. It is possible that we could lose multiple cell banks from multiple locations and have our manufacturing severely impacted by the need to replace the cell banks. However, we believe we have adequate backup should any particular cell bank be lost in a catastrophic event.

Governmental Regulation

United States Food and Drug Administration Regulation

The United States Food and Drug Administration, or FDA, and other U.S. regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, safety, efficacy, import, export, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of drugs and biologics such as those we are developing. We, along with our vendors, collaboration partners, clinical research organizations, or CROs, clinical trial investigators, and CMOs will be required to navigate the various preclinical, clinical, manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our product candidates. The process of obtaining regulatory approvals of drugs and ensuring subsequent compliance with appropriate United States federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable regulatory requirements at any time during the product development process or post-approval may subject an applicant to delays in development or approval, as well as administrative and judicial sanctions.

In the United States, the FDA regulates drugs under the FDCA, and biologics under the FDCA and the Public Health Service Act, or PHSA, and their implementing regulations. Both drugs and biologics are also subject to other federal, state and local statutes and regulations. Our product candidates are early-stage and have not been approved by the FDA for marketing in the United States.

Our product candidates must be approved for therapeutic indications by the FDA before they may be marketed in the United States. For our drug product candidates regulated under the FDCA, such as CLN-081, FDA must approve a New Drug Application, or NDA. For our biologic product candidates regulated under the FDCA and PHSA, such as CLN-049 and CLN-619, FDA must approve a Biologics License Application, or BLA. The process is similar and generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with Good Laboratory Practice, or GLP, requirements;
- submission to the FDA of an Investigational New Drug, or IND application which must become effective before clinical trials may begin and must be updated annually and when certain changes are made;
- approval by an Institutional Review Board, or IRB, or independent ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with Good Clinical Practice, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- preparation and submission to the FDA of an NDA or BLA;
- payment of user fees for FDA review of the NDA or BLA, unless waived;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the product will be produced to assess compliance with current Good Manufacturing Practices, or cGMPs to assure that the facilities, methods and controls are adequate to ensure and preserve the drug or biological product’s identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the clinical trial sites that generated the data in support of the NDA or BLA; and

- FDA review and approval of the NDA or BLA, including, where applicable, consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States.

Preclinical and Clinical Trials

Before testing any drug or biologic in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of chemistry, formulation and stability, as well as *in vitro* and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP requirements for safety and toxicology studies. In the United States, the results of the preclinical studies, together with manufacturing information and analytical data must be submitted to the FDA as part of an IND.

An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before clinical trials may begin. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational product. In the United States, the IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Some long-term preclinical testing may continue after the IND is submitted. Accordingly, submission of an IND may or may not result in FDA authorization to begin a trial.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness, including stopping rules that assure a clinical study will be stopped if certain adverse events should occur. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB, either centrally or at each institution at which the clinical trial will be conducted, to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable related to the anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

The FDA may, at any time during the initial 30-day IND review period or while clinical trials are ongoing under the IND, impose a partial or complete clinical hold based on concerns for patient safety and/or noncompliance with regulatory requirements. This order issued by the FDA would delay 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. Imposition of a clinical hold could cause significant delays or difficulties in completing planned clinical studies in a timely manner. In addition, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trials to public registries. In the United States, information about applicable clinical trials, including clinical trials results, must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website.

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

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

- Phase 1—Phase 1 clinical trials involve initial introduction of the investigational product in a limited population of healthy human volunteers or patients with the target disease or condition in the case of some products for severe or life-threatening diseases. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, evaluate the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- Phase 2—Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3—Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA or BLA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA. Failure to exhibit due diligence with regard to conducting required Phase 4 clinical trials could result in withdrawal of approval for products.

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

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the drug or biological characteristics of the product candidate and finalize a process for manufacturing the drug product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life and to identify appropriate storage conditions for the product candidate.

Expanded Access

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. 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 the following groups: 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.

There is no requirement for a company to provide expanded access to its investigational product. However, if a company decides to make its investigational product available for expanded access, FDA reviews each request for expanded access and determines if treatment may proceed. Expanded access may be appropriate when all of the following criteria apply: the patient has 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 benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context of the disease or condition to be treated; and providing the investigational product for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides an additional mechanism for patients with a life-threatening condition who have exhausted approved treatments and are unable to participate in clinical trials to access certain investigational products that have completed a Phase I clinical trial, are the subject of an active IND, and are undergoing investigation for FDA approval. Unlike the expanded access framework described above, Right to Try does not require FDA to review or approve requests for use of the investigational product. There is no obligation for a company to make its investigational products available to eligible patients under the Right to Try Act.

Under the FDCA, sponsors of one or more investigational products for the treatment of a serious disease or condition must make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. 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. There is no obligation for a sponsor to make its investigational products available to eligible patients as a result of the Right to Try Act, but the sponsor must develop an internal policy and respond to patient requests according to that policy.

FDA Marketing Application Review and Approval Process

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

In addition, under the Pediatric Research Equity Act, or PREA, certain NDAs and BLAs and certain supplements to an NDA or BLA must contain data to assess the safety and effectiveness of the drug or biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act requires that a sponsor who is planning to submit a marketing application or supplement to an application for a drug or biological product that includes a new active ingredient or clinically active component, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan within 60 days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. Unless otherwise required by regulation, PREA does not apply to a drug or biological product for an indication for which orphan designation has been granted.

In the United States, the FDA reviews all submitted NDAs and BLAs to ensure they are sufficiently complete to permit substantive review before it accepts them for filing and may request additional information rather than accepting the NDA or BLA for filing. The FDA makes a decision on accepting an NDA or BLA for filing within 60 days of receipt, and such decision could include a refusal to file by the FDA. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the application. The FDA reviews an NDA or BLA to determine, among other things, whether the product is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards, including cGMP requirements, designed to assure and preserve the product's identity, strength, quality and purity. Under the goals and polices agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA targets ten months, from the filing date, in which to complete its initial review of an original NDA or BLA and respond to the applicant, and six months from the filing date of an original NDA or BLA filed for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

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

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

Before approving an NDA or 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 compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA. To assure GMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

After evaluating the application and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter will usually describe all of the deficiencies that the FDA has identified in the NDA or BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may recommend actions that the applicant might take to place the NDA or BLA in condition for approval, including requests for additional information or clarification. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed, the FDA may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a product's safety or efficacy after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a risk evaluation and mitigation strategy, or REMS, which can materially affect the potential market and profitability of the product. 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-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation, or ODD, to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with either a patient population of fewer than 200,000 individuals in the United States, or a patient population of greater than 200,000 individuals in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States of that drug or biologic. ODD must be requested before submitting an NDA or BLA. After the FDA grants ODD, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The granting of ODD does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has received ODD and subsequently receives the first FDA approval for that drug for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same drug or biologic for the same indication for seven years from the approval of the NDA or BLA, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of ODD are tax credits for certain research and a waiver of the NDA or BLA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received ODD. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Development and Review Programs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs and biologics to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, priority review and accelerated approval. Fast Track designation, Breakthrough Therapy designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

A new drug or biologic is eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the FDA may initiate review of sections of a Fast Track product’s application before the application is complete upon satisfaction of certain conditions.

In addition, a new drug or biological product may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic, alone or in combination with or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track, or Breakthrough Therapy designation, may also be eligible for priority review. A product is eligible for priority review if it is intended to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness. For original NDAs and BLAs, priority review designation means the FDA’s goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

The FDA may grant accelerated approval to a product intended to treat a serious or life-threatening disease or condition that generally provides a meaningful therapeutic advantage to patients over available treatments, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, 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.

For drugs granted accelerated approval, the FDA generally requires sponsors to conduct, in a diligent manner, adequate and well-controlled post-approval confirmatory studies to verify and describe the product's clinical benefit. Failure to conduct required post-approval studies with due diligence, failure to confirm a clinical benefit during the post-approval studies, or dissemination of false or misleading promotional materials would allow the FDA to withdraw the product approval on an expedited basis. All promotional materials for product candidates approved under accelerated approval are subject to prior review by the FDA unless FDA informs the applicant otherwise.

FDA Approval or Clearance of Companion Diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to the development and approval of therapeutic products intended for use with *in vitro* companion diagnostics. According to the guidance, for novel drugs and biologics, 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 therapeutic products and *in vitro* companion diagnostic devices on issues related to co-development of the products.

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 a 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.

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 investigational device exemption, or IDE, regulation. The IDE regulations distinguish 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. Many companion diagnostics are considered significant risk devices due to their role in diagnosing a disease or condition. 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.

In the United States, device manufacturers are also subject to FDA's medical device reporting regulations, which require that a manufacturer report to the FDA if a device it markets may have caused or contributed to a death or serious injury, or has malfunctioned and the device or a similar device that it markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur, and FDA's correction and removal reporting regulations, which require that manufacturers report to the FDA corrections or removals if undertaken to reduce a risk to health posed by the device or to remedy a violation of the FDCA that may present a risk to health. 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.

Post-Approval Requirements for Drugs and Biologics in the United States

In the United States, drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, reporting of adverse experiences with the product, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe approved products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, including not only by Company employees but also by agents of the Company or those speaking on the Company's behalf, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties, including liabilities under the False Claims Act where products carry reimbursement under federal health care programs. Promotional materials for approved drugs and biologics must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the product, including proposed changes to the indication, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new or supplemental NDA or BLA, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-market testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug and biologics manufacturers and their subcontractors involved in the manufacture and distribution of approved products 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, which impose certain procedural and documentation requirements upon us and our CMOs. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution. There is also a continuing, annual program fee for any marketed product.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- mandated modification of promotional materials and labeling and issuance of corrective information;

- fines, warning letters, or untitled letters;
- holds on clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product recall, seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs.

United States Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of our future product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit restoration of the patent term of up to five years as compensation for patent term lost during the FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Regulatory exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

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

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

United States Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars in the United States. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or 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, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its 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.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the ACA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and regulatory interpretation of the BPCIA remain subject to significant uncertainty.

Other United States Regulatory Matters

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

Other Healthcare Laws in the United States

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

- The federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bride, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid; a person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. On December 2, 2020, OIG published further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others, although the portion of the rule eliminating safe harbor protection for certain rebates related to the sale or purchase of a pharmaceutical product from a manufacturer to a plan sponsor under Medicare Part D was delayed to January 2026 under the Infrastructure Investment and Jobs Act. Implementation of the this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. We continue to evaluate what effect, if any, these rules will have on our business;
- The federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using, or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government;
- Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- The federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies;
- The Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for knowingly and willfully executing a scheme, or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, or falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity need not have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, imposes, among other things, specified requirements on covered entities and their business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- The Physician Payments Sunshine Act, enacted as part of the ACA, imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, for certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. In addition, many states also require reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts; and

- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party-payors, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, and restrict marketing practices or require disclosure of marketing expenditures and pricing information; state and local laws that require the registration of pharmaceutical sales representatives; state and foreign laws that govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts.

In addition, pharmaceutical manufacturers may also be subject to United States federal and state consumer protection and unfair competition laws and regulations, which broadly regulate marketplace activities and that potentially harm consumers.

The distribution of drugs and biological products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

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

United States Coverage and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, 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 regulatory approvals. Factors payors consider in determining reimbursement are based on whether the product is a covered benefit under its health plan; safe, effective and medically necessary; appropriate for the specific patient; cost-effective; and neither experimental nor investigational. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

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

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the United States Congress enacted the ACA, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court and members of Congress have introduced several pieces of legislation aimed at significantly revising or repealing the ACA. The United States Supreme Court is expected to rule on a legal challenge to the constitutionality of the ACA in early 2021. The implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030 unless additional Congressional action is taken. These will be suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, with a 1% reduction being reinstated from April 2022 through June 2022 and the full 2% reduction resuming thereafter, . In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, in the United States, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Further, the Trump administration previously released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has already implemented certain measures. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. However, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions. In addition, individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, it is possible that additional governmental action is taken to address the COVID-19 pandemic.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

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 or 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 healthcare 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, i.e., 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 products, if approved in those countries.

Compliance with Other Federal and State Laws or Requirements; Changing Legal Requirements

If any products that we may develop are made available in the United States to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, labeling, packaging, distribution, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws, among other requirements to we may be subject.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, exclusion from federal healthcare programs, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, relabeling or repackaging, or refusal to allow a firm to enter into supply contracts, including government contracts. Any claim or action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on marketing, sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling or packaging; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

European Drug Development

In the European Union, our future products also may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. 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. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will apply following confirmation of full functionality of the Clinical Trials Information System (CTIS), the centralized EU portal and database for clinical trials foreseen by the Regulation, through an independent audit, currently expected to occur in December 2021. The new Regulation will be directly applicable in all Member States (and so does not require national implementing legislation in each Member State), and aims at simplifying and streamlining the approval of clinical studies in the EU, for instance by providing for a streamlined application procedure via a single point and strictly defined deadlines for the assessment of clinical study applications.

We are in the process of applying to renew our status with EMA as a small and medium-sized enterprise, or SME. If we obtain SME status with EMA, it will provide access to administrative, regulatory and financial support, including fee reductions for scientific advice and regulatory procedures.

European Drug Marketing

Much like the Anti-Kickback Statue prohibition in the United States, 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 also prohibited in the European Union. The provision of benefits or advantages to induce or reward improper performance generally is governed by the national anti-bribery laws of European Union Member States, and the Bribery Act 2010 in the U.K. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the EU.

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 EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

European Drug Review and Approval

In the European Economic Area, or EEA, which is comprised of the Member States of the European Union together with Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a marketing authorization, or MA. There are two types of marketing authorizations.

- The centralized MA is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and is valid throughout the entire territory of the EEA. The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines) and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union. Under the centralized procedure, the maximum timeframe for the evaluation of a MA application by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MA application considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a MA application under the accelerated assessment procedure is of 150 days, excluding stop-clocks, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this national MA can be recognized in other Member States through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure. Under the decentralized procedure, an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SmPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Concerned Member States, or CMSs) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the CMSs).

Under the procedures described above, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized MAs (under the Northern Irish Protocol, centralized MAs will continue to be recognized in Northern Ireland). All medicinal products with a current centralized MA were automatically converted to Great Britain MAs on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain MA. A separate application will, however, still be required.

European Data and Marketing Exclusivity

In the EEA, innovative medicinal products (including both small molecules and biological medicinal products), sometimes qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization, for a period of eight years from the date on which the reference product was first authorized in the EEA. During the additional two-year period of market exclusivity. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. The overall ten-year period will be extended to a maximum of 11 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 their authorization, are determined to bring a significant clinical benefit in comparison with currently approved therapies.

European Orphan Designation and Exclusivity

In the EEA, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions which either affect not more than 5 in 10,000 persons in the European Union community, or where it is unlikely that the development of the medicine would generate sufficient return to justify the necessary investment in its development. In each case, no satisfactory method of diagnosis, prevention or treatment must have been authorized (or, if such a method exists, the product in question would be of significant benefit to those affected by the condition).

In the EEA, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following marketing approval for the orphan product. This period may be reduced to six years if, at the end of the fifth year, it is established that the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. During the period of market exclusivity, marketing authorization may only be granted to a "similar medicinal product" for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the marketing authorization holder for the authorized product consents to a second orphan medicinal product application; or (iii) the marketing authorization holder for the authorized product cannot supply enough orphan 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. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

European Pediatric Investigation Plan

In the EEA, companies 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. 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 PDCO can grant a deferral 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. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when this data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP (even where such results are negative) are eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval). 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

In June 2016, the electorate in the UK voted in favor of leaving the EU (commonly referred to as "Brexit"). Thereafter, in March 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty and the UK formally left the EU on January 31, 2020. A transition period began on February 1, 2020, during which EU pharmaceutical law remained applicable to the UK, which ended on December 31, 2020. Since the regulatory framework in the UK covering the quality, safety and efficacy of medicinal products, clinical trials, marketing authorization, commercial sales and distribution of medicinal products is derived from EU Directives and Regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the UK, as UK legislation now has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the UK in the long-term. The MHRA, the UK medicines and medical devices regulator, 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.

European Data Collection

The collection and use of personal health data in the European Economic Area, or the EEA, governed by the GDPR, which became effective May 25, 2018. The GDPR applies to any company established in the EEA and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EU or the monitoring of the behavior of data subjects in the European Union. The GDPR enhances data protection obligations for data controllers of personal data, including stringent requirements relating to the consent of data subjects, expanded disclosures about how personal data is used, requirements to conduct privacy impact assessments for "high risk" processing, limitations on retention of personal data, special provisions for "sensitive information" including health and genetic information of data subjects, mandatory data breach notification and "privacy by design" requirements, and direct obligations on service providers acting as data processors. The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the U.S. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA Member States may result in fines up to 20 million euros or 4% of a company's global annual revenues for the preceding financial year, whichever is higher. Moreover, the GDPR grants data subjects the right to request deletion of personal information in certain circumstances, and claim material and non-material damages resulting from infringement of the GDPR. Given the breadth and depth of changes in data protection obligations, maintaining compliance with the GDPR, will require significant time, resources and expense, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations, and prospects.

Corporate Information

Cullinan Pharmaceuticals, LLC was formed in September 2016 and was subsequently renamed Cullinan Oncology, LLC, or the LLC entity, in November 2017. The LLC entity's, wholly-owned subsidiary, Cullinan Management, Inc., or the Corporation, was formed in September 2016.

Immediately before to our initial public offering, or IPO, in January 2021 we completed a reorganization with the LLC entity. Pursuant to a contribution agreement, where the LLC entity contributed all of the stock it owned of each of Cullinan Amber Corp., Cullinan Apollo Corp., Cullinan Florentine Corp., Cullinan MICA Corp. and Cullinan Amber Corp., Cullinan Pearl Corp., and Cullinan MICA Corp., or collectively, the Asset Subsidiaries, to the Corporation in exchange for the Corporation's common stock, and as a result, the Asset Subsidiaries became subsidiaries of the Corporation, or the Contribution. The LLC entity then merged with and into the Corporation with the Corporation being the surviving entity of such merger, or the LLC Merger. As a result of the LLC Merger, the holders of existing units in the LLC entity exchanged those units for corresponding shares of capital stock of the Corporation.

On January 8, 2021, our common stock began trading on the Nasdaq Global Select Market under the symbol "CGEM." On February 25, 2021, our corporate name was changed to Cullinan Oncology, Inc. Our principal executive offices are located at One Main Street, Suite 520, Cambridge, MA 02142 and our telephone number is (617) 410-4650.

We use various trademarks and trade names in our business, including, without limitation, our corporate name and logo. All other trademarks or trade names referred to in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of: (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of the IPO, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Employees

As of December 31, 2021, we had 31 full-time employees and three consultants. Twelve of our employees have M.D. or Ph.D. degrees. Within our workforce, 17 employees are engaged in research and development and 14 are engaged in business development, finance, legal, and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Available Information

Our corporate website address is https://www.cullinanoncology.com. Information contained on or accessible through our website is not a part of this Annual Report, and the inclusion of our website address in this Annual Report is an inactive textual reference only.

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Electronic Data Gathering, Analysis and Retrieval system at *http://www.sec.gov*. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our consolidated financial statements and related notes appearing elsewhere in this Annual Report and the section of this Annual Report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" before you make an investment decision. The risks described below are not the only risks that we face. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and prospects. As a result, the market price of our common stock could decline, and you may lose all or part of your investment in our common stock.

Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may adversely affect our business. See "Special Note Regarding Forward-Looking Statements" In this Annual Report on Form 10-K.

Risks Related to the Development of Our Product Candidates

Our preclinical studies and clinical trials may fail to demonstrate adequately the safety and efficacy of any of our product candidates, which would prevent or delay development, regulatory approval, and commercialization.

Before obtaining regulatory approvals for the commercial sale of our product candidates, including CLN-081, CLN-049, and CLN-619, we must demonstrate the safety and efficacy of our investigational product candidates for use in each target indication through lengthy, complex, and expensive preclinical studies and clinical trials. If the results of our ongoing or future preclinical studies and clinical trials are inconclusive with respect to the safety and efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for such product candidates. In some instances, there can be significant variability in safety or efficacy results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants.

In addition to our ongoing clinical trial of CLN-081, patients have been, and will likely continue to be, treated with CLN-081 under an expanded access or "compassionate use" program. To the extent the experiences of patients being treated in this program are inconsistent with or less favorable than the results of our ongoing or planned company-sponsored trials with CLN-081, it may negatively affect perceptions of CLN-081, our other product candidates, or our business. In addition, the U.S. Food and Drug Administration, or the FDA, or foreign regulatory authorities may require us to obtain and submit additional clinical data due to these inconsistent or unfavorable results, which could delay clinical development or marketing approval of CLN-081 or potentially our other product candidates.

Our approach to the identification, discovery, and development targeted oncology and product candidates may never lead to marketable products.

The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. The patient populations for certain of our product candidates are limited to those with specific target mutations, and we will need to screen and identify these patients with the targeted mutations. Successful identification of patients is dependent on several factors, including achieving certainty as to how specific genetic alterations and larger classes of mutations, such as EGFR exon 20 mutations, respond to our product candidates, and developing companion diagnostics to identify such genetic alterations. Furthermore, even if we are successful in identifying patients, we cannot be certain that the resulting patient populations for each mutation or class of mutations will be large enough to allow us to successfully obtain indications for each mutation type and to commercialize our products and achieve profitability. The FDA and other regulatory authorities may not agree with our approach to seek labeling for groups of related mutations, rather than individual mutations, and may require us to conduct additional trials and obtain separate approvals for each individual mutation, which may further affect our ability to successfully commercialize our products, if approved. In addition, even if our approach is successful in showing clinical benefit for tumors harboring certain targeted mutations, we may never successfully identify additional oncogenic mutations. Therefore, we do not know if our approach of treating patients with targeted oncology therapies will be successful, and if our approach is unsuccessful, our business will suffer.

If we are unable to successfully validate, develop, and obtain regulatory approval for any required companion diagnostic tests for our product candidates or experience significant delays in doing so, we may fail to obtain approval or may not realize the full commercial potential of these product candidates.

In connection with the clinical development of our product candidates for certain indications, we need to develop or obtain access to *in vitro* companion diagnostic tests to identify patient subsets within a disease category who may derive benefit from our product candidates, as we are targeting certain genetically defined populations for our treatments. Such companion diagnostics may be used during our clinical trials and may be required in connection with the FDA approval of our product candidates. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory, and logistical challenges. Companion diagnostics are subject to regulation by the FDA, European Medicines Agency, or EMA, and other regulatory authorities as medical devices and require separate regulatory approval prior to commercialization.

Given our limited experience in developing and commercializing diagnostics, we may rely on third parties for the design, development, and manufacture of companion diagnostic tests for our product candidates that may require such tests. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. We and our future collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics. We and our future collaborators also may encounter difficulties in developing, obtaining regulatory approval for, manufacturing, and commercializing companion diagnostics similar to those we face with respect to our product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for these product candidates, or experience delays in doing so, the development of these therapeutic product candidates may be adversely affected or these product candidates may not obtain marketing approval or such approval may be delayed, and we may not realize the full commercial potential of any of these product candidates that obtain marketing approval. As a result, our business, results of operations, and financial condition could be materially harmed. In addition, a diagnostic company with whom we contract may decide to discontinue developing, selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

Preclinical and clinical development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future preclinical studies or clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate.

Our preclinical studies and future clinical trials may not be successful. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates.

Additionally, some of the clinical trials we conduct may be open-label in study design and may be conducted at a limited number of clinical sites on a limited number of patients. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect, as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Given that our Phase 1/2a clinical trial of CLN-081 includes an open-label dosing design, the results from this clinical trial may not be predictive of future clinical trial results with this or other product candidates for which we conduct an open-label clinical trial when studied in a controlled environment with a placebo or active control.

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

If a sufficient number of our product candidates generally prove to be ineffective, unsafe or commercially unviable, our entire pipeline may have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations and prospects.

We may encounter substantial delays in preclinical and clinical trials, or may not be able to conduct or complete preclinical or clinical trials on the expected timelines, if at all.

We may experience delays in initiating or completing preclinical studies or clinical trials, including as a result of delays in obtaining, or failure to obtain, the FDA's clearance to initiate clinical trials under future investigational new drug applications, or INDs. Additionally, we cannot be certain that preclinical studies or clinical trials for our product candidates will not require redesign, enroll an adequate number of subjects on time, or be completed on schedule, if at all. We may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or terminate our trials, or delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- we may receive feedback from regulatory authorities that requires us to modify the design or implementation of our preclinical studies or clinical trials, including our ability to commence a clinical trial;
- we may fail or be delayed in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- we may be unable to add or be delayed in adding a sufficient number of clinical trial sites and obtaining institutional review board, or IRB, or independent ethics committee approval at each clinical trial site;
- preclinical studies or clinical trials of our product candidates may fail to show safety or efficacy or otherwise produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or abandon our research efforts for our other product candidates;
- preclinical studies or clinical trials of our product candidates may not produce differentiated or clinically significant results across tumor types or indications;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of our clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls or be unable to provide us with sufficient product supply to conduct and complete preclinical studies or clinical trials of our product candidates in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate, for example, if we experience delays or challenges in identifying patients with the mutations required for our clinical trials, we may have to reimburse sites for genetic sequencing costs in order to encourage sequencing of additional patients;
- we may experience difficulties in having subjects complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites may deviate from clinical trial protocol or drop out of a clinical trial;
- we may be unable to obtain or be delayed in obtaining sufficient product supply of product candidate for use in preclinical studies or clinical trials from third-party suppliers;
- the quality of our product candidates or other materials necessary to conduct preclinical studies or clinical trials of our product candidates may be insufficient or inadequate, and any transfer of manufacturing activities may require unforeseen manufacturing or formulation changes;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about our product candidates;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- future collaborators may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

If we are required to conduct additional preclinical studies or clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these studies, trials or tests are not positive or are only moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs, or ethics committees of the institutions in which such clinical trials are being conducted, by the data safety monitoring board, if any, for such clinical trial or by the FDA or other regulatory authorities. Such authorities may suspend, place on clinical hold, or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from the product candidates, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

We are early in our development efforts and are substantially dependent on our lead product candidates, CLN-081, CLN-049 and CLN-619. If we are unable to advance these or any of our other product candidates through clinical development, or to obtain regulatory approval and ultimately commercialize any such product candidates, either by ourselves or with or by third parties or if we experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts. Our lead program, CLN-081, is in a Phase 1/2a clinical trial. In December 2021, we initiated Phase 1 clinical trials for CLN-049 and CLN-619. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful clinical development and eventual commercialization of CLN-081, CLN-049, and CLN-619, and one or more of our other product candidates, if approved. The success of our product candidates will depend on several factors, including the following:

- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- successful completion of preclinical studies;

- regulator acceptance of and maintenance of INDs or comparable foreign applications that allow commencement and continuation of our planned clinical trials or future clinical trials;
- successful initiation of clinical trials;
- successful patient enrollment in and completion of clinical trials;
- positive results from our preclinical data and clinical trials that support a demonstration of safety and effectiveness and an acceptable risk-benefit profile for our product candidates that are satisfactory to the FDA or any foreign regulatory authority for marketing approval in the intended population;
- receipt of marketing approvals for our product candidates and any companion diagnostics from applicable regulatory authorities;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates, if any product candidates are approved;
- establishing sales, marketing, and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other cancer therapies;
- obtaining and maintaining third-party coverage and adequate reimbursement; and
- maintaining a continued acceptable safety, tolerability, and efficacy profile of our products following approval.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays in our ability to successfully commercialize product candidates, or be unable to commercialize product candidates at all. If we are unable to advance our preclinical stage product candidates to clinical development, successfully complete clinical trials for our product candidates, obtain regulatory approval, and ultimately commercialize our product candidates, our business will be materially harmed.

There is no guarantee that the results obtained in current preclinical studies or our ongoing clinical trials of CLN-81 in EGFR exon 20 insertion mutation non-small-cell lung carcinoma, or NSCLC, patients, CLN-049 in patients with relapsed or refractory acute myeloid leukemia, or r/r AML, or CLN-619 in patients with solid tumors will be sufficient to obtain regulatory approval or marketing authorization for such product candidates. For example, the FDA may require us to complete trials in addition to our ongoing Phase 1/2a trial prior to granting regulatory approval. Although we believe our product candidates and programs are uncorrelated, negative results in the development process of one product candidate could impact other product candidates or programs. For each of our product candidates, antitumor activity may be different in each of the different tumor types we plan on evaluating in our clinical trials. Even as we build clinical experience with our product candidates, we may need to further discuss or meet with the FDA to agree on the optimal patient population, study design, and size for each trial in order to obtain regulatory approval, any of which may require significant additional resources and delay the timing of our clinical trials and ultimately the approval, if any, of any of our product candidates.

Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates, and ultimately delay or prevent regulatory approval.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of completion of our clinical trials depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical trials if we encounter difficulties in enrollment. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. In particular, because we are focused on patients with specific genetic mutations for the development of CLN-081, our ability to enroll eligible patients may be limited or enrollment may be slower than we anticipate due to the small eligible patient population. For our Phase 1 trial evaluating CLN-049 in r/r AML patients, our ability to enroll eligible patients may be limited or enrollment may be slower than we anticipate due to enrollment criteria and the single ascending dose design. In addition, our ability to enroll patients has been delayed and may continue to be significantly delayed by the evolving COVID-19 pandemic.

In addition to the potentially small populations, the eligibility criteria of our planned clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics, such as a certain severity or stage of disease progression, to include them in a study. Additionally, the process of finding eligible patients may prove costly. We also may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidate under study, the availability and efficacy of competing therapies and clinical trials, the proximity and availability of clinical study sites for prospective patients, the availability of genetic sequencing information for patient tumors so that we can identify patients with the targeted genetic mutations, and the patient referral practices of physicians. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed.

The enrollment of patients further depends on many factors, including:

- the proximity of patients to clinical trial sites;
- the design of the clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents;
- our ability to enroll a diverse patient base in our clinical trials to meet FDA recommended guidance;
- reporting of the preliminary results of any of our clinical trials;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion; and
- factors we may not be able to control, such as current or potential pandemics that may limit patients, principal investigators or staff or clinical site availability (e.g., the COVID-19 pandemic).

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us because some patients who might have opted to enroll in our clinical trials may instead opt to enroll in a clinical trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because certain of our product candidates represent a departure from more commonly used methods for cancer treatment and because certain of our product candidates have not been tested in humans before, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy, rather than enroll patients in any future clinical trial of our product candidates.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented.

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

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. From time to time, we may also disclose interim data from our clinical trials. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment and treatment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects and our ability to obtain approval for, and commercialize, our product candidates may be harmed. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

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

We submitted our INDs for CLN-081 in May 2019 and for both CLN-049 and CLN-619 in May 2021, which are all currently in effect. However, we may not be able to file future INDs for our other product candidates on the timelines we expect. Additionally, we may experience manufacturing delays or other delays with IND-enabling studies, or the FDA or other regulatory authorities may require additional preclinical studies that we did not anticipate. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that result in a decision by us, by IRBs or independent ethics committees, or by the FDA or other regulatory authorities to suspend or terminate clinical trials, including as a result of a clinical hold. Additionally, even if the FDA or other regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that they will not change their requirements or expectations in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND. Any failure to file INDs on the timelines we expect or to obtain regulatory approvals for our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

We intend to develop CLN-619 and potentially other product candidates in combination with other therapies, which exposes us to additional risks.

We intend to develop CLN-619 and potentially other product candidates in combination with one or more approved or unapproved therapies to treat cancer or other diseases. Even if any product candidate we develop were to receive marketing approval for use in combination with other approved therapies, the FDA, the EMA, or comparable foreign regulatory authorities outside of the United States could still revoke approval of the therapy used in combination with our product. If the therapies used in combination with our product candidates are replaced as the standard of care for the indications, we choose for any of our product candidates, the FDA, EMA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

Further, we will not be able to market and sell any product candidate we develop in combination with an unapproved cancer therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved cancer therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

If the FDA, EMA or comparable foreign regulatory authorities do not approve these other products or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the products we choose to evaluate in combination with our product candidate we develop, we may be unable to obtain approval of or market such combination therapy.

Our product candidates may cause undesirable side effects or have other properties that delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.

Our product candidates may cause undesirable side effects. Additionally, the administration process or related procedures also can cause adverse side effects. Adverse events that occur in our trials may cause us, or cause the FDA, the EMA or other regulatory authorities, or IRBs to order us to halt, delay or amend preclinical development or clinical development of our product candidates and could result in more restrictive labelling or the denial of regulatory approval of our product candidates for any or all targeted indications. Even if serious adverse events are unrelated to study treatment, such occurrences could affect patient enrollment or the ability of enrolled patients to complete the trial. In addition, if any of our product candidates are tested or used in combination with other drugs, such as our plans to potentially use CLN-619 in combination with other agents, these combinations may have additional side effects, which could be more severe than those caused by either therapy alone.

Furthermore, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates or those of our competitors may only be uncovered when a significantly larger number of patients have been exposed to the drug. For example, while we believe that CLN-081 has demonstrated a manageable tolerability profile thus far, there can be no assurance that it or any of our other product candidates will not cause more severe side effects in a greater proportion of patients.

Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any of our product candidates, the commercial prospects of such product candidates or our other product candidates may be harmed, and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates and may harm our business, financial condition, results of operations, and prospects significantly.

If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar drugs or biologics) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates;
- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contraindication;
- we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such product candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our product candidates, if approved, and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

Since the number of patients that have been and will be dosed in our Phase 1/2a clinical trial of CLN-081, and our Phase 1 clinical trials of CLN-049 and CLN-619, and those that we plan to dose in future clinical trials, is small, the results from such clinical trials, once completed, may be less reliable than results achieved in larger clinical trials, which may hinder our efforts to obtain regulatory approval for our product candidates.

The preliminary results of clinical trials with smaller sample sizes, such as our Phase 1/2a clinical trial of CLN-081 and our Phase 1 clinical trials of CLN-049 and CLN-619, can be disproportionately influenced by various biases associated with the conduct of small clinical trials, such as the potential failure of the smaller sample size to accurately depict the characteristics of the broader patient population, which limits the ability to generalize the results across a broader community, thus making the clinical trial results less reliable than clinical trials with a larger number of patients. As a result, there may be less certainty that such product candidates would achieve a statistically significant effect in any future clinical trials. Further, the FDA or other regulatory authorities may require us to conduct additional and larger trials than we may plan to support applications for marketing authorization. If we conduct any future clinical trials of CLN-081, CLN-049, or CLN-619 or of our other product candidates, we may not achieve a positive or statistically significant result or the same level of statistical significance, if any, that we might have anticipated based on prior results.

We are currently conducting and may in the future conduct clinical trials for product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are evaluating CLN-081 in a Phase 1/2a trial that includes centers located inside and outside of the United States. We may also in the future choose to conduct one or more additional clinical trials outside the United States, including in Europe and Australia. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. If data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice, and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice, or GCP, regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. We would need to conduct additional trials if the FDA or any comparable foreign regulatory authority does not accept data from trials conducted outside of the United States or the applicable foreign jurisdiction, which could be costly and time-consuming, and which may result in product candidates that we may develop not receiving approval for commercialization in the United States or any such foreign jurisdiction.

Risks Related to Our Financial Condition and Capital Requirements

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We began substantive operations in 2017. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital for us and our subsidiaries, filing patent applications, identifying and acquiring and investing in potential product candidates, undertaking clinical trials, building our intellectual property portfolio, and establishing arrangements and collaborating with third parties for identification, discovery and research activities, preclinical studies, clinical trials, and the manufacture of initial quantities of our product candidates and component materials. We have not yet demonstrated our ability to successfully conduct late-stage clinical trials, complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales, marketing, and distribution activities necessary for successful product commercialization.

Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future.

Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We are still in the early stages of development of our product candidates. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. We have financed our operations primarily through the sale of equity securities.

We have incurred significant net losses in each period since we began substantive operations. For the years ended December 31, 2021 and 2020, we reported net losses $67.5 million and $59.5 million, respectively. As of December 31, 2021, we had an accumulated deficit of $158.9 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- continue our research and development efforts and submit investigational new drug applications, or INDs, for our product candidates;
- conduct preclinical studies and clinical trials for our current and future product candidates;
- take temporary measures to help minimize the risk of COVID-19 to our employees;
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges;
- develop the necessary processes, controls, and manufacturing capabilities to obtain marketing approval for our product candidates and to support manufacturing on a commercial scale;
- seek regulatory approvals for any product candidates that successful complete clinical trials, if any;
- hire and retain additional personnel, such as non-clinical, clinical, pharmacovigilance, quality assurance, regulatory affairs, manufacturing, distribution, legal, compliance, medical affairs, finance, general and administrative, commercial, and scientific personnel;
- establish a sales, marketing, and distribution infrastructure and scale-up manufacturing capabilities, whether alone or with third parties, to commercialize any product candidates for which we may obtain regulatory approval; and
- develop, maintain, expand, and protect our intellectual property portfolio.

Because of the numerous risks and uncertainties associated with developing pharmaceutical product candidates, particularly during the COVID-19 pandemic, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop and seek regulatory approval for additional product candidates or additional indications. We may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We have not generated any revenue from the sale of our product candidates and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. In the first quarter of 2021, we recognized $18.9 million of license revenue from our license agreement with Zai Lab Shanghai Company, Limited. To date, we have not generated any other license or collaboration revenue or any sale from any of our product candidates. We do not expect to generate significant sales revenue or commercial revenue from the sale or license of one or more of our preclinical programs or product candidates unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, at least one of our product candidates or, alternatively, enter into agreements with third parties for the purchase, collaboration, or license of one of our product candidates. We are currently advancing CLN-081, CLN-049 and CLN-619 in clinical development, but most of our product candidates are in the preclinical stages of development and will require additional preclinical studies. All of our product candidates will require additional clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity, and significant marketing efforts before we can generate any revenue from product sales. Our ability to generate revenue depends on a number of factors, including, but not limited to:

- timely completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- our ability to complete IND-enabling studies and successfully submit INDs or comparable applications for our product candidates;
- whether we are required by the FDA or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates or any future product candidates;
- our ability to timely seek and obtain regulatory and marketing approvals for any of our product candidates or any future product candidates for which we complete clinical trials, and such regulatory authorities' acceptance of our tumor-agnostic development strategy (i.e., our pursuit of approval based on a biomarker rather than a specific cancer indication);
- the prevalence, duration, and severity of potential side effects or other safety issues experienced by patients receiving our product candidates or future product candidates;
- the willingness of physicians, operators of clinics, and patients to utilize or adopt any of our product candidates or future product candidates over alternative or more conventional therapies, such as chemotherapy;
- the actual and perceived availability, cost, risk profile, and side effects, and efficacy of our product candidates, if approved, relative to existing and future alternative cancer therapies and competitive product candidates and technologies;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities and develop, validate, and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMP;
- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates or any future product candidates in the United States and internationally, if approved for marketing, reimbursement, sale, and distribution in such countries and territories, whether alone or in collaboration with others;
- patient demand for our product candidates and any future product candidates, if approved; and
- our ability to establish and enforce intellectual property rights in and for our product candidates or any future product candidates.

Many of the factors listed above are beyond our control and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercializing our product candidates. Even if we are able to commercialize our product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the commercial sale of our product candidates or any future product candidates, or from agreements with third parties for the purchase, collaboration, or license of one or more of our product candidates, we may be unable to continue operations without continued funding.

We will require substantial additional funding to develop and commercialize our product candidates and identify and invest in new product candidates. If we are unable to raise capital when needed, we would be compelled to delay, reduce, or eliminate our product development programs or other operations.

The development of pharmaceutical products is capital intensive. We are currently advancing CLN-081, CLN-049 and CLN-619 in clinical development and making further investments in our preclinical programs. We expect our expenses to increase in parallel with our ongoing activities, as described above under the risk factor entitled "We have incurred significant losses since inception, and we expect to incur losses over the next several years and may not be able to achieve or sustain revenues or profitability in the future." Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations, which may include raising funding by one or more of our subsidiaries that could dilute our equity interest in the subsidiary. We have estimated our current additional funding needs based on assumptions that may prove to be wrong. Changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We cannot be certain that additional funding will be available on acceptable terms, or at all. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of public or private equity offerings, debt financings, governmental funding, collaborations, strategic partnerships, and alliances, or marketing, distribution, or licensing arrangements with third parties, either by Cullinan Oncology, Inc., or Cullinan, or by one or more of our subsidiaries. If we or our subsidiaries are unable to raise capital when needed or on attractive terms, we or the applicable subsidiary would be forced to delay, reduce, or eliminate our identification, discovery, and preclinical or clinical development programs, or any future commercialization efforts.

We had cash and cash equivalents and short-term investments of $290.5 million and long-term investments of $140.4 million as of December 31, 2021. We believe that, based upon our current operating plan, our existing capital resources will be sufficient to fund our anticipated operations through 2024. Our future capital requirements will depend on many factors, including:

- the scope, progress, results, and costs of drug discovery, laboratory testing, manufacturing and preclinical and clinical development for our current and future product candidates;
- the extent to which we enter into additional collaboration arrangements with regard to product discovery or acquire or in-license products or technologies;
- our ability to establish additional discovery collaborations on favorable terms, if at all;
- the costs, timing, and outcome of regulatory review of our product candidates;
- the costs of future commercialization activities, including product sales, marketing, manufacturing, and distribution, for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval, or from licensing or collaboration agreements pursuant to which we may receive milestone, royalty, or other revenue from third parties developing or commercializing our product candidates; and
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

If we or our subsidiaries engage in acquisitions or strategic partnerships, this may increase our or their capital requirements, dilute our or their stockholders, cause us or them to incur debt or assume contingent liabilities, and subject us or them to other risks.

We intend to engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring products, intellectual property rights, technologies, or businesses, carried out either by Cullinan or by one or more of our wholly- or partially-owned subsidiaries, including a newly-formed subsidiary formed for the purpose of such transaction. Any acquisition or strategic partnership may entail numerous risks to us or the applicable subsidiary, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;
- the issuance of equity securities which would result in dilution;
- assimilation of operations, intellectual property, products, and product candidates of an acquired company, including difficulties associated with integrating new personnel;

- the diversion of financial and managerial resources from our existing product programs and initiatives in pursuing such an acquisition or strategic partnership;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals;
- our inability to generate revenue from acquired intellectual property, technology, and/or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs;
- risk of conducting research and development activities in new therapeutic areas or treatment modalities in which we have little to no experience;
- successfully negotiating a proposed acquisition, in-license or investment in a timely manner and at a price or on terms and conditions favorable to us;
- successfully combining and integrating a potential acquisition into our existing business to fully realize the benefits of such acquisition;
- the impact of regulatory reviews on a proposed acquisition, in-license or investment; and
- the outcome of any legal proceedings that may be instituted with respect to the proposed acquisition, in-license or investment.

If we fail to properly evaluate potential acquisitions, in-licenses, investments or other transactions associated with the creation of new research and development programs or the maintenance of existing ones, we might not achieve the anticipated benefits of any such transaction, we might incur costs in excess of what we anticipate, and management resources and attention might be diverted from other necessary or valuable activities.

Risks Related to Our Corporate Structure

We may not be successful in our efforts to use our differentiated hub-and-spoke business model to build a pipeline of product candidates with commercial value.

A key element of our strategy is to use our differentiated hub-and-spoke business model to form or seek strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties for programs, product candidates, technologies or intellectual property that we believe are novel, employ differentiated mechanisms of action, are more advanced in development than competitors, or have a combination of these attributes. We face significant competition in seeking appropriate strategic partners and licensing and acquisition opportunities, and the negotiation process is time-consuming and complex. We may not be successful in our efforts in building a pipeline of product candidates for the treatment of various cancers through acquisitions, licensing or through internal development or in progressing these product candidates through clinical development. Although we analyze whether we can replicate scientific results observed prior to our acquisition or investment in a product candidate, we may not be successful in doing so after our investment. Our differentiated hub-and-spoke business model is evolving and may not succeed in building a pipeline of product candidates. For example, we may not be successful in identifying additional genetic mutations which are oncogenic and which can be "basketed" into a group that is large enough to present a sufficient commercial opportunity or that is druggable with one chemical compound.

Additionally, pursuing additional in-licenses or acquisitions of development-stage assets or programs, which entails additional risk to us. While we believe our hub-and-spoke model offers an attractive platform for these transactions and for potential partners, our model is unique and we may not be able to attract or execute transactions with licensors or collaborators who may choose to partner with companies that employ more traditional licensing and collaboration approaches. Identifying, selecting, and acquiring promising product candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a successful product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. For example, if we are unable to identify programs that ultimately result in approved products, we may spend material amounts of our capital and other resources evaluating, acquiring, and developing products that ultimately do not provide a return on our investment. We have terminated programs and expect to terminate programs in the future if they do not meet our criteria for advancement.

Our subsidiaries are party to certain agreements that provide our licensors, collaborators or other shareholders in our subsidiaries with rights that could delay or impact the potential sale of our subsidiaries or could impact the ability of our subsidiaries to sell assets, or enter into strategic alliances, collaborations or licensing arrangements with other third parties.

Each of our subsidiaries licenses intellectual property from third parties and several, including our partially-owned subsidiary Cullinan Pearl Corp., or Cullinan Pearl, and Cullinan MICA Corp., or Cullinan MICA, have raised capital from third party investors. These third parties have certain rights that could delay collaboration, licensing or other arrangement with another third party, and the existence of these rights may adversely impact the ability to attract an acquirer or partner. These rights include rights of negotiation and fees payable upon a sale of assets or change of control of a subsidiary that are contained in license agreements, as well as rights such as drag-along rights in agreements with shareholders of the subsidiary.

For example, Cullinan Pearl is party to a license agreement, or the Taiho Agreement, with Taiho Pharmaceuticals, Inc., or Taiho, pursuant to which Taiho has a right of negotiation that requires Cullinan Pearl to negotiate in good faith with Taiho prior to proceeding with a transaction to license, sell, assign, transfer or otherwise dispose of a majority of the assets of Cullinan Pearl to a third party, or any transaction with respect to any of the rights licensed from Taiho to Cullinan Pearl. While Cullinan Pearl is not obligated to enter into a transaction with Taiho, the right of negotiation could delay a potential sale or adversely impact our ability to attract a partner or acquirer and could negatively impact prospects for a larger company to acquire Cullinan Pearl or its assets or enter into a collaboration or licensing transaction that would benefit us. Further, Cullinan Pearl must pay Taiho a percentage of the proceeds from the sale, assignment or transfer of less than all or substantially all of Cullinan Pearl's assets. In addition, our partially-owned subsidiaries Cullinan Florentine Corp., or Cullinan Florentine, and Cullinan Amber Corp., or Cullinan Amber, will also owe licensors a success fee in the event of a sale or other disposition of the majority of its assets. These fees will reduce the net proceeds we receive from any such sale or disposition of assets.

We have also entered into investor rights and voting agreements with third party investors, which may delay or impact our ability to sell our equity interests in or the assets of our partially-owned subsidiaries. For example, we would need to comply with certain notice and other provisions, such as a drag-along provision in the event of sale of the subsidiary, which may delay or prevent a specific transaction or make transacting with our subsidiaries and us less attractive to third parties.

We may form additional subsidiaries and enter into similar agreements with future partners or investors, or our subsidiaries may enter into further agreements, that in each case may contain similar provisions or other terms that are not favorable to us.

Our ability to realize value from our subsidiaries may be impacted if we reduce our ownership to a minority interest or otherwise cede control to other investors through contractual agreements or otherwise.

In the event that any of our subsidiaries require additional capital and its respective board of directors authorizes the transaction, our equity interest in our subsidiaries may be further reduced to the extent such additional capital is obtained from third party investors rather than from us. However, such transactions would still need to be approved by the board of directors of our respective subsidiary over which we maintain full or, in the case of Cullinan MICA, majority control. For example, in the event Cullinan MICA were to undertake a transaction that could lead to further dilution of our interest, such action would still be subject to protective provisions requiring the consent of a majority in interest of the then-outstanding shares of Series A Senior Preferred Stock, or the Protective Voting Rights, including, among other things, any authorization, designation, recapitalization or issuance of any new class or series of stock or any other securities convertible into equity securities of Cullinan MICA. Cullinan currently holds a majority of the Series A Senior Preferred Stock. These Protective Voting Rights give holders of Series A Senior Preferred voting control over any actions that would result in redemptions of equity securities.

However, if we do not wish to or cannot provide additional capital to any of our subsidiaries, we may approve of an issuance of equity by a subsidiary that dilutes our ownership and may lose control over the subsidiary. In addition, if the affairs of such minority-owned subsidiaries such as Cullinan MICA were to be conducted in a manner detrimental to our interests or intentions, our business, reputation, and prospects may be adversely affected. For example, other shareholders of Cullinan MICA could take actions without our consent, including that a majority of shareholders could demand a registration of their shares beginning in April 2025 and such a liquidity event by the other shareholders could have an adverse impact on our investment in the subsidiary.

A single or limited number of subsidiaries may comprise a large proportion of our value.

A large proportion of our value may at any time reside in one or two of our subsidiaries, including intellectual property rights and the value ascribed to the product candidate or program that it is developing. Our consolidated financial condition and prospects may be materially diminished if the clinical development or potential commercialization prospects of a subsidiary's product candidate or program or one or more of the intellectual property rights held by a specific subsidiary becomes impaired. Furthermore, a large proportion of our consolidated revenue may at any time be derived from one, or a small number of, licensed technologies, and termination or expiration of licenses to these technologies would likely have a material adverse effect on our consolidated revenue. Any material adverse impact on the value of a particular subsidiary, including its intellectual property rights or the clinical development of its product candidate or program, could have a material adverse effect on our consolidated business, financial condition, results of operations or prospects.

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

Because we have limited financial and managerial resources, we must focus on a limited number of research programs and product candidates and on specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or fail to recognize or acquire assets that may be more promising than those we acquire. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future identification, discovery, and preclinical development programs and product candidates for specific indications may not yield any commercially viable products.

Our reliance on a central team consisting of a limited number of employees presents operational challenges that may adversely affect our business.

As of December 31, 2021, we had 31 full-time employees upon which we rely for various administrative, research and development, and other support services shared among our other operating subsidiaries. We also have three consultants who we rely on for research and development, business development, and other services. While we believe this structure enables us to reduce certain infrastructure costs, the small size of our centralized team may limit our ability to devote adequate personnel, time, and resources to support the operations of all of our subsidiaries, including their research and development activities, and the management of financial, accounting, and reporting matters. Given that our employees and management are primarily incentivized at the parent company level, these employees and management team members may not be sufficiently incentivized to maximize the overall value of our entire organization. If our centralized team fails to provide adequate administrative, research and development, or other services across our entire organization, our business, financial condition, and results of operations could be harmed.

Some of our officers and directors currently serve, and in the future may serve, as directors or officers of our subsidiaries, and, as a result, have and may continue to have, fiduciary and other duties to our subsidiaries causing conflicts of interest with respect to their duties to us and their duties to our subsidiaries and in determining how to devote themselves to our affairs and the affairs of our subsidiaries. Our subsidiaries' partners may also disagree with the sufficiency of resources that we provide to each subsidiary.

Certain of our officers are also directors and/or officers of one or more of our subsidiaries and, as a result, have fiduciary or other duties both to us and our subsidiaries. The conflicts of interest that arise from such duties could interfere with the management of our subsidiaries and their programs and product candidates, or result in disagreements with our subsidiaries' partners. For example, an individual who is both a director of one of our subsidiaries and a director of Cullinan owes fiduciary duties to the subsidiary and to the Company as a whole, and such individual may encounter circumstances in which his or her decision or action may benefit the subsidiary while having a detrimental impact on the Company, or vice versa, or on another subsidiary, including one for which he or she also serves as a director. Further, our officers and directors who are also officers and directors of our subsidiaries will need to allocate his or her time to responsibilities owed to Cullinan and each of the subsidiaries for which he or she serves as an officer or director, and will make decisions on behalf of one entity that may negatively impact others. In addition, while most of our subsidiaries have waived any interest or expectation of corporate opportunities that is presented to, or acquired, created or developed by, or which otherwise comes into possession of any director or officer who is also a director or officer of Cullinan disputes could arise between us and our subsidiary's partners regarding a conflict of interest. These partners also may disagree with the amount and quality of resources that our officers and employees devote to the subsidiary they are invested in. Any such disputes or disagreements could distract our management, interfere with our relations with our partners, and take significant time to resolve, which could disrupt the development of our product candidates, delay our potential commercialization efforts, result in increased costs or make it less likely that other third parties will choose to partner with us in the future.

Risks Related to Potential Commercialization

Even if we obtain regulatory approval of our product candidates, the products may not gain market acceptance among physicians, patients, hospitals, cancer treatment centers, and others in the medical community.

The use of targeted oncology medicines as a potential cancer treatment is a recent development and may not become broadly accepted by physicians, patients, hospitals, cancer treatment centers, and others in the medical community. Various factors will influence whether our product candidates are accepted in the market, including:

- the clinical indications for which our product candidates are licensed;
- physicians, hospitals, cancer treatment centers, and patients considering our product candidates as a safe and effective treatment;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the prevalence and severity of any side effects caused by our product candidates;
- the prevalence and severity of any side effects for other precision medicines and public perception of other precision medicines;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA;
- the timing of market introduction of our product candidates as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate coverage, reimbursement and pricing by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts.

If our product candidates are licensed but fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we will not be able to generate significant revenue.

Even if our product candidates achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The biotechnology and pharmaceutical industries are characterized by the rapid evolution of technologies and understanding of disease etiology, intense competition, and a strong emphasis on intellectual property. We face, and will continue to face, competition from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. We believe that our differentiated business model, approach, scientific capabilities, know-how, and experience provide us with competitive advantages. However, we expect substantial competition from multiple sources, including major pharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions, governmental agencies, and public and private research institutions worldwide. Many of our competitors, either alone or through collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and recruiting patients in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

Product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We expect that CLN-081 will compete against small molecule EGFR inhibitor Exkivity (TAK-788) from Takeda Pharmaceuticals, Inc. and EGFR/cMET bispecific antibody Rybrevant from Johnson & Johnson. CLN-081 may also compete against EGFR inhibitors poziotinib from Spectrum Pharmaceuticals, Inc. BDTX-189 from Black Diamond Therapeutics, Inc. and DZD-9008 from Dizal Pharmaceutical Co., Ltd., as well as other molecules in preclinical development. CLN-081 may also compete with a number of agents in preclinical development for EGFR exon 20. We expect that CLN-049 will compete against bispecifics for the treatment of AML, including those targeting CD3 and CD33 (Amgen Inc., or Amgen, and Amphivena Therapeutics, Inc.), CD123 (Macrogenics, Inc. and Xencor, Inc.), FLT3 (Amgen), and CCL1/CLEC12A (Merus N.V. and Genentech, Inc.). We expect that CLN-619 will compete against cancer therapies targeting MICA/B as a monotherapy and/or in combination with other agents, including: Innate Pharma, Inc. (in collaboration with AstraZeneca Inc.), CanCure LLC, Genentech Inc., Fate Therapeutics, Inc. and Bristol Myers Squibb Company.

If our product candidates, including CLN-081, CLN-049, and CLN-619, are approved for their currently proposed target indication, they will likely compete with the competitor products mentioned above and with other products that are currently in development. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition, and the availability of reimbursement from government and other third-party payors. Our competitors may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. The availability of reimbursement from government and other third-party payors will also significantly affect the pricing and competitiveness of our products. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. If our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable label than our product candidates, we could see a reduction or elimination in our commercial opportunity. For additional information regarding our competition, see the section of this Annual Report titled “Business—Competition.”

The insurance coverage and reimbursement status of newly-approved products is uncertain. Our product candidates may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices, or healthcare reform initiatives, which would harm our business. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments such as gene therapy products. Sales of these or other product candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

A primary trend in the United States healthcare industry and elsewhere is cost containment. Governmental authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by Centers for Medicare & Medicaid Services, or the CMS, an agency within the United States Department of Health and Human Services or HHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates, and our overall financial condition.

Net prices for drugs 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 drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third-party payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Additionally, we may develop companion diagnostic tests for use with our product candidates. We, or our collaborators, may be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. Even if we obtain regulatory approval or clearance for such companion diagnostics, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our product candidates. Medicare reimbursement methodologies, whether under Part A, Part B, or clinical laboratory fee schedule may be amended from time to time, and we cannot predict what effect any change to these methodologies would have on any product candidate or companion diagnostic for which we receive approval. Our inability to promptly obtain coverage and adequate reimbursement from both third-party payors for the companion diagnostic tests that we develop and for which we obtain regulatory approval could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Affordable Care Act, or ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the United States pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court and members of Congress have introduced several pieces of legislation aimed at significantly revising or repealing the ACA. The implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results.

United States federal government agencies currently face potentially significant spending reductions. The Budget Control Act of 2011, or the BCA, established a Joint Select Committee on Deficit Reduction, which was tasked with achieving a reduction in the federal debt level of at least $1.2 trillion. That committee did not draft a proposal by the BCA's deadline. As a result, automatic cuts, referred to as sequestration, in various federal programs were scheduled to take place, beginning in January 2013, although the American Taxpayer Relief Act of 2012 delayed the BCA's automatic cuts until March 1, 2013. While the Medicare program's eligibility and scope of benefits are generally exempt from these cuts, Medicare payments to providers and Part D health plans are not exempt. The BCA did, however, provide that the Medicare cuts to providers and Part D health plans would not exceed two percent unless additional Congressional action is taken. President Obama issued the sequestration order on March 1, 2013, and cuts went into effect on April 1, 2013. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, and subsequent legislation, these reductions were suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic and the reduction will be one percent from April 1, 2022 through June 30, 2022.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent United States Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. The former Trump administration's budget proposal for fiscal year 2021 included a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the former Trump administration sent “principles” for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Additionally, the former Trump administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. HHS has already implemented certain measures. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS’s policy change that was effective January 1, 2019. However, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions.

In 2020, former President Trump signed four Executive Orders aimed at lowering drug prices. In response, the FDA released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit for approval importation plans for certain prescription drugs from Canada. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all United States and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, in response to a lawsuit filed by several industry groups, on December 28, the United States District Court for the Northern District of California issued a nationwide preliminary injunction enjoining government defendants from implementing the MFN Rule pending completion of notice-and-comment procedures under the Administrative Procedure Act. On January 13, 2021, in a separate lawsuit brought by industry groups in the United States District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the United States District Court for the Northern District of California and that performance for any final regulation stemming from the MFN Interim Final Rule shall not commence earlier than 60 days after publication of that regulation in the Federal Register. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our product candidates. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to an order entered by the United States District Court for the District of Columbia, the portion of the rule eliminating safe harbor protection for certain rebates related to the sale or purchase of a pharmaceutical product from a manufacturer to a plan sponsor under Medicare Part D has been delayed to January 1, 2023. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed.

Further, 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 new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

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 product candidates or additional pricing pressures.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement approval for a product;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

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

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury 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 product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even 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 product candidates or products that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- 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;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; and
- a decline in our share price.

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of product candidates we develop, alone or with corporate collaborators. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

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.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. 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.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

The market opportunities for our product candidates may be relatively small since the patients who may potentially be treated with our product candidates are those who are ineligible for or have failed prior treatments, and our estimates of the prevalence of our target patient populations may be inaccurate.

Cancer therapies are sometimes characterized by line of therapy (first line, second line, third line, fourth line, etc.), and the FDA often approves new therapies initially only for a particular line or lines of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery, and new technologies. There is no guarantee that our product candidates, even if approved as a second or third or subsequent line of therapy, would be approved for an earlier line of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

Our projections of both the number of people who have the cancers we are targeting, who may have their tumors genetically sequenced, as well as the subset of people with these cancers in a position to receive a particular line of therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new therapies may change the estimated incidence or prevalence of the cancers that we are targeting. Consequently, even if our product candidates are approved for a second or third line of therapy, the number of patients that may be eligible for treatment with our product candidates may turn out to be much lower than expected. In addition, we have not yet conducted market research to determine how treating physicians would expect to prescribe a product that is approved for multiple tumor types if there are different lines of approved therapies for each such tumor type.

We currently have no marketing and sales organization and have no experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue.

We currently have no sales, marketing or distribution capabilities and have no experience in marketing products. If we commercialize ourselves any of our product candidates that may be approved, we will need to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel.

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

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

Risks Related to Government Regulation

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

Our 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, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Before we can commercialize any of our product candidates, we must obtain marketing approval. Whether the results from our current ongoing clinical trials and other trials will suffice to obtain approval will be a review issue and the FDA may not grant approval and may require that we conduct one or more controlled clinical trials to obtain approval. Additionally, even if FDA does grant approval for one or more of our product candidates, it may be for a more narrow indication than we seek. For example, we intend to develop our product candidates and seek approval for a tumor-agnostic indication based on a biomarker. FDA has approved only a small number of oncology products with tumor-agnostic indications, and there is a risk that FDA may disagree with or strategy or data and approve only a more narrow indication. Regulatory authorities, including the FDA, also may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require labeling that includes precautions or contra-indications with respect to conditions of use, or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we may develop.

To date, we have had interactions with regulatory authorities outside of the United States in France, the Netherlands, China, Hong Kong, Singapore, and Taiwan. We intend to engage with EMA regarding regulatory requirements for registration in the European Union, or EU for our CLN-081, CLN-049, and CLN-619 programs. There is limited experience of regulatory authorities outside of the United States with the approval of tumor-agnostic precision cancer medicines.

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. Further, our 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 regulatory approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted IND, Biologics License Application, or BLA, New Drug Application, or NDA, or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- the FDA or comparable foreign regulatory authorities may disagree with our tumor-agnostic development strategy;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication or a related companion diagnostic is suitable to identify appropriate patient populations;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA, NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may determine that the manufacturing processes or controls or the facilities of third-party manufacturers with which we contract for clinical and commercial supplies are inadequate; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of product candidates in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations, and prospects.

We may in the future seek orphan drug status for CLN-081, CLN-049, and some of our other future product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA or NDA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug or biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular drug for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA or NDA, to market the same drug for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our product candidates receives orphan exclusivity, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve a later product candidate that is the same drug as the drug with orphan exclusivity for the same condition if the FDA concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. Orphan drug exclusivity may also be lost if the FDA 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 orphan drug designation for CLN-081, CLN-049, and some or all of our other future product candidates in additional orphan indications in which there is a medically plausible basis for the use of these products. Even when we obtain orphan drug designation, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we intend to seek orphan drug designation for other product candidates, we may never receive such designations. For example, the FDA has expressed concerns regarding the regulatory considerations for orphan drug designation as applied to tumor-agnostic therapies, and the FDA may interpret the federal Food, Drug and Cosmetic Act, as amended, or the FDCA, and regulations promulgated thereunder in a way that limits or blocks our ability to obtain orphan drug designation or orphan drug exclusivity, if our product candidates are approved, for our targeted indications.

On August 3, 2017, the United States Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The legislation was made in response to a court ruling holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period of a company obtains approval of a drug designated as an orphan drug, regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where FDA issued an orphan designation before the enactment of FDARA but where product approval came after the enactment of FDARA. The FDA and legislators may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

A Fast Track designation by the FDA, even if granted for CLN-081, CLN-049, and CLN-619, or any other future product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

If a drug or biologic is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for FDA Fast Track designation for a particular indication. We may seek Fast Track designation for CLN-081, CLN-049, and CLN-619, and certain of our future product candidates, but there is no assurance that the FDA will grant this status to any of our proposed product candidates. Marketing applications filed by sponsors of products in Fast Track development may qualify for priority review under the policies and procedures offered by the FDA, but the Fast Track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant Fast Track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any Fast Track designation at any time.

The Breakthrough Therapy designation by the FDA we received for CLN-081, and if granted for any of our other product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that CLN-081 or our other product candidates will receive marketing approval.

We received Breakthrough Therapy designation for CLN-081 in January 2022 and may seek this designation for CLN-049 and CLN-619, and some or all of our future product candidates. A Breakthrough Therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Sponsors of product candidates that have been designated as Breakthrough Therapies are eligible to receive more intensive FDA guidance on developing an efficient drug development program, an organizational commitment involving senior managers, and eligibility for rolling review and priority review. Drugs and biologics designated as Breakthrough Therapies by the FDA may also be eligible for other expedited approval programs, including accelerated approval.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to candidate products developed and considered for approval that have not received Breakthrough Designation and does not assure ultimate approval by the FDA. In addition, even though CLN-081 qualifies as a Breakthrough Therapy, the FDA may later decide that the product candidate no longer meets the conditions for qualification. Thus, even though we may seek Breakthrough Therapy designation for CLN-049, and CLN-619, and some or all of our future product candidates for the treatment of various cancers, there can be no assurance that we will receive breakthrough therapy designation for such product candidates.

Accelerated approval by the FDA, even if granted for CLN-081 or any other future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek approval of CLN-081, and certain of our other current and future product candidates using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of approval, the FDA requires that a sponsor of a product receiving accelerated approval perform a post-marketing confirmatory clinical trial or trials. These confirmatory trials must be completed with due diligence. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate full FDA approval. Accelerated approval may also be withdrawn if, among other things, a confirmatory trial required to verify the predicted clinical benefit of the product fails to verify such benefit or if such trial is not conducted with due diligence.

If approved, our investigational products regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

Most of our pipeline products, with the exception of CLN-081, will be regulated by the FDA as biologics, which must be licensed by FDA prior to marketing under a BLA. The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biologic products that are biosimilar to or interchangeable with an FDA-licensed reference biologic product. Under the BPCIA, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a BLA for the competing 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 the other company's product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our investigational medicines to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once licensed, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our small molecule investigational products that receive marketing approval, or such authorities do not grant our products appropriate periods of exclusivity before approving generic versions of those products, the sales of our products, if approved, could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials to assess safety and efficacy. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labelling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug is typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. Specifically, in cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference listed drug.

Generic drug manufacturers may seek to launch generic products following the expiration of any applicable exclusivity period we obtain if our products are approved, even if we still have patent protection for such products. Competition that our products could face from generic versions of our products could materially and adversely affect our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing, and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties, and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we receive regulatory approval of our 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 product candidates.

Any product candidate for which we obtain marketing approval will be subject to extensive and ongoing regulatory requirements governing, among other things, the research, development, testing, manufacturing, labeling, packaging, distribution, storage, advertising, promotion, import, export, recordkeeping, monitoring, and reporting of our products. These requirements include submissions of safety and other post-marketing information and reports, facility registration and drug listing requirements, as well as continued compliance with cGMPs, good laboratory practice, or GLP, regulations, and GCPs, for any clinical trials that we conduct post-approval. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product.

The FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; 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 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 marketing approval that we may have obtained and we may not achieve or sustain profitability.

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

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of products 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. If any of our product candidates are approved and we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. Violation of the FDCA, and other statutes, including the False Claims Act, or FCA, and equivalent legislation in other countries relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state and other countries' health care fraud and abuse laws and state consumer protection laws. Even if it is later determined we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the United States 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 or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns or other disruptions could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis after foreign and domestic inspection of facilities were largely placed on hold due to the COVID-19 pandemic. The FDA may not be able to maintain this pace and delays or setbacks are possible in the future. Should the FDA determine that an inspection is necessary for approval, and an inspection cannot be completed during the review cycle due to restrictions on travel, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. Additionally, regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

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

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to: comply with the regulations of the FDA and other similar foreign regulatory authorities, provide true, complete and accurate information to the FDA and other similar foreign regulatory authorities, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws and regulations will increase significantly, and our costs associated with compliance with such laws and regulations are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the FCA which impose criminal and civil penalties, including through civil “qui tam” or “whistleblower” actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- the federal Physician Payment Sunshine Act, created under the ACA and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; 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 that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

We adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. 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. 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 criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, and we may be required to curtail or restructure our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

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 also prohibited in the EU. The provision of benefits or advantages to induce or reward improper performance generally is usually governed by the national anti-bribery laws of EU Member States, and the Bribery Act 2010 in the United Kingdom, or the Bribery Act. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the United Kingdom despite its departure from the EU. Payments made to physicians in certain EU 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 EU Member States.

These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States.

Failure to comply with these requirements could result in administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, individual imprisonment, reputational harm, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws.

Data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR increased our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, the United Kingdom's vote in favor of exiting the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

In addition, California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA went into effect on January 1, 2020, and the California Attorney General commenced enforcement actions for violations on July 1, 2020. Further, a new California privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020. The CPRA will create additional obligations with respect to processing and storing personal information that are scheduled to take effect on January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). While there are currently exceptions for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. While clinical trial data and information governed by HIPAA are currently exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope. We continue to monitor the impact the CCPA may have on our business activities.

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

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent and other intellectual property protection for our current and future product candidates and technology, or if the scope of intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize CLN-081, CLN-049 and CLN-619 or any other product candidates or technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our product candidates, including CLN-081, CLN-049 and CLN-619, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment and development that are important to our business, as well as successfully defending these patents against third-party challenges. If we do not adequately protect our intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

We intend to rely upon a combination of patent applications, confidentiality agreements, trade secret protection and license agreements to protect the intellectual property related to our product candidates and technologies. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. We, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to establish our patent position.

To protect our proprietary position, we have filed or in-licensed, and plan to file or in-license, patents and patent applications in the United States and abroad relating to our product candidates that are important to our business. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. If we are unable to secure or maintain patent protection with respect to CLN-081, CLN-049 and CLN-619, or any other proprietary products and technology we develop, our business, financial condition, results of operations, and prospects would be materially harmed.

The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any patents we may own or in-license in the future will have, or that any of our patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. In addition, to the extent that we currently or in the future license intellectual property, we cannot assure you that those licenses will remain in force. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan, and the term of any patents we may own or in-license may be inadequate to protect our competitive position of our product candidates or technology for an adequate amount of time. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Even if they are unchallenged, our patent applications, if issued, and any patents we may own or in-license, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent any patents we may own or in-license by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to one or more of our product candidates but that uses a formulation and/or a device that falls outside the scope of any patent protection we may have in the future. If the patent protection provided by our patent applications or any patents, we may pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business.

Patent positions of life sciences companies can be uncertain and involve complex factual and legal questions. Changes in either the patent laws or their interpretation in any jurisdiction that we seek patent protection may diminish our ability to protect our inventions, maintain and enforce our intellectual property rights; and, more generally, may affect the value of our intellectual property, including the narrowing of the scope of our patent applications or any patents we may own or in-license.

The patent prosecution process is complex, expensive, time-consuming and inconsistent across jurisdictions. Patent license negotiations also can be complex and protracted, with uncertain results. We may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent rights at a commercially reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is possible that we will fail to identify important patentable aspects of our research and development efforts in time to obtain appropriate or any patent protection. While we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development efforts, including for example, our employees, corporate collaborators, external academic scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose results before a patent application is filed, thereby endangering our ability to seek patent protection. In addition, publications of discoveries in the scientific and scholarly literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Consequently, we cannot be certain that we were the first to file for patent protection on the inventions claimed in our patent applications.

It is possible that defects of form in the preparation or filing of our patent applications, or any patents we may own or in-license, may exist or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, licensees or licensors fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patent applications or patents we may own or in-license, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

Additionally, we cannot be certain that the claims in our patent applications covering composition of matter of our product candidates or technology will be considered patentable by United States Patent and Trademark Office, or the USPTO, or by patent offices in foreign countries, or that the claims in any issued patents we may own or in-license will be considered patentable by courts in the United States or foreign countries.

Method of use patents protect the use of a product for the specified method. These types of patents do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may induce or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain and involves complex legal and factual questions for which many legal principles remain unresolved. In recent years, patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability and commercial value of any rights we may have from our patent applications are highly uncertain. Our patent applications may not result in patents being issued in the United States or in other jurisdictions which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Moreover, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art, including our own previously filed patent applications and scientific publications, allow our inventions to be patentable over the prior art. Even if our patent applications issue as patents, third parties could challenge the validity of such patents based on such scientific publications and we could potentially lose valuable patent rights. Further, the scope of the invention claimed in a patent application can be significantly reduced before the patent is issued, and this scope can be reinterpreted after issuance. Even where our patent applications, whether owned or in-licensed, issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with a competitive advantage. Any patents that eventually issue may be challenged, narrowed or invalidated by third parties. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by valid and enforceable patent rights. Our competitors or other third parties may be able to evade any rights we may have by developing new compounds or alternative technologies or products in a non-infringing manner.

The issuance or grant of a patent is not irrefutable as to its inventorship, scope, validity or enforceability, and any of our current or future patents, whether owned or in-licensed may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in the patent claims of any such patents being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. We may in the future, become subject to a third-party pre-issuance submission of prior art or opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceeding and other similar proceedings challenging any rights we may have from our patent applications or the patent rights of others in the USPTO or other foreign patent office, or in declaratory judgment actions or counterclaims. An unfavorable determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, any rights we may have from our patents or patent applications, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or extinguish our ability to manufacture or commercialize products without infringing third-party patent rights.

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

If we fail to comply with our obligations in any agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are currently, and may in the future be, party to license or collaboration agreements with third parties to advance our research or allow commercialization of product candidates. Our current agreements impose, and we expect that future agreements may impose numerous obligations, such as development, diligence, payment, commercialization, funding, milestone, royalty, sublicensing, insurance, patent prosecution, enforcement and other obligations on us and may require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. If our licensors conclude that we have materially breached our license agreements they may seek to terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technologies covered by these license agreements.

Any termination of these licenses, or if the underlying patents fail to provide the intended exclusivity, could result in the loss of significant rights and could harm our ability to commercialize our product candidates, and competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe, misappropriate or otherwise violate intellectual property rights of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- the priority of invention of any patented technology; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

In addition, licensing agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. For example, under the Taiho Agreement, while Cullinan Pearl is not obligated to enter into a transaction with Taiho, the right of negotiation could delay a potential sale or adversely impact our ability to attract a partner or acquirer and could negatively impact prospects for a larger company to acquire Cullinan Pearl or its assets or enter into a collaboration or licensing transaction that would benefit us. In addition, Cullinan Florentine and Cullinan Amber will also owe licensors a success fee in the event of a sale or other disposition of the majority of its assets. These fees will reduce the net proceeds we receive from any such sale or disposition of assets.

Moreover, if disputes over intellectual property prevent or impair our ability to maintain licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

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

In addition to the protection afforded by our owned and in-licensed patents, we seek to rely on trade secret protection, confidentiality agreements, and license agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product identification, discovery, and development processes, including our differentiated hub-and-spoke business model that involve proprietary know-how, information, or technology that is not covered by patents. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, trade secrets can be difficult to protect and we have limited control over the protection of trade secrets used by our collaborators and suppliers. We cannot be certain that we have or will obtain these agreements in all circumstances and we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary information. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

Third-party claims of intellectual property infringement, misappropriation or other violations may be costly and time consuming and may prevent or delay our product identification, discovery and development efforts.

The intellectual property landscape around precision medicine is crowded, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability, or the ability of our third parties, to develop, manufacture, market and sell our current and future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including derivation, interference, reexamination, *inter partes* review, and post grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We or any of our licensors or strategic partners may be party to, exposed to, or threatened with, future adversarial proceedings or litigation by third parties having patent or other intellectual property rights alleging that our current or future product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. We cannot assure you that our product candidates and other technologies that we have developed, are developing or may develop in the future do not or will not infringe, misappropriate or otherwise violate existing or future patents or other intellectual property rights owned by third parties. Numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third party claims that we infringe, misappropriate or otherwise violate its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement, misappropriation and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business and may impact our reputation;
- substantial damages for infringement, misappropriation or other violations, which we may have to pay if a court decides that the product candidate or technology at issue infringes, misappropriates or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, including CLN-081, CLN-049 and CLN-619, or from using our proprietary technologies, unless the third party licenses its product rights to us, which it is not required to do, on commercially reasonable terms or at all;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products, or the license to us may be non-exclusive, which would permit third parties to use the same intellectual property to compete with us;
- redesigning our product candidates or processes so they do not infringe, misappropriate or violate third party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time; and
- there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations or prospects.

We may choose to challenge the patentability of claims in a third party's United States patent by requesting that the USPTO review the patent claims in an *ex-parte* re-exam, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the European Patent Office, or the EPO, or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies.

Third parties may assert that we are employing their proprietary technology without authorization. Patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Patent applications can take many years to issue. In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications covering our product candidates or technology. If any such patent applications issue as patents, and if such patents have priority over our patent applications or patents we may own or in-license, we may be required to obtain rights to such patents owned by third parties which may not be available on commercially reasonable terms or at all, or may only be available on a non-exclusive basis. There may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates or other technologies, could be found to be infringed by our product candidates or other technologies. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement, misappropriation or other violation against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

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

We have in-licensed four patent families and own a fifth patent family related to CLN-081. We have in-licensed one patent family related to CLN-049. We own three patent families related to CLN-619. Because additional product candidates may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations to work effectively and efficiently, and these rights may be held by others. Similarly, efficient production or delivery of our product candidates may also require specific compositions or methods, and the rights to these may be owned by third parties. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be nonexclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. Moreover, the molecules that will be used with our product candidates may be covered by the intellectual property rights of others.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program and allowing third parties to compete with us. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business, results of operations, financial condition and prospects could suffer.

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

Competitors may infringe any patents we may own or in-license. In addition, any patents we may own or in-license may become involved in inventorship, priority, validity or unenforceability disputes. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that one or more of any patents we may own or in-license is not valid or is unenforceable or that the other party's use of our technology that may be patented falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). There is also the risk that, even if the validity of these patents is upheld, the court may refuse to stop the other party from using the technology at issue on the grounds that any of our owned or in-licensed patents do not cover the technology in question or that such third party's activities do not infringe our patents. An adverse result in any litigation or defense proceedings could put one or more of our owned or in-licensed patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Post-grant proceedings provoked by third parties or brought by the USPTO may be necessary to determine the validity or priority of inventions with respect to our owned or in-licensed patents or patent applications. These proceedings are expensive and an unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. In addition to potential USPTO review proceedings, we may become a party to patent opposition proceedings in the EPO or similar proceedings in other foreign patent offices, where our foreign patents are challenged. The costs of these opposition or similar proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result at the USPTO, EPO or other patent office may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business.

Litigation or post-grant proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

We may not be able to detect infringement against any of our owned or in-licensed patents. Even if we detect infringement by a third party, we may choose not to pursue litigation against or settlement with the third party. If we later sue such third party for patent infringement, the third party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us to enforce any patents we may own or in-license against such third party.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in some cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market with similar or identical products or platforms, which could have a material adverse effect on our business prospects and financial condition.

Changes to patent law in the United States and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and are therefore costly, time-consuming and inherently uncertain. Recent United States Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we might obtain in the future. For example, in the case *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the United States Supreme Court held that certain claims to DNA molecules are not patentable. Any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition. Changes in the laws and regulations governing patents in other jurisdictions could similarly have an adverse effect on our ability to obtain and effectively enforce any rights we may have in our patent applications or any patents we may own or in-license.

Recent or future patent reform legislation could also increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents we may own or in-license. The United States has enacted and implemented wide-ranging patent reform legislation. On September 16, 2011, the Leahy-Smith America Invents Act, or America Invents Act, was signed into law, which includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation, establish a new post-grant review system and switch the United States patent system from a “first-to-invent” system to a “first-to-file” system. Under a “first-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier.

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

We may not be able to pursue generic coverage of our product candidates outside of the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the United States. These products may compete with our product candidates and in jurisdictions where we do not have any issued patents or patent applications or other intellectual property rights may not be effective or sufficient to prevent them from competing. Our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of any patents we may own or in-license or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce any rights we may have in our patents and patent applications in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put any of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any of our owned or in-licensed patents that are relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

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

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

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information or alleged trade secrets of third parties or competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

We have received confidential and proprietary information from third parties. In addition, as is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors, in some cases until recently. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information or trade secrets of these third parties or our employees' former employers or our consultants' or contractors' current or former clients or customers. In addition, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation or arbitration may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims and possible aftermath could result in substantial cost and be a distraction to our management and employees. Any litigation or the threat thereof may adversely affect our ability to hire employees. A loss of key personnel or their work product could hamper or prevent our ability to commercialize product candidates, which could have an adverse effect on our business, results of operations and financial condition. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

If we do not obtain patent term extension and data exclusivity for any of our current or future product candidates we may develop, our business may be materially harmed.

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

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

Our trademarks or trade names may be challenged, infringed, diluted, circumvented or declared generic or determined to be infringing on other marks. We intend to rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to obtain a registered trademark or establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Our Reliance on Third Parties

We currently rely and expect to continue to rely on the outsourcing of the majority of our development functions to third parties to conduct our preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.

We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, contract manufacturing organizations, or CMOs, and strategic partners to conduct and support our preclinical studies and clinical trials under agreements with us, and expect to rely on such parties in the future.

We negotiate budgets and contracts with CROs, trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. We rely heavily on these third parties over the course of our preclinical studies and clinical trials, and we control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of our preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we relied entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with good manufacturing, clinical, laboratory practices, or GxPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GxPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GxP regulations, 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 assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GxP regulations. In addition, our clinical trials must be conducted with pharmaceutical product produced under GxP regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may delay ongoing or planned clinical trials or require us to repeat clinical trials, which would delay the regulatory approval process. Failure by us or by third parties we engage to comply with regulatory requirements can also result in fines, adverse publicity, and civil and criminal sanctions. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials are not and will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing, clinical and preclinical product candidates. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties 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 or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

Switching or adding third parties to conduct our preclinical studies and clinical trials involves substantial cost and requires extensive time and focus of our management. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines.

Additionally, we do not directly control the manufacturing facilities where our product candidates are made, and we must depend on CMOs to make our product candidates according to standards for quality and reliability. We do not own any manufacturing facilities or equipment and do not employ any manufacturing personnel. We cannot assure you that we will be able to obtain qualified contract manufacturing services on reasonable terms. If any CMO with whom we contract fails to perform its obligations or has changes sourcing raw materials, we may be forced to enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In such scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability or bridging study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to advance clinical trials or otherwise develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently, which may increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

We may form or seek additional collaborations or strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such collaborations, alliances or licensing arrangements.

We may form or seek additional strategic alliances, create joint ventures or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization of our product candidates 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;
- 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;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights 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 potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and 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 product candidates; and

- collaborators may own or co-own intellectual property covering our product candidates that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, if we enter into additional collaboration agreements and strategic partnerships or license our product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

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

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must currently rely on outside vendors to manufacture our product candidates. We will need to negotiate and maintain contractual arrangements with these outside vendors for the supply of our product candidates and we may not be able to do so on favorable terms. We have not yet caused our product candidates to be manufactured on a commercial scale and may not be able to do so for any of our product candidates.

Our anticipated reliance on a limited number of third-party manufacturers exposes us to a number of risks, including the following:

- we may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must inspect any manufacturers for cGMP compliance as part of our marketing application;
- a new manufacturer would have to be educated in, or develop substantially equivalent processes for, the production of our product candidates;
- our third-party manufacturers might be unable to timely manufacture our product candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any;
- contract manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;
- our future contract manufacturers may not perform as agreed, may not devote sufficient resources to our product candidates or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store, and distribute our products, if any;
- manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies, as well as foreign regulatory authorities, to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards and we have no control over third-party manufacturers' compliance with these regulations and standards;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates;
- our third-party manufacturers could breach or terminate their agreements with us;
- raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects; and
- our contract manufacturers and critical reagent suppliers may be subject to inclement weather, as well as natural or man-made disasters.

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

Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

The manufacture of drug products, and particularly biologics, is complex and our third-party manufacturers may encounter difficulties in production. If any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our current product candidates or any future product candidates for clinical trials or our products for patients, if approved, could be delayed or prevented.

Manufacturing drugs, particularly biologics, especially in large quantities, is often complex and may require the use of innovative technologies to handle living cells. Each lot of an approved biologic must undergo thorough testing for identity, strength, quality, purity, potency and stability. Manufacturing biologics requires facilities specifically designed for and validated for this purpose, and sophisticated quality assurance and quality control procedures are necessary. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business.

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if we obtain marketing approval for any of our current product candidates or any future product candidates, there is no assurance that our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

Risks Related to Managing Growth and Employee Matters

COVID-19 has and may continue to adversely impact our business, including our preclinical studies and clinical trials and our ability to source drug supply.

The COVID-19 pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. As a result of the COVID-19 pandemic, we have experienced delays in our clinical trial and preclinical development activities, including our ability to enroll and retain patients in our ongoing clinical trials, and we could continue to experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- further delays or difficulties in enrolling and retaining patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in receiving authorizations from regulatory authorities to initiate our planned clinical trials;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, our product candidates or supplies for our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruptions in preclinical studies due to restricted or limited operations at our laboratory facility;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- changes in local regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; and
- interruption or delays to our sourced identification, discovery and clinical activities.

Additionally, the demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. The COVID-19 pandemic continues to rapidly evolve. The extent to which the pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

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

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our senior management, including scientific and medical personnel and other key employees. While we expect to engage in an orderly transition process as we integrate newly appointed officers and managers, we face a variety of risks and uncertainties relating to management transition, including diversion of management attention from business concerns, failure to retain other key personnel or loss of institutional knowledge. In addition, the loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business. In particular, due to our small number of employees, the loss of one employee may have a larger impact on our business than compared to a loss at one of our peers.

We conduct our operations at our facilities in Cambridge, Massachusetts. The Massachusetts region is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. Changes to United States immigration and work authorization laws and regulations, including those that restrain the flow of scientific and professional talent, can be significantly affected by political forces and levels of economic activity. Our business may be materially adversely affected if legislative or administrative changes to immigration or visa laws and regulations impair our hiring processes and goals or projects involving personnel who are not United States citizens.

To encourage valuable employees to remain at our company, in addition to salary and cash incentives, we have provided other equity that vests over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. 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 any of our employees could leave our employment at any time, with or without notice. 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 personnel.

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

As of December 31, 2021, we had 31 full-time employees and three consultants. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize any product candidates that are approved for marketing will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and potentially commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

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

Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, and telecommunication and electrical failures. While we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of data from completed or future preclinical studies and clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as name, mailing address, email addresses, phone number and clinical trial information. A successful cyberattack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (*e.g.*, state breach notification laws), federal (*e.g.*, HIPAA, as amended by HITECH), and international law (*e.g.*, the GDPR) and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business.

In addition, the computer systems of various third parties on which we rely, including our CROs and other contractors, consultants and law and accounting firms, may sustain damage from computer viruses, unauthorized access, data breaches, phishing attacks, cybercriminals, natural disasters (including hurricanes and earthquakes), terrorism, war and telecommunication and electrical failures. We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business.

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

Our operations, and those of our CROs, CMOs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Risks Related to Ownership of Our Common Stock

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report, these factors include:

- the results of our ongoing, planned or any future preclinical studies, clinical trials or clinical development programs;
- the commencement, enrollment, or results of clinical trials of our product candidates or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results or delays in preclinical studies and clinical trials, including as a result of clinical holds;
- our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial;
- any delay in our regulatory filings or any adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- changes in laws or regulations applicable to our products, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers or our manufacturing plans;
- our inability to obtain adequate product supply for any licensed product or inability to do so at acceptable prices;
- our inability to establish collaborations if needed;
- our failure to commercialize our product candidates;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- the size and growth of our initial cancer target markets;
- our ability to successfully treat additional types of cancers or at different stages;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or immunotherapy in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;

- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to intellectual property or proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including intellectual property or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and The Nasdaq Global Select Market and market for biopharmaceutical companies in particular, 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 may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, financial condition, results of operation and future prospects.

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

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

We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, we may enter into agreements that prohibit us from paying cash dividends without prior written consent from our contracting parties, or which other terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock, which may never occur.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval.

Our executive officers, directors, and 5% stockholders beneficially owned approximately 61.3% of our voting stock, based on 44,292,102 shares of our common stock deemed to be outstanding as of December 31, 2021. These stockholders have the ability to influence us through their ownership position. Accordingly, these stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

We are an emerging growth company and a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act, or JOBS Act, enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700.0 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to not "opt out" of this exemption from complying with new or revised accounting standards and, therefore, we will adopt new or revised accounting standards at the time private companies adopt the new or revised accounting standard and will do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We may take advantage of scaled disclosures available to smaller reporting companies until the fiscal year following the determination that either (i) the market value of our voting and nonvoting common stock held by non-affiliates is greater than $700.0 million, as measured on the last business day of the most recently completed second fiscal quarter, or (ii) the market value of our voting and nonvoting common stock held by non-affiliates, as measured on the last business day of our most recently completed second fiscal quarter, is less than $700.0 million but greater than $250.0 million and our annual revenues during our most recently completed fiscal year are greater than $100.0 million. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership by 5% stockholders over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income may be limited. As a result of our most recent private placements and other transactions that have occurred over the past three years, we may have experienced, and may experience, an "ownership change." We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As of December 31, 2021, we had United States federal and state net operating loss carryforwards of $117.4 million and $119.0 million, respectively. The Company generated federal net operating losses of $5.8 million prior to 2018, which begin to expire in 2036. State losses also begin to expire in 2036. The Company generated federal NOLs of $111.6 million, which can be carried forward indefinitely. As of December 31, 2021, the Company had federal and state research and development tax credit carryforwards of $1.3 million and $0.1 million, respectively, each of which will begin to expire at various dates through 2037 and 2033, respectively, and which could be limited if we experience an "ownership change." The reduction of the corporate tax rate under the Tax Cuts and Jobs Act of 2017, or the TCJA, may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Under the TCJA, federal net operating losses generated after December 31, 2017 will not be subject to expiration but will not be permitted to be carried back. In addition, under the TCJA, the amount of post 2017 net operating losses that we are permitted to deduct in any taxable year is limited to 80% of our taxable income in such year, where taxable income is determined without regard to the net operating loss deduction itself. As of December 31, 2020, we had United States federal net operating loss carryforwards of $78.1 million and United States federal and state research and development tax credit carryforwards of $1.4 million, each of which will begin to expire at various dates through 2036 and which could be limited if we experience an "ownership change."

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our second amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These antitakeover provisions and other provisions in our second amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer, or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims 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 arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws will further provide that unless we consent in writing to the selection of an alternative forum, the United States District Court for the District of Delaware will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision, as the Company is incorporated in the State of Delaware. In addition, our amended and restated bylaws will provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the United States federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, these forum selection clauses may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the United States District Court for the District of Delaware may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing, and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we will need as a public company.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell our service to new and existing customers.

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

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. In the event one or more of the analysts who cover us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our corporate headquarters is located in Cambridge, Massachusetts, where we sublease and occupy approximately 7,531 square feet of office space. The current term of our Cambridge lease expires June 30, 2024. We believe our existing facilities are sufficient for our needs for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

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

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Our common stock is publicly traded on the Nasdaq Global Select Market under the symbol "CGEM".

Stockholders

As of December 31, 2021, there were 73 stockholders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never paid or declared any cash dividends on our common stock and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors that our board of directors deems relevant.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Use of Proceeds from our Public Offering of Common Stock

On January 7, 2021, our Registration Statement on Form S-1, as amended (Registration No. 333-251512) was declared effective by the SEC for our initial public offering. At the closing of the offering on January 12, 2021, we sold 13,685,000 shares of common stock, including the exercise in full by the underwriters of their option to purchase up to 1,785,000 additional shares of common stock, at a public offering price of $21.00 per share. The aggregate net proceeds to us from the public offering, inclusive of the over-allotment exercise and after underwriting discounts and offering expenses, were approximately $264.5 million.

As of December 31, 2021, we estimate that we have used approximately $110.3 million of our existing cash and cash equivalents prior to the time of the initial public offering, or IPO. We have invested the net proceeds from the IPO and any unused proceeds from our prior equity financings into money market funds and marketable securities. Information related to use of proceeds from registered securities is incorporated herein by reference to the "Use of Proceeds" section of our initial public offering as described in our final prospectus dated January 7, 2021 and filed with the SEC on January 11, 2021 pursuant to Rule 424(b)(4) of the Securities Act. There has been no material change in the planned use of proceeds as described in our final prospectus.

Item 6. Reserved.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report. This discussion and other parts of this Annual Report contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section of this Annual Report.

Overview

We are a biopharmaceutical company focused on developing a diversified pipeline of targeted therapeutic candidates across multiple modalities in order to bring important medicines to cancer patients. Our strategy is to source innovation through both internal discovery efforts and external collaborations, focusing on advanced stage assets with novel technology platforms and differentiated mechanisms. Before we advance a product candidate into clinical development, we evaluate its potential for anti-tumor activity as a single agent as well as its ability to generate an immune system response or to inhibit oncogenic drivers. Using this strategy, we have efficiently developed or in-licensed a portfolio of therapeutic candidates that currently includes eight distinct programs. We currently employ or have consulting agreements with all of our team members.

Our lead product candidate, CLN-081, is an orally available small molecule, irreversible EGFR inhibitor that is designed to selectively target cells expressing mutant EGFR variants, including EGFR exon 20 insertion mutations, with relative sparing of cells expressing wild type EGFR. We are currently evaluating CLN-081 as a treatment for non-small cell lung cancer, or NSCLC, in adult patients with EGFRex20ins mutations in a Phase 1/2a trial. In December 2021, we presented efficacy and safety data from this trial that we believe supports CLN-081's differentiated clinical profile. In January 2022, we announced that the United States Food and Drug Administration, or FDA, granted CLN-081 Breakthrough Therapy Designation, or BTD.

Following CLN-081, our most advanced product candidates include CLN-049, a bispecific antibody targeting FLT3 and CD3, and CLN-619, a monoclonal antibody designed to stimulate natural killer, or NK, and T cell responses by engaging a unique target, MICA/B. We initiated enrollment in clinical trials in the fourth quarter of 2021 for CLN-619 for patients with advanced solid tumors and CLN-049 for patients with relapsed/refractory acute myeloid leukemia, or r/r AML.

In addition, through our AMBER platform, we are developing CLN-617, a fusion protein combining two potent antitumor cytokines, interleukin-2, or IL-2, and interleukin-12, or IL-12, with a tumor retention domain for the treatment of solid tumors. In November, we announced that we had selected a lead candidate and advanced CLN-617 into IND-enabling studies. We presented preclinical AMBER data at the Society for Immunotherapy of Cancer annual meeting in November 2021. Our pipeline includes four additional preclinical oncology programs: NexGem (CLN-978), an internally developed half-life extended T cell engaging antibody construct designed to simultaneously engage CD19 and CD3; Opal, a bispecific fusion protein that blocks the PD-1 axis and selectively activates the 4-IBB/CD137 pathway on T cells in tumors; Jade, a cell therapy targeting a novel senescence and cancer-related protein we are developing in collaboration with the Fred Hutchinson Cancer Research Center; and a collaboration with Mt. Sinai to optimize and develop HPK1 protein degraders. We currently hold worldwide development and commercialization rights to each of our product candidates, except for CLN-081, where Japan and Greater China rights have been partnered.

Since our inception in 2016, we have focused all of our efforts and financial resources on raising capital, organizing and staffing our company, identifying, acquiring or in-licensing and developing product and technology rights, establishing and protecting our intellectual property portfolio and developing and advancing our programs. To support these activities, we (i) identify and secure new programs, (ii) set up new subsidiaries to further advance individual programs, (iii) recruit key management team members, (iv) raise and allocate capital across the portfolio and (v) provide certain shared services, including research and development operations, administrative services, and business development, to our subsidiaries. We do not have any products approved for sale and have not generated any revenue from product sales.

We have four partially-owned development subsidiaries, together the Asset Subsidiaries: Cullinan Pearl Corp., or Cullinan Pearl, which is advancing CLN-081; Cullinan Florentine Corp., or Cullinan Florentine, which is advancing CLN-049; Cullinan MICA Corp., or Cullinan MICA, which is advancing CLN-619; and Cullinan Amber Corp., or Cullinan Amber, which is developing our AMBER platform and advancing CLN-617 as its first product candidate. We hold IP rights and exclusive options for worldwide IP for our earlier-stage programs, NexGem, Opal, Jade and the HPK1 degrader collaboration with Mt. Sinai.

Since inception, we have funded our operations primarily through the sale of equity securities. As of December 31, 2021, we have received net proceeds of $541.2 million from equity financings, inclusive of our net proceeds of $264.5 million from our IPO. Furthermore, we received $18.9 million in net collaboration revenue from the license agreement, or the Zai License Agreement with Zai Lab Shanghai Company, Limited, or Zai Lab.

As of December 31, 2021, we had cash, cash equivalents and short-term investments of $290.5 million and long-term investments of $140.4 million. We have incurred operating losses and have had negative cash flows from operations since our inception. As of December 31, 2021, we had an accumulated deficit of $158.9 million. We expect to continue to generate operating losses for the foreseeable future. Our future viability is dependent on the success of our research and development and our ability to access additional capital to fund our operations. There can be no assurance that our current operating plan will be achieved or that additional funding will be available on terms acceptable to us, or at all.

We are subject to risks and uncertainties common to early-stage companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the ability to obtain additional capital to fund operations. Our therapeutic programs will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require additional capital, adequate personnel and extensive compliance-reporting capabilities. There can be no assurance that our research and development will be successfully completed, that adequate protection for our intellectual property will be obtained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable.

Impact of COVID-19 Pandemic

In December 2019, a novel strain of coronavirus, or COVID-19, was reported in China and subsequently was declared a pandemic in March 2020 by the World Health Organization. Many countries around the world imposed quarantines and restrictions on travel and mass gatherings to slow the spread of the virus and closed non-essential businesses. The duration and scope of the COVID-19 pandemic continues to be uncertain. Infection rates remain high in many parts of the world, and the virulence and spread of different strains of the virus have caused many local jurisdictions to continue or re-implement quarantines and restrictions on travel and mass gatherings. The level and timing of COVID-19 vaccine distribution across the world will impact the economic recovery and growth and the general economic consequences of the pandemic.

The Company implemented remote working and other protective measures, but thus far, has not experienced a significant disruption or delay in its operations as it relates to the clinical development or drug production of the Company's product candidates. However, COVID-19 has impacted the pace of our enrollment in our clinical trials and our preclinical studies. In the future, COVID-19-related restrictions may adversely impact our operations. Such events may result in a period of business, supply and drug product manufacturing disruption, and in reduced operations, any of which could materially affect our business, financial condition and results of operations.

To date, COVID-19 has not had a financial impact on us. The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the ultimate economic impact brought by, and the duration of, the COVID-19 pandemic remain difficult to assess or predict, including new information which may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others, the pandemic has resulted in significant disruptions in the general commercial activity and the global economy and caused financial market volatility and uncertainty in significant and unforeseen ways. A continuation or worsening of the levels of market disruption and volatility seen in the recent past could have an adverse effect on our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business.

The full extent and duration of the impact of COVID-19 on our operations and financial performance is currently unknown and depends on future developments that are uncertain and unpredictable. While the situation caused by COVID-19 is unprecedented and dynamic, we have considered its impact when developing our estimates and assumptions. Actual results and outcomes may differ from our estimates and assumptions. For additional information of risks related to COVID-19, refer to Part I, Item 1A. Risk Factors of this Annual Report.

Basis of Presentation and Consolidation

Since our inception, we have created wholly-owned subsidiaries or made investments in certain controlled entities. Losses attributed to noncontrolling interests are reported separately in our consolidated statements of operations and comprehensive loss.

The following Asset Subsidiaries are consolidated into our financial statements:

Consolidated Entities	Current Relationship	Date Control First Acquired	Ownership as of December 31, 2021%[1]
Cullinan Pearl Corp.	Partially-owned Subsidiary	November 2018	80%
Cullinan Amber Corp.[2]	Partially-owned Subsidiary	December 2019	92%
Cullinan Florentine Corp.[3]	Partially-owned Subsidiary	December 2019	95%
Cullinan MICA Corp.[4]	Partially-owned Subsidiary	May 2020	45%
Cullinan Apollo Corp.[5]	N/A	November 2018	N/A

(1) Ownership percentages are reflected on a fully-diluted basis.

(2) Reflects the closing of an additional tranche of Series A Preferred Stock financing of Cullinan Amber and the issuance of common stock of Cullinan Amber to MIT in June 2021.

(3) Reflects the Company's ownership after the closing of an additional tranche of Series B Preferred Stock financing of Cullinan Florentine in July 2021.

(4) Reflects the Company's ownership after the First Additional Closing of Series A Senior Preferred Stock financing of Cullinan MICA in June 2021.

(5) Cullinan Apollo Corp. was dissolved in August 2021.

Cullinan Pearl

Cullinan Pearl, incorporated in November 2018, is our partially-owned operating subsidiary that has exclusive worldwide rights, excluding Japan and Greater China, to CLN-081, our orally available small molecule designed as a next generation, irreversible EGFR inhibitor that is in development for the treatment of NSCLC patients with EGFR exon 20 insertion mutations.

In February 2019, Cullinan Pearl entered into a licensing and collaboration agreement with Taiho Pharmaceutical, Co., Ltd., or Taiho Pharma, for the worldwide rights to CLN-081 outside of Japan, which Taiho Pharma retained. Cullinan Pearl also issued to Taiho Ventures, LLC, or Taiho Ventures, an affiliate of Taiho Pharma, 1,860,000 shares of Series A Preferred Stock at a price of $1.00 per share for an aggregate purchase price of $1.9 million. In August 2020, at the election of the board of directors of Cullinan Pearl, Cullinan Pearl completed its subsequent closing of its Series A Preferred Stock financing and issued to Taiho Ventures an additional 1,206,000 shares of Series A Preferred Stock for an aggregate purchase price of $1.2 million.

As of December 31, 2021, we and Taiho Ventures, have purchased an aggregate of $23.0 million in Series A Preferred Stock of Cullinan Pearl.

As of December 31, 2021, we own 87% and Taiho Ventures owns 13% of the Series A Preferred Stock of Cullinan Pearl. Assuming conversion of the Series A Preferred Stock, we own 80%, Taiho Ventures owns 10%, and Taiho Pharma owns 10% of the fully-diluted common stock outstanding of Cullinan Pearl. Pursuant to a voting agreement, by and among Cullinan Pearl, us, Taiho Ventures, and other stockholders of Cullinan Pearl, the Series A Preferred stockholders, acting by majority vote, have the right to appoint two members of the board of directors, Taiho Ventures has the right to appoint one director; our chief executive officer, Nadim Ahmed, serves as the fourth board member; and two independent directors are appointed by a majority of the other four Cullinan Pearl board of directors.

Cullinan Amber

Cullinan Amber, incorporated in December 2019, is our partially-owned operating subsidiary that has exclusive worldwide rights to the patents related to the technology that originated in the laboratory of Professor Dane Wittrup at the Massachusetts Institute of Technology, or MIT. In December 2019, Cullinan Amber entered into an Exclusive Patent License Agreement with MIT.

In June 2021, upon election by Amber's board of directors, Amber issued an additional 3,000,000 shares of its Series A Preferred Stock for gross proceeds of $3.0 million to the Company and 153,229 shares of its common stock to MIT in exchange for no consideration as set forth in the license agreement.

As of December 31, 2021, we own 92% of the issued equity of Cullinan Amber, on a fully-diluted basis, including 100% of Series A Preferred Stock.

Pursuant to the Series A Preferred Stock Purchase Agreement, by and among Cullinan Amber and us, upon election by the Cullinan Amber board of directors, we will purchase up to an additional 6,000,000 Series A Preferred Stock at a purchase price of $1.00 per share of Series A Preferred Stock in one or more closings. Pursuant to a voting agreement by and among Cullinan Amber, us, and other stockholders, of the three person board of directors, the holders of Series A Preferred Stock, acting by majority vote, have the right to designate two members of the board of directors.

Cullinan Florentine

Cullinan Florentine, incorporated in December 2019, is our partially-owned operating subsidiary that has exclusive worldwide rights to CLN-049, our bispecific antibody targeting FLT3 and CD3, pursuant to an Exclusive License Agreement, or the Tübingen License Agreement with Deutsches Krebsforschungszentrum, or DKFZ, Eberhard Karls University of Tübingen, Faculty of Medicine, or University of Tübingen, and Universitätsmedizin Gesellschaft für Forschung und Entwicklung mbH, Tübingen, or UFE.

Through December 31, 2021, we have purchased an aggregate of $12.0 million of shares of Series A Preferred Stock and $8.1 million of shares of Series B Preferred Stock of Cullinan Florentine. In connection with the issuance of additional shares of Series A Preferred Stock to us and pursuant to the Tübingen License Agreement, Cullinan Florentine issued to each of DKFZ and UFE an additional 261,540 and 120,270 shares of common stock of Cullinan Florentine, respectively.

As of December 31, 2021, we own 95% of the fully-diluted shares outstanding of Cullinan Florentine, including 100% of Series A Preferred Stock. DKFZ and University of Tübingen currently own, in the aggregate, 5% of the equity of Cullinan Florentine on a fully-diluted basis.

Pursuant to a voting agreement between Cullinan Florentine, we and other stockholders of Series A Preferred Stock, acting by majority vote, have the right to designate two members of the four person board of directors, DKFZ and UFE, acting jointly, have the right to appoint one director, our current chief executive officer, Mr. Ahmed, is the fourth board member.

Cullinan MICA

Cullinan MICA Corp. (formerly known as PDI Therapeutics, Inc.), or Cullinan MICA, of which we assumed operational control in May 2020, is our partially-owned operating subsidiary that owns intellectual property related to CLN-619, our MICA/B-targeted humanized IgG1 monoclonal antibody. We purchased 24% of the issued equity of Cullinan MICA, on a fully-diluted basis, including 89% of the outstanding shares of Series A Senior Preferred Stock. Pursuant to the Series A Senior Preferred Stock Purchase Agreement by and among us, Cullinan MICA, and other stockholders of Cullinan MICA, we will purchase up to an additional $16.0 million of the aggregate $18.0 million Series A Senior Preferred Stock in two additional closings upon the determination of Cullinan MICA's board of directors. At the first additional closing, the purchasers were required to invest an additional $8.0 million. At the Second Additional Closing, the purchasers are required to invest an additional $10.0 million.

In December 2020, the stockholders and the board of directors of Cullinan MICA approved an amendment to its equity plan that decreased the authorized amount of shares under its equity plan such that no further grants could be made under its equity plan. Any authorized but unissued shares under the equity plan were returned to the status of authorized, unissued shares of common stock. In December 2020, we purchased an aggregate of 3,367,804 shares of common stock of Cullinan MICA.

In June 2021, Cullinan MICA's board of directors authorized the first additional closing where investors of Series A Senior Preferred Stock purchased an additional $8.0 million of Series A Senior Preferred Stock of Cullinan MICA. The Company purchased 5,385,787 shares while other investors purchased 702,495 shares for $7.1 million and $0.9 million, respectively. As a result of these transactions, our ownership percentage in Cullinan MICA increased to 45%, which remains as of December 31, 2021.

Subject to the completion of Cullinan MICA's Series A financing, we will own 54% of the fully-diluted capital stock outstanding. Pursuant to a voting agreement, by and among Cullinan MICA, us, and other stockholders of Cullinan MICA, of the five-person board of directors, we have the right to appoint three members of the board of directors.

Cullinan Apollo

Cullinan Apollo, incorporated in November 2018, was our partially-owned operating subsidiary that was formed around VK-2019. In December 2018, Cullinan Apollo licensed the exclusive worldwide rights to VK-2019, an Epstein-Barr Nuclear Antigen 1 inhibitor, from The Wistar Institute, or Wistar. Cullinan Apollo also entered into a Collaborative Research Agreement with Wistar to continue preclinical research and development of VK-2019. In May 2020, Cullinan Apollo discontinued development of VK-2019 and terminated its license and collaboration agreements with Wistar. Cullinan Apollo was dissolved in August 2021.

Components of Our Results of Operations

Revenue

For the year ended December 31, 2021, we recognized $18.9 million of revenue, relating to the upfront fee earned from the Zai License Agreement. We have not generated any revenue from the sale of products since our inception and do not expect to generate any revenue from the sale of products in the near future, if at all. If our development efforts for our product candidates are successful and result in regulatory approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

Operating Expenses

Research and development expenses

Research and development expenses consist primarily of costs incurred in connection with the research and development of our product candidates and programs. We expense research and development costs and intangible assets acquired that have no alternative future use as incurred. These expenses include:

- employee-related expenses, including salaries, related benefits and equity-based compensation expense, for employees engaged in research and development functions;
- expenses incurred under agreements with organizations that support our drug discovery and development activities;
- expenses incurred in connection with the preclinical and clinical development of our product candidates and programs, including under agreements with contract research organizations, or CROs;
- costs related to contract manufacturing organizations, or CMOs, that are primarily engaged to provide drug substance and product for our clinical trials, research and development programs, as well as investigative sites and consultants that conduct our clinical trials, nonclinical studies and other scientific development services;
- the costs of acquiring and manufacturing nonclinical and clinical trial materials, including manufacturing registration and validation batches;
- costs related to compliance with quality and regulatory requirements;
- payments made under third-party licensing agreements; and
- direct and allocated costs related to facilities, information technology, personnel and other overhead.

Advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or consumed or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will increase substantially in connection with our planned clinical development activities in the near term and in the future. At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of any current or future product candidates.

Our clinical development costs may vary significantly based on factors such as:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up periods;
- the cost and timing of manufacturing our product candidates;
- the phase of development of our product candidates;
- the efficacy and safety profile of our product candidates; and
- the number of product candidates we are developing.

The successful development and commercialization of product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the following:

- the timing and progress of nonclinical and clinical development activities;
- the number and scope of nonclinical and clinical programs we decide to pursue;
- raising necessary additional funds;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current development programs and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of drug substance and drug product for use in the production of our product candidates;
- establishing and maintaining agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- our ability to protect our rights in our intellectual property portfolio;

- the commercialization of our product candidates, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other products; and
- a continued acceptable safety profile of our therapies following approval.

A change in the outcome of any of these variables with respect to the development of our product candidates could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any of our product candidates or programs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel in executive management, finance, corporate and business development, and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; professional fees for accounting, auditing, tax, and administrative consulting services; insurance costs; administrative travel expenses; marketing expenses; and other operating costs.

We incurred increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with being a public company. We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support development of our product candidates and programs and our continued research activities.

Other Income

Other income consists primarily of interest income earned on our cash, cash equivalents, short-term investments and long-term investments.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A reduction in the carrying value of the deferred tax assets is required when it is not more likely than not that such deferred tax assets are not realizable.

Results of Operations

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020:

(in thousands)	Year Ended December 31, 2021	2020
License revenue	$ 18,943	$ —
Operating expenses:		
Research and development	57,751	43,211
General and administrative	29,146	17,124
Total operating expenses	86,897	60,335
Loss from operations	(67,954)	(60,335)
Other income (expense):		
Interest income	477	888
Other income (expense), net	(8)	(11)
Net loss	(67,485)	(59,458)
Net loss attributable to noncontrolling interest	(1,915)	(7,659)
Net loss attributable to common stockholders of Cullinan	$ (65,570)	$ (51,799)

Research and Development Expenses

(in thousands)	Year Ended December 31, 2021	2020	Change
Cullinan Pearl (CLN-081)	$ 22,723	$ 8,253	$ 14,470
Cullinan MICA (CLN-619)	8,797	10,352	(1,555)
Cullinan Florentine (CLN-049)	6,442	9,659	(3,217)
Cullinan Amber (CLN-617)	2,231	720	1,511
Total Asset Subsidiaries expenses	$ 40,193	$ 28,984	$ 11,209
Early stage research	4,878	6,031	(1,153)
Other personnel and unallocated	3,802	2,296	1,506
Equity-based compensation	8,878	5,900	2,978
Total research and development expenses	$ 57,751	$ 43,211	$ 14,540

Research and development expenses were $57.8 million for the year ended December 31, 2021, compared to $43.2 million for the year ended December 31, 2020. We separately disclosed additional details for the research and development expenses incurred in connection with the research and development activities conducted for the product candidates and programs being developed by our partially-owned subsidiaries Cullinan Amber, Cullinan Florentine, Cullinan MICA and Cullinan Pearl, as we believe they represent key portfolio value drivers.

The net increase of $11.2 million of research and development expenses of the Asset Subsidiaries were primarily due to the following ongoing research and development activities for our active programs: (i) increase in trial enrollment and chemistry, manufacturing and controls, or CMC costs relating to CLN-081 of $14.5 million, (ii) increase in preclinical and CMC costs to support IND enabling activities for CLN-619 of $5.0 million offset by a non-recurring non-cash charge of $6.5 million taken in May 2020 for the asset acquisition of CLN-619, (iii) a decrease in preclinical and CMC activity for CLN-049 of $3.2 million relating to the completion of development and manufacturing activity of the drug product and (iv) increase in preclinical and CMC costs to support IND enabling activities for CLN-617 of $1.5 million.

The remaining net increase of $3.3 million in research and development expenses were primarily related to equity-based compensation expense for stock options granted under the 2021 Stock Option and Incentive Plan of $3.0 million, increased headcount and expansion of operations of $1.5 million, offset by a $2.4 million decrease in expenses from the wind down of clinical trial activities for VK-2019 and $1.2 million increase in early stage research activities.

General and Administrative Expenses

General and administrative expenses were $29.1 million for the year ended December 31, 2021 compared to $17.1 million for the year ended December 31, 2020. The increase of $12.0 million was primarily due to a net increase of $6.4 million in equity-based compensation expense where the Company recorded a non-recurring charge of $6.7 million in the fourth quarter of 2021 due to the transition of our chief executive officer, $2.5 million in directors' and officers' liability insurance and other corporate fees, $1.7 million due to increased headcount to support operations of a public company, $0.5 million for patent fees and $0.6 million costs for system upgrades to enhance information technology environment.

Other Income, Net

Other income, net was $0.5 million during the year ended December 31, 2021 compared to $0.9 million during the year ended December 31, 2020. The decrease of $0.4 million was primarily related to a higher interest income earned in the prior year.

Net Loss Attributable to Noncontrolling Interest

Net loss attributable to noncontrolling interests were $1.9 million and $7.7 million for the years ended December 31, 2021 and 2020, respectively. Net loss attributable to noncontrolling interests was lower in 2021 compared to 2020, which was primarily due to the allocation of income from the Zai License Agreement to the noncontrolling interests shareholders of Cullinan Pearl. Net loss attributable to noncontrolling interests of $7.7 million for the year ended December 31, 2020 was primarily related to the acquisition of our Asset Subsidiary, Cullinan MICA, of $5.4 million and the issuance of anti-dilution shares in our Asset Subsidiaries, of $1.2 million.

Liquidity and Capital Resources

Overview

Since our inception, we have incurred significant operating losses. We have not yet commercialized any products and we do not expect to generate revenue from sales of products for several years, if at all. To date, we have funded our operations primarily with proceeds from the sale of equity securities. As of December 31, 2021, we had cash, cash equivalents and short-term investments of $290.5 million and long-term investments of $140.4 million.

In January 2021, the Company completed its IPO and received net proceeds of $264.5 million from the offering, after deducting underwriting discounts, commissions and other offering expenses. Based on our current operational plans and assumptions, we expect that our current cash, cash equivalents, and short-term investments, will be sufficient to fund operations through 2024. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We cannot guarantee that we will be able to raise additional capital on reasonable terms or at all.

Cash Flows

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,	
(in thousands)	**2021**	**2020**
Net cash used in operating activities	$ (43,433)	$ (29,772)
Net cash used in investing activities	(333,775)	(5,420)
Net cash provided by financing activities	268,784	140,140
Net (decrease) increase in cash and cash equivalents	$ (108,424)	$ 104,948

Cash Flow from Operating Activities

For the year ended December 31, 2021, operating activities used $43.4 million of cash and primarily consisted of our net loss of $67.5 million, changes in net operating assets and liabilities of $3.5 million, and offset by non-cash charges of $27.6 million. Our non-cash charges of $27.6 million primarily consisted of $24.4 million from equity-based compensation expense and a $3.1 million from amortization or accretion on marketable securities.

For the year ended December 31, 2020, operating activities used $29.8 million of cash and primarily consisted of our net loss of $59.5 million, offset by changes in net operating assets and liabilities of $6.9 million, and non-cash charges of $22.8 million. Our non-cash charges of $22.8 million primarily consisted of $14.9 million from equity-based compensation expense, $6.4 million relating to the IPR&D charge in connection with the acquisition of MICA and a $1.2 million license expense in exchange for subsidiary capital stock.

Cash Flow from Investing Activities

For the year ended December 31, 2021, investing activities used $333.8 million of cash and primarily consisted of $525.8 million used for the purchases of marketable securities offset by $192.0 million proceeds from the sales and maturities of marketable securities.

For the year ended December 31, 2020, investing activities used $5.4 million of cash and primarily consisted of net $6.8 million used for the purchases of marketable securities, less than $0.1 million for the purchases of property and equipment, offset by $1.5 million of cash acquired in the MICA asset acquisition.

Cash Flow from Financing Activities

For the year ended December 31, 2021, net cash provided by financing activities was $268.8 million, which primarily consisted of net proceeds from our initial public offering of $267.3 million, proceeds from stock option exercises of $3.3 million, offset by payment of deferred offering costs of $2.7 million.

For the year ended December 31, 2020, net cash provided by financing activities was $140.1 million, which primarily consisted of net proceeds from the issuance of common stock equivalents of $138.9 million and net proceeds related to the issuance of noncontrolling interests of $1.2 million.

Future Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities, manufacturing and clinical trials of our product candidates. In addition, we have and will continue to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company. Our expenses will also increase as we:

- continue our research and development efforts and submit investigational new drug applications, or INDs, for our product candidates and programs;
- conduct preclinical studies and clinical trials for our current and future product candidates;
- take temporary precautionary measures to help minimize the risk of COVID-19 to our employees;
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges;
- develop the necessary processes, controls, and manufacturing capabilities to obtain marketing approval for our product candidates and to support manufacturing on a commercial scale;
- develop and implement plans to establish and operate in-house manufacturing operations and facility;
- seek regulatory approvals for any product candidates that successfully complete clinical trials, if any;
- hire and retain additional personnel, such as non-clinical, clinical, pharmacovigilance, quality assurance, regulatory affairs, manufacturing, distribution, legal, compliance, medical affairs, finance, general and administrative, commercial, and scientific personnel; and
- develop, maintain, expand, and protect our intellectual property portfolio.

As a publicly-traded company, we incurred significant legal, accounting and other expenses. We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act, or JOBS Act, enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

To achieve compliance with Section 404 after we no longer qualify as an emerging growth company, we will be required to provide an attestation of our internal controls over financial reporting processes, or ICFR, which will require additional costs and personnel. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. We expect these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

Based on our current operational plans and assumptions, we expect that our current cash, cash equivalents, short-term and long-term investments, will be sufficient to fund operations through 2024. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. As we progress with our development programs and the regulatory review process, we expect to incur significant commercialization expenses related to product manufacturing, pre-commercial activities and commercialization. We may also require additional capital to pursue in-licenses or acquisitions of other programs to further expand our pipeline.

Because of the numerous risks and uncertainties associated with research, development and commercialization of our product candidates and programs, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results, and costs of drug discovery, laboratory testing and preclinical and clinical development for our current and future product candidates;
- timely completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- the prevalence, duration and severity of potential side effects or other safety issues experienced by patients receiving our product candidates or future product candidates;
- our ability to establish and maintain collaborations and license agreements on favorable terms, if at all, and the extent to which we acquire or in-license technologies or programs, if at all;
- our ability to enroll clinical trials in a timely manner and to quickly resolve any delays or clinical holds that may be imposed on our development programs;
- timing delays with respect to preclinical and clinical development of our current and future product candidates, including as result of the COVID-19 pandemic;
- the costs of expanding our facilities to accommodate our expected growth in personnel;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities and develop, validate, and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMP;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending intellectual property-related claims;
- the extent to which we acquire or in-license technologies or programs;

- the sales price and availability of adequate third-party coverage and reimbursement for our product candidates, if and when approved; and
- the ongoing costs of operating as a public company.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements, and other collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity, current ownership interests will be diluted. If we raise additional funds through government or third-party funding, collaboration agreements, strategic alliances, licensing arrangements, or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Contractual Obligations and Other Commitments

We have certain payment obligations under various license and collaboration agreements. Under these agreements, we are required to make milestone payments upon successful completion and achievement of certain intellectual property, clinical, regulatory, and sales milestones. The payment obligations under the license and collaboration agreements are contingent upon future events, such as our achievement of specified development, clinical, regulatory, and commercial milestones, and we will be required to make milestone and royalty payments in connection with the sale of products developed under these agreements. As the achievement and timing of these future milestone payments are not probable or estimable, such amounts have not been included in our consolidated balance sheet as of December 31, 2021 and 2020.

We have entered into an operating lease commitment for $3.8 million for our corporate headquarter. Operating lease obligations as of December 31, 2021 were $1.5 million, with $0.6 million payable within 12 months. See Note 10, to our consolidated financial statements for further detail on our obligations and the timing of expected future payments.

In addition, we enter into agreements in the normal course of business with CROs for clinical trials and with vendors for preclinical studies, manufacturing services, and other services and products for operating purposes, which are generally cancelable upon written notice.

Critical Accounting Policies and Estimates

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

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

Net Loss Attributable to Noncontrolling Interests

Net loss attributable to noncontrolling interests in our consolidated statements of operations is a result of our investments in our consolidated entities, which include Cullinan Amber, Cullinan Florentine, Cullinan Pearl and Cullinan MICA, and consists of the portion of the net loss of those consolidated entities that is not allocated to us. Earnings or losses are attributed to noncontrolling interests under the hypothetical liquidation at book value, or HLBV, method. The HLBV method is a point in time calculation that utilizes inputs to determine the amount that we and our noncontrolling interest holders would receive upon a hypothetical liquidation at each balance sheet date based on the liquidation provisions of the respective articles of incorporation. We calculate the share of the noncontrolling interests' earning or losses based on the change to the noncontrolling interests' claim on the net asset of each Asset Subsidiaries. Management's estimates of assets, liabilities, costs and expenses impacted the determination of the net asset value of each Asset Subsidiaries.

Revenue Recognition

The Company recognizes revenue in accordance with Accounting Standards Codification, or ASC, Topic 606, Revenue from Contracts with Customers, or ASC 606. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. Upon satisfaction of our performance obligation to Zai Lab in the first quarter of 2021, we recognized revenue of $18.9 million from our license agreement with Zai Lab. The amount recognized represented the upfront fee less foreign tax withholdings as Pearl does not expect to recover such amounts.

Research and Development Contract Costs and Accruals

We record accrued liabilities for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies, clinical trials and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced and include these costs in accrued research and development liabilities in our consolidated balance sheets and within research and development expense in our consolidated statements of operations and comprehensive loss. These costs are a significant component of our research and development expenses.

We accrue for these costs based on factors such as estimates of the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and in accordance with agreements established with our third-party service providers for such services. We make significant judgments and estimates in determining the accrued research and development liabilities balance at each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, the status and timing of services performed, the number of patients enrolled in clinical trials and the rate of patient enrollment may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party service providers. We record advance payments to service providers as prepaid assets, which are expensed as the contracted services are performed. To date, there have been no material differences between our accrued costs and actual costs.

Equity-Based Compensation Expense

We estimate the fair value of the stock options using the Black-Scholes option pricing model, which requires the input of objective and subjective assumptions. Certain assumptions used, including the fair value of our common stock prior to the time of the initial public offering and stock price volatility, represent management’s estimates and involve inherent uncertainties and the application of management’s judgment and selection of comparable companies. We do not have sufficient historical or implied volatility data for our common stock necessary to estimate expected volatility over a period of time commensurate with the expected term of our stock option awards. For such reporting periods, we estimated expected volatility based the common stock of a selected peer group of similar publicly traded companies for which sufficient historical volatility data was available. As a result, if factors change and management uses different assumptions, equity-based compensation expense could be materially different for future awards.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. A reduction in the carrying value of the deferred tax assets is required when it is not more likely than not that such deferred tax assets are not realizable. Judgement is required to if certain income tax positions are more likely than not of being sustained and may change from period to period when there is a change in judgement. Due to the Company's lack of earnings history, management determined that a full valuation allowance is required to offset the net deferred tax assets at December 31, 2021 and 2020.

Emerging Growth Company and Smaller Reporting Status

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an “emerging growth company,” or an EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, we may adopt certain new or revised accounting standards early.

We will remain an emerging growth company until the earliest to occur of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

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

Recently Issued and Adopted Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to of our consolidated financial statements appearing at the end of this Annual Report.

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

We are a smaller reporting company as defined by Item 10 of Regulation S-K and are not required to provide the information otherwise required under this Item.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15, Exhibits and Financial Statement Schedules, of this Annual Report on Form 10-K.

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

There has been no change of accountants nor any disagreements with accountants on any matter of accounting principles or practices of financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

The Company has established disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) designed to ensure that information required to be disclosed in the reports that the Company files or submits under the Securities Exchange Act of 1934, as amended, or Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated, as of December 31, 2021, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) were effective at the reasonable assurance level as of December 31, 2021.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting (as defined in Rules 13a-15(f) and 15(d)-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) or 15(d)-15(f) under the Exchange Act) that occurred during the fiscal quarter ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Except to the extent provided below, the information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

(3) The exhibits filed as part of this Annual Report are set forth on the Exhibit Index immediately following our consolidated financial statements. The Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary.

The Company has elected not to include summary information.

CULLINAN ONCOLOGY, INC.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Cullinan Oncology, Inc.

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Cullinan Oncology, Inc. and subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

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

Boston, Massachusetts

March 17, 2022

CULLINAN ONCOLOGY, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31, 2021	December 31, 2020[1]
Assets		
Current assets:		
Cash and cash equivalents	$ 59,774	$ 168,198
Short-term investments	230,692	42,008
Prepaid expenses and other current assets	6,098	2,072
Total current assets	296,564	212,278
Property and equipment, net	77	130
Other assets	147	2,300
Long-term investments	140,397	—
Total assets	$ 437,185	$ 214,708
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,169	$ 9,679
Accrued expenses and other current liabilities	8,577	4,641
Total current liabilities	11,746	14,320
Long-term liabilities:		
Deferred rent	65	74
Total liabilities	11,811	14,394
Commitments and contingencies (Note 10)		
Stockholders' equity:		
Common stock, $0.0001 par value, 150,000,000 and 34,900,878 shares authorized as of December 31, 2021 and December 31, 2020, respectively; 44,292,102 and 29,831,125 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively.	4	3
Additional paid-in capital	584,714	292,348
Accumulated other comprehensive loss	(838)	(2)
Accumulated deficit	(158,909)	(93,339)
Total Cullinan stockholders' equity	424,971	199,010
Noncontrolling interests	403	1,304
Total stockholders' equity	425,374	200,314
Total liabilities and stockholders' equity	$ 437,185	$ 214,708

See accompanying notes to the consolidated financial statements.

(1) The consolidated balance sheet as of December 31, 2020 is derived from the consolidated financial statements as of that date and was retroactively adjusted, including shares and per share amounts, as a result of the Reorganization and Reverse Stock Split. See Note 3 to the consolidated financial statements for additional details.

CULLINAN ONCOLOGY, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2021	2020[1]
License revenue	$ 18,943	$ —
Operating expenses:		
Research and development	57,751	43,211
General and administrative	29,146	17,124
Total operating expenses	86,897	60,335
Loss from operations	(67,954)	(60,335)
Other income (expense):		
Interest income	477	888
Other income (expense), net	(8)	(11)
Net loss	(67,485)	(59,458)
Net loss attributable to noncontrolling interest	(1,915)	(7,659)
Net loss attributable to common stockholders of Cullinan	$ (65,570)	$ (51,799)
Net loss per share, basic and diluted	$ (1.52)	$ (2.60)
Total weighted-average shares used in computing net loss per share, basic and diluted	43,077,330	19,887,307
Comprehensive loss:		
Net loss	$ (67,485)	$ (59,458)
Unrealized gain/(loss) on investments	(836)	2
Comprehensive loss	$ (68,321)	$ (59,456)
Comprehensive loss attributable to noncontrolling interest	(1,915)	(7,659)
Comprehensive loss attributable to Cullinan	$ (66,406)	$ (51,797)

See accompanying notes to the consolidated financial statements.

(1) The shares and per share amounts for the year ended December 31, 2020 were derived from the consolidated financial statements as of that date and were retroactively adjusted as a result of the Reorganization and Reverse Stock Split. See Note 3 to the consolidated financial statements for additional details.

CULLINAN ONCOLOGY, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share amounts)

	Common Stock		Noncontrolling Interests in Subsidiaries	Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount					
Balances at December 31, 2019 [1]	18,738,734	$2	$864	$138,543	$(4)	$(41,540)	$97,865
Issuance of common stock equivalents [1] net of issuance costs of $213	1,297,700	—	—	14,037	—	—	14,037
Issuance of common stock equivalents [1] net of issuance costs of $6,359	9,461,414	1	—	124,840	—	—	124,841
Noncontrolling interest acquired in MICA	—	—	5,673	—	—	—	5,673
Issuance subsidiary preferred stock	—	—	1,206	—	—	—	1,206
Issuance subsidiary common stock	—	—	1,183	—	—	—	1,183
Equity-based compensation	320,228	—	38	14,872	—	—	14,910
Stock option exercises	13,049	—	—	56	—	—	56
Unrealized gain on investments	—	—	—	—	2	—	2
Net loss	—	—	(7,659)	—	—	(51,799)	(59,458)
Balances at December 31, 2020[1]	29,831,125	$3	$1,305	$292,348	$(2)	$(93,339)	$200,315
Initial public offering net of issuance costs of $22,870	13,685,000	1	—	264,515	—	—	264,516
Issuance of common stock under employee stock purchase plan	12,977	—	—	218	—	—	218
Issuance subsidiary preferred stock	—	—	923	—	—	—	923
Issuance subsidiary common stock	—	—	67	—	—	—	67
Equity-based compensation	—	—	23	24,352	—	—	24,375
Stock option exercises	763,000	—	—	3,281	—	—	3,281
Unrealized loss on investments	—	—	—	—	(836)	—	(836)
Net loss	—	—	(1,915)	—	—	(65,570)	(67,485)
Balances at December 31, 2021	44,292,102	$4	$403	$584,714	$(838)	$(158,909)	$425,374

See accompanying notes to the consolidated financial statements.

(1) The consolidated balance sheets as of December 31, 2020 and 2019 are derived from the consolidated financial statements as of such date and was retroactively adjusted, including shares and per share amounts, as a result of the Reorganization and Reverse Stock Split. See Note 3 to the consolidated financial statements for additional details.

CULLINAN ONCOLOGY, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2021	2020
Operating activities:		
Net loss	$ (67,485)	$ (59,458)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	53	62
Equity-based compensation expense	24,375	14,910
Amortization or accretion on marketable securities	3,098	233
License expense in exchange for subsidiary common stock	67	1,183
Acquired in-process research and development assets	—	6,447
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(3,269)	(462)
Other assets	—	(18)
Accounts payable	(4,835)	5,581
Accrued expenses and other current liabilities	4,563	1,750
Net cash used in operating activities	(43,433)	(29,772)
Investing activities:		
Purchases of property and equipment	—	(10)
Net cash acquired in Mica asset acquisition	—	1,450
Purchase of marketable securities	(525,813)	(69,763)
Proceeds from sales and maturities of marketable securities	192,038	62,903
Net cash used in investing activities	(333,775)	(5,420)
Financing activities:		
Proceeds from issuance of common stock equivalents[(1)]	—	145,450
Proceeds from initial public offering	267,268	—
Payment of issuance costs related to common stock equivalents[(1)]	—	(6,572)
Payment of deferred offering costs	(2,688)	—
Proceeds from issuance of noncontrolling interests	923	1,206
Proceeds from stock options exercises	3,281	56
Net cash provided by financing activities	268,784	140,140
Net decrease in cash and cash equivalents	(108,424)	104,948
Cash and cash equivalents at beginning of period	168,198	63,250
Cash and cash equivalents at end of period	$ 59,774	$ 168,198
SUPPLEMENTAL NONCASH DISCLOSURE		
Noncash financing activities		
Deferred offering costs paid in the prior year	$ 65	$ —
Deferred offering costs in accounts payable and accrued expenses	$ —	$ 2,093

See accompanying notes to consolidated financial statements.

(1) Changes in equity activities for the year ended December 31, 2020 were retroactively adjusted, including shares and per share amounts, as a result of the Reorganization and Reverse Stock Split. See Note 3 to the consolidated financial statements for additional details.

(1) Nature of Business and Basis of Presentation

Organization

Cullinan Oncology, Inc., together with its consolidated subsidiaries (Cullinan or the Company), is a biopharmaceutical company developing a diversified pipeline of targeted oncology therapies for cancer patients. Cullinan's predecessor company, Cullinan Pharmaceuticals, LLC was formed in September 2016 and was subsequently renamed Cullinan Oncology, LLC (the LLC) in November 2017. The LLC's wholly-owned subsidiary, Cullinan Management, Inc. (Management), was formed in September 2016 and became the surviving entity in a reverse merger with the LLC in January 2021. In February 2021, the Company changed its name from Cullinan Management, Inc. to Cullinan Oncology, Inc.

As of December 31, 2021, the Company had four development subsidiaries, or Asset Subsidiaries: Cullinan Amber Corp. (Amber), Cullinan Florentine Corp. (Florentine), Cullinan MICA Corp. (MICA) and Cullinan Pearl Corp. (Pearl). As of December 31, 2020, the LLC had five development subsidiaries: Amber, Cullinan Apollo Corp. (Apollo), Florentine, MICA and Pearl. Apollo was dissolved in August 2021.

Reorganization, Reverse Stock Split and Initial Public Offering

In January 2021, the Company completed its initial public offering (IPO) in which it issued and sold 13,685,000 shares of its common stock, including 1,785,000 shares sold pursuant to the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $21.00 per share. The shares began trading on the Nasdaq Global Select Market on January 8, 2021 under the symbol "CGEM". The net proceeds received by the Company from the offering were $264.5 million, after deducting underwriting discounts, commissions and other offering expenses.

Immediately prior to the effectiveness of the Company's registration statement, the Company completed its reorganization, whereby the LLC merged with and into Management and Management was the surviving entity. Management was the registrant in the IPO. Pursuant to the Reorganization, all outstanding Redeemable Preferred Units, Non-Voting Incentive Units and common units converted into shares of Management common stock while common unit options were exchanged for stock options. Immediately following the Reorganization, the Company effected a one-for-7.0390 reverse stock split of its issued and outstanding shares of common stock (the Reverse Stock Split).

Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements prior to the Reorganization and notes thereto have been adjusted retroactively, where applicable, to reflect the effect of the Reorganization and Reverse Stock Split. Refer to Note 3 for additional details relating to the Reorganization and Reverse Stock Split.

Liquidity

The Company has incurred operating losses and negative cash flows from operations since its inception and expects to continue to generate operating losses for the foreseeable future. The Company's ultimate success depends on the outcome of its research and development activities as well as the ability to commercialize the Company's product candidates. The Company is subject to a number of risks including, but not limited to, the need to obtain adequate additional funding for the ongoing and planned clinical development of its product candidates. Due to the numerous risks and uncertainties associated with pharmaceutical products and development, the Company is unable to accurately predict the timing or amount of funds required to complete development of its product candidates, and costs could exceed the Company's expectations for a number of reasons, including reasons beyond the Company's control. The Company has incurred losses since inception and has an accumulated deficit of $158.9 million as of December 31, 2021.

Since inception, the Company has funded its operations primarily through the sale of equity securities. The Company expects that its cash, cash equivalents and short-term investments of $290.5 million and long-term investments of $140.4 million as of December 31, 2021, will be sufficient to fund its operating expenses and capital expenditure requirements through at least the next twelve months from the date of issuance of these consolidated financial statements.

(2) Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements of the Company have been prepared in conformity with accounting principles generally accepted in the United States of America (GAAP) and in accordance with applicable rules and regulations of the United States Securities and Exchange Commission (SEC) for financial reporting. The consolidated financial statements include accounts of the Company and its consolidated subsidiaries. All intercompany balances have been eliminated in consolidation. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Updates (ASUs) of the Financial Accounting Standards Board (FASB).

In the opinion of the Company's management, the consolidated financial statements reflect all adjustments, consisting of normal and recurring adjustments, considered necessary for a fair statement of the Company's financial position, its results of operations and comprehensive loss and its cash flows for the periods presented.

Use of Estimates

The preparation of the accompanying consolidated financial statements in accordance with GAAP requires the Company's management to make estimates and judgments that may affect the reported amounts of assets, liabilities, revenues, expenses and related disclosure of contingent assets and liabilities. On an ongoing basis, the Company's management evaluates the estimates, including those related to expenses and accruals. The Company's management bases its estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the fair value of the royalty transfer agreements, accrued research and development costs, the valuation of acquired in-process research and development asset and the fair value of equity awards issued by the Company and its subsidiaries prior to the IPO. Actual results may differ from these estimates under different assumptions or conditions.

Principles of Consolidation

The Company consolidates entities in which it has a controlling financial interest. The Company evaluates each of its subsidiaries to determine whether the entity represents a variable interest entity (VIE) for which consolidation should be evaluated under the VIE model, or alternatively, if the entity is a voting interest entity, for which consolidation should be evaluated using the voting interest model (VOE). The Company concluded that none of its subsidiaries is a VIE and has consolidated each subsidiary under the VOE. Under the VOE, the Company consolidates the entity if it determines 1) that it directly, or indirectly, has greater than 50% of the voting shares or other equity holders do not have substantive voting, participation, or liquidation rights, or 2) when the company has a controlling financial interest through its control of the board of directors, and the significant decisions of the entity are made at the board level.

The Company has either created or made investments in the following Asset Subsidiaries:

Consolidated Entities	Relationship as of December 31, 2021	Date Control First Acquired
Cullinan Amber Corp.	Partially-owned Subsidiary	December 2019
Cullinan Florentine Corp.	Partially-owned Subsidiary	December 2019
Cullinan Mica Corp.	Partially-owned Subsidiary	May 2020
Cullinan Pearl Corp.	Partially-owned Subsidiary	November 2018

Noncontrolling Interests

To the extent that ownership interests in the subsidiaries are held by entities other than the Company, management reports these as noncontrolling interests on the consolidated balance sheets. Earnings or losses are attributed to noncontrolling interests under the hypothetical liquidation at book value (HLBV) method. The HLBV method is a point in time calculation that utilizes inputs to determine the amount that the Company and the noncontrolling interest holders would receive upon a hypothetical liquidation at each balance sheet date based on the liquidation provisions of the respective articles of incorporation. At December 31, 2021, investors and licensors held noncontrolling interests in Amber, Florentine, MICA and Pearl. At December 31, 2020, investors and licensors held noncontrolling interests in Amber, Apollo, Florentine, MICA and Pearl. Refer to Note 4 for details relating to the license agreements and Note 6 for details relating to the noncontrolling interests.

For the years ended December 31, 2021 and 2020, $1.9 million and $7.7 million of net loss, respectively, were attributable to noncontrolling interests and are recorded in the consolidated statements of operations and comprehensive loss and disclosed within the noncontrolling interests in subsidiaries column in the consolidated statements of stockholders' equity.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from nonowner sources. For years ended December 31, 2021 and 2020, the Company recognized $0.8 million in unrealized loss and less than $0.1 million in unrealized gain on investments, respectively.

Segments

The Company has determined that its Chief Executive Officer is the Chief Operating Decision Maker (CODM). The Company operates and manages the business as one reporting and one operating segment, which is the business of developing early stage cancer therapeutics. The Company's CODM reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance. All of the Company's assets are located in the United States.

Concentration of Credit Risk and Other Risks and Uncertainties

The Company has no significant off-balance sheet risk. Cash and cash equivalents are primarily maintained with two major financial institutions in the United States. Deposits at banks may exceed the insurance provided on such deposits. These deposits may be redeemed upon demand, and therefore, bear minimal risk.

The Company is subject to certain risks and uncertainties and believes that changes in any of the following areas could have a material adverse effect on future financial position or results of operations: ability to obtain future financing; regulatory approval and market acceptance of, and reimbursement for, product candidates; performance of third-party clinical research organizations and manufacturers upon which the Company relies; protection of the Company's intellectual property; litigation or claims against the Company based on intellectual property, patent, product, regulatory or other factors; and the Company's ability to attract and retain employees necessary to support its growth.

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for drug substance and drug products related to these programs. These programs could be adversely affected by a significant interruption in the supply.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the time of purchase to be cash equivalents. As of December 31, 2021 and 2020, cash equivalents consist of government-backed money market funds.

Investments

Investments not classified as cash equivalents with maturities of less than twelve months are classified as short-term investments in the consolidated balance sheets. Investments with maturities greater than twelve months for which the Company has the intent and ability to hold the investment for greater than twelve months are classified as long-term investments in the consolidated balance sheets. The Company generally holds investments in marketable securities.

Marketable securities are carried at estimated fair value, with unrealized gains or losses included in accumulated other comprehensive income (loss) in stockholders' equity. The fair value of marketable securities is based on available market information. The amortized cost of marketable securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Interest and dividends are also included in interest income. The Company periodically reviews its marketable securities for impairment and adjusts these investments to their fair value when a decline in market value is deemed to be other than temporary. Declines in fair value judged to be other-than-temporary on marketable securities, if any, are included in other income (expense), net.

The Company recognized its short-term and long-term investments by security type at December 31, 2021:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		(in thousands)		
Short-term investments				
Corporate notes	$ 98,642	$ —	$ (95)	$ 98,547
Commercial paper	114,174	—	(27)	114,147
U.S. government notes	18,033	—	(35)	17,998
Total short-term investments	230,849	—	(157)	230,692
Long-term investments				
Corporate notes	117,868	—	(596)	117,272
Asset-backed securities	3,044	—	(8)	3,036
U.S. government notes	20,166	—	(77)	20,089
Total long-term investments	141,078	—	(681)	140,397
Total investments	$ 371,927	$ —	$ (838)	$ 371,089

The Company recognized its short-term investments by security type at December 31, 2020:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		(in thousands)		
Corporate notes	$ 12,780	$ —	$ (3)	$ 12,777
Commercial paper	24,473	—	—	24,473
Asset-backed securities	4,757	1	—	4,758
Total investments	$ 42,010	$ 1	$ (3)	$ 42,008

Fair Value of Financial Instruments

Certain assets and liabilities are carried at fair value under GAAP. The fair value hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets (Level 1) and the lowest priority to unobservable inputs (Level 3). As required by FASB ASC Topic 820, *Fair Value Measurement* (ASC Topic 820) the Company's financial assets are classified within the fair value hierarchy based on the lowest level of input that is significant to the fair value measurement. The three levels of the fair value hierarchy under ASC Topic 820, and its applicability to the Company's financial assets, are described below:

Level 1—Unadjusted quoted prices in active markets that are accessible at the measurement date of identical, unrestricted assets.

Level 2—Quoted prices for similar assets, or inputs that are observable, either directly or indirectly, for substantially the full term through corroboration with observable market data.

Level 3—Pricing inputs are unobservable for the asset, that is, inputs that reflect the reporting entity's own assumptions about the assumptions market participants would use in pricing the asset.

Asset-backed securities, commercial paper and corporate and U.S. government notes are primarily valued using market quotations or prices obtained from independent pricing sources which may employ various pricing methods to value the investments including matrix pricing.

The following table sets forth the fair value of the Company's financial assets as of December 31, 2021, allocated into Level 1, Level 2 and Level 3, that was measured on a recurring basis:

	Level 1	Level 2	Level 3	Total
		(in thousands)		
Cash and cash equivalents				
Cash	$ 35,925	$ —	$ —	$ 35,925
Money market funds	23,849	—	—	23,849
Total cash and cash equivalents	59,774	—	—	59,774
Short-term investments				
Corporate notes	—	98,547	—	98,547
Commercial paper	—	114,147	—	114,147
U.S. government notes	—	17,998	—	17,998
Total short-term investments	—	230,692	—	230,692
Long-term investments				
Corporate notes	—	117,272	—	117,272
Asset-backed securities	—	3,036	—	3,036
U.S. government notes	—	20,089	—	20,089
Total long-term investments	—	140,397	—	140,397
Total cash, cash equivalents and investments	$ 59,774	$ 371,089	$ —	$ 430,863

The following table sets forth the fair value of the Company's financial assets as of December 31, 2020, allocated into Level 1, Level 2 and Level 3, that was measured on a recurring basis:

	Level 1	Level 2	Level 3	Total
		(in thousands)		
Cash and cash equivalents				
Cash	$ 22,007	$ —	$ —	$ 22,007
Money market funds	146,191	—	—	146,191
Total cash and cash equivalents	168,198	—	—	168,198
Short-term investments				
Corporate notes	—	12,777	—	12,777
Commercial paper	—	24,473	—	24,473
Asset-backed securities	—	4,758	—	4,758
Total short-term investments	—	42,008	—	42,008
Total cash, cash equivalents and investments	$ 168,198	$ 42,008	$ —	$ 210,206

Prepaid expenses and other current assets, accounts payable and accrued expenses and other current liabilities are carried at cost, which management believes approximates fair value due to their short term nature.

Deferred Offering Costs

The Company capitalizes costs that are directly associated with in-process equity financings until such financings are consummated at which time such costs are recorded against the gross proceeds of the offering. Should the in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statements of operations and comprehensive loss. The Company incurred $2.7 million of deferred offering costs in 2020 and recorded such amounts against the gross proceeds of the Company's IPO within the statements of stockholders' equity for the year ended December 31, 2021.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

Computers	3 years
Office furniture and equipment	5 years
Leasehold improvements	Shorter of the useful life of the asset or the lease term

Maintenance and repairs that do not improve or extend the life of the assets are expensed when incurred. Upon sale or retirement of assets, the cost and accumulated depreciation and amortization are removed from the consolidated balance sheet and any resulting gain or loss is reflected in the consolidated statements of operations and comprehensive loss in the period realized.

Property and equipment consisted of the following:

	December 31,	
	2021	2020
	(in thousands)	
Computers	$ 70	$ 70
Office furniture and equipment	134	134
Leasehold improvements	105	105
Total property and equipment, gross	309	309
Less: accumulated depreciation	(232)	(179)
Total property and equipment, net	$ 77	$ 130

Depreciation expense was less than $0.1 million for each of the years ended December 31, 2021 and 2020.

Accrued liabilities and other current liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2021	2020
	(in thousands)	
Accrued bonus	$ 2,576	$ 1,763
Professional fees and other	973	1,049
Research and development costs	5,028	1,829
	$ 8,577	$ 4,641

Asset Acquisitions

The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes transactions costs. Goodwill is not recognized in asset acquisitions. In an asset acquisition, the cost allocated to acquire in-process research and development (IPR&D) with no alternative future use is charged to research and development expense at the acquisition date.

Impairment of Long-Lived Assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to future undiscounted net cash flows expected to be generated. Impairment charges are recognized at the amount by which the carrying amount of an asset exceeds the fair value of the asset. Assets to be disposed of are reported at the lower of the carrying amount or the fair value less costs to sell. There was no impairment of long-lived assets for any of the periods presented.

Revenue Recognition

The Company recognizes revenue in accordance with ASC Topic 606, Revenue from Contracts with Customers, or ASC 606. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a 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) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company enters into licensing arrangements for research and development, manufacturing and commercialization activities, which have components within the scope of ASC 606. Payments pursuant to these arrangements typically include non-refundable, upfront payments, milestone payments upon achieving significant development events, research and development reimbursements, sales milestones and royalties on future product sales. The amount of variable consideration is constrained until it is probable that the revenue is not at a significant risk of reversal in a future period. The contracts into which the Company enters generally do not include significant financing components. As part of the accounting for these arrangements, the Company must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above, and d) the measure of progress in step (v) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below.

Non-Exclusive Licenses

If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a promise or performance obligation is distinct from the other elements, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining elements, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

Milestone Payments

At the inception of each arrangement that includes milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to 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 revenues and earnings in the period of adjustment.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license of intellectual property is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Research and Development Expenses

Research and development costs are expensed as incurred and consist primarily of funds for employee wages and funds paid to third parties for the provision of services for product candidate development, clinical and preclinical development and related supply and manufacturing costs, and regulatory compliance costs. At the end of the reporting period, the Company compares payments made to third-party service providers to the estimated progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the progress that the Company estimates has been made as a result of the service provided, the Company may record net prepaid or accrued expense relating to these costs.

Costs incurred to obtain licenses are recognized as research and development expense as incurred if the technology licensed has no alternative future use. Advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are received or services are performed.

The Company has entered into various research and development related contracts with parties both inside and outside of the United States. The payments related to these agreements are recorded as research and development expenses as incurred. The Company records accrued liabilities for estimated ongoing research and development costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. To date, there have been no material differences between the Company's accrued costs and actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Equity-Based Compensation

Equity-based compensation is measured at the grant date for all equity-based awards made to employees and non-employees based on the fair value of the awards and is recognized as expense on a straight-line basis over the requisite service period, which is generally the vesting period. The Company has elected to recognize the actual forfeitures by reducing the equity-based compensation expense in the same period as the forfeitures occur.

The Company estimated the fair of the stock options using the Black-Scholes option pricing model, which requires the input of objective and subjective assumptions. Certain assumptions used, including the fair value of the Company's common stock prior to IPO and stock price volatility, represent management's estimates and involve inherent uncertainties and the application of management's judgment. As a result, if factors change and management uses different assumptions, equity-based compensation expense could be materially different for future awards.

The Company classifies equity-based compensation in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

Income Taxes

The Company accounts for income taxes using the asset and liability method in accordance with FASB ASC Topic 740, Income Taxes. Current income taxes are based on taxable income for federal and state reporting purposes. Deferred income tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. A valuation allowance is provided when it is more likely than not that some portion, or all of a deferred tax asset will not be realized. Due to the Company's lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance at both December 31, 2021 and 2020.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount of benefit that is greater than fifty percent likely to be realized upon settlement. Changes in measurement are reflect in the period in which the change in judgment occurs.

Net Loss per Share

Basic and diluted net loss per share is determined by dividing net loss attributable to common stockholders by the weighted-average shares of common stock outstanding during the period, without consideration for potential dilutive shares of common stock, such as stock options, unvested restricted stock awards and shares issuable under the employee stock purchase plan. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive shares of common stock are not assumed to have been issued if their effect is anti-dilutive. Therefore, the weighted-average shares used to calculate both basic and diluted net loss per share are the same for the periods presented. The Company excluded unvested shares of restricted stock awards, stock options and shares issuable under the employee stock purchase plan from the computation of diluted weighted-average shares outstanding as they would be antidilutive.

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

The JOBS Act does not preclude an emerging growth company from adopting a new or revised accounting standard earlier than the time that such standard applies to private companies. The Company expects to use the extended transition period for any other new or revised accounting standards during the period in which it remains an emerging growth company.

Recently Adopted Accounting Pronouncements

In August 2020, FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* (ASU 2020-06), which, among other things, provides guidance on how to account for contracts on an entity's own equity. ASU 2020-06 simplifies the accounting for certain financial instruments with characteristics of liabilities and equity. Specifically, ASU 2020-06 eliminated the need for the Company to assess whether a contract on the entity's own equity (1) permits settlement in unregistered shares, (2) whether counterparty rights rank higher than shareholder's rights, and (3) whether collateral is required. In addition, ASU 2020-06 requires incremental disclosure related to contracts on the entity's own equity and clarifies the treatment of certain financial instruments accounted for under this ASU on earnings per share. ASU 2020-06 may be applied on a full retrospective or modified retrospective basis. ASU 2020-06 became effective January 1, 2022 including interim periods presented within that year. Early adoption of the ASU is permitted by the Company effective January 1, 2021. The Company adopted ASU 2020-06 beginning on January 1, 2021. The adoption of ASU 2020-06 did not materially impact the Company's consolidated financial statements and associated disclosures.

Recently Issued Accounting Pronouncements Not Yet Adopted

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), to increase transparency and comparability among organizations by recognizing a right-of-use asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either operating or financing, with such classifications affecting the pattern of expense recognition in the income statement. ASU 2016-02 is effective for fiscal years beginning after December 15, 2019, and early adoption is permitted. ASU 2016-02 was recently delayed for emerging growth companies that elected to adopt new accounting standards on the adoption date required for private companies and will be effective for the Company's annual reporting period beginning on January 1, 2022 and interim periods beginning in the first quarter of 2023.

The Company will adopt ASU 2016-02 in the first quarter of 2022 using a modified retrospective approach under which the cumulative effect of initially applying the standard will be recognized as an adjustment to its opening 2022 retained earnings, with no restatement of prior year amounts. The Company will apply an optional package of practical expedients intended to ease transition to the standard for existing leases by, among its provisions, allowing the Company to carry forward its original lease classification conclusions without reassessment. The Company also intends to elect application of the practical expedient to not separate non-lease components from lease components for purposes of measuring its lease-related balances.

Based on assessment efforts to date, the Company estimates that the adoption of ASU 2016-02 will result in initial increases in its long-term assets and liabilities of approximately $1.3 million to $1.4 million relating to its existing lease commitments that will become subject to balance sheet recognition. These balances will fluctuate over time as the Company's lease portfolio changes as a result of ongoing lease-related activity. The standard also requires enhanced quantitative and qualitative lease-related disclosures. Recognition of lease expense in the consolidated statement of operations and comprehensive loss will not significantly change.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* (ASU 2019-12), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard became effective beginning January 1, 2022. The Company does not expect the adoption of ASU 2019-12 to have a material impact on its consolidated financial position and consolidated results of operations upon adoption.

(3) Reorganization and Reverse Stock Split

Immediately prior to the completion of the IPO in January 2021, the LLC completed the Reorganization. Prior to the Reorganization, Management was a wholly-owned subsidiary of the LLC. The LLC was also the direct parent company of the Company's development subsidiaries. Pursuant to the Reorganization, Management acquired all the assets of the LLC, including all of the stock the LLC owned of Amber, Apollo, Florentine, MICA and Pearl (collectively the Asset Subsidiaries), and assumed all of the LLC's liabilities and obligations.

Following the Reorganization, all of Management's outstanding Preferred Stock automatically converted on a one-for-one basis into common stock of Management. The Company then effected the Reverse Stock Split. Immediately prior to completion of the Company's IPO, the existing units of the LLC were cancelled and the number of shares of common stock exchanged and issued to the LLC's unitholders in the Reorganization is shown in the below table by unit class, on a split adjusted basis:

Cullinan Oncology, LLC Unit Type	Number of Management's Shares Issued	Adjusted for the Reverse Stock Split
Series C Preferred Units	66,599,045	9,461,414
Series B Preferred Units	63,141,016	8,970,154
Series A1 Preferred Units	50,000,000	7,103,280
Series Seed Preferred Units	16,000,000	2,273,050
Non-Voting Incentive Units	11,896,500	1,689,949
Common Units	34,747,722	4,936,415
Total shares issued	242,384,283	34,434,262

The amount presented for Non-Voting Incentive Units included unvested outstanding Non-Voting Incentive Units that were exchanged for restricted stock of Management. The amount presented for Common Units included the unvested outstanding Restricted Common Units, exchanged for Management's restricted stock, and issued and unvested Common Unit Options, that were exchanged for Management's stock options. The unvested awards are subject to the same time-based vesting conditions as the original awards.

The Reorganization was accounted for as a reverse acquisition, where the LLC was determined to be the accounting acquirer and Management to be the legal acquiree, and recapitalization for financial reporting purposes. Accordingly, the historical financial statements of the LLC became the Company's historical financial statements, including the comparative prior periods. All share and per share amounts in these consolidated financial statements and related notes have been retroactively adjusted, where applicable, for all periods presented. The shares of the Company's common stock for periods prior to the Reorganization represent the outstanding units of the LLC recalculated to give effect to the Reorganization and Reverse Stock Split.

All LLC units that were previously reported as Redeemable Preferred Units, or temporary equity, were converted to common stock of the Company upon the execution of the Reorganization and have been reclassified to stockholders' equity for all periods presented, as if the Reorganization occurred at the beginning of the earliest period presented in the Company's financial statements for the years ended December 31, 2020 and 2019:

	As of December 31, 2020		
	As Reported	Adjustment	As Adjusted
		(in thousands)	
Redeemable Preferred Units			
Series Seed Redeemable Preferred Units	$ 3,956	$ (3,956)	$ —
Series A1 Redeemable Preferred Units	49,946	(49,946)	—
Series B Redeemable Preferred Units	97,909	(97,909)	—
Series C Redeemable Preferred Units	124,841	(124,841)	—
Total Redeemable Preferred Units	276,652	(276,652)	—
Stockholders' Equity (Members' Deficit)			
Non-Voting Incentive Units	1	(1)	—
Common Stock	—	3	3
Additional paid-in capital	15,698	276,650	292,348
Accumulated other comprehensive loss	(2)	—	(2)
Accumulated deficit	(93,339)	—	(93,339)
Total Cullinan Stockholders' Equity (Members' Deficit)	(77,642)	276,652	199,010
Non-controlling interests in subsidiaries	1,304	—	1,304
Total Stockholders' Equity (Members' Deficit)	$ (76,338)	$ 276,652	$ 200,314

	As of December 31, 2019		
	As Reported	Adjustment	As Adjusted
		(in thousands)	
Redeemable Preferred Units			
Series Seed Redeemable Preferred Units	$ 3,956	$ (3,956)	$ —
Series A1 Redeemable Preferred Units	49,946	(49,946)	—
Series B Redeemable Preferred Units	83,872	(83,872)	—
Series C Redeemable Preferred Units	—	—	—
Total Redeemable Preferred Units	137,774	(137,774)	—
Stockholders' Equity (Members' Deficit)			
Non-Voting Incentive Units	1	(1)	—
Common Stock	—	2	2
Additional paid-in capital	770	137,773	138,543
Accumulated other comprehensive loss	(4)	—	(4)
Accumulated deficit	(41,540)	—	(41,540)
Total Cullinan Stockholders' Equity (Members' Deficit)	(40,773)	137,774	97,001
Non-controlling interests in subsidiaries	864	—	864
Total Stockholders' Equity (Members' Deficit)	$ (39,909)	$ 137,774	$ 97,865

(4) License and Collaboration Agreements

The following table summarizes the impact of research and development costs related to the collaboration and license agreements on the Company's consolidated statements of operations and comprehensive loss for the years ended December 31, 2021 and 2020.

	December 31,	
	2021	2020
	(in thousands)	
Adimab	$ 46	$ 1,318
Amber - MIT	71	333
Apollo - Wistar	—	355
Florentine - Tubigen	—	912
Pearl - Taiho	3,000	531
	$ 3,117	$ 3,449

Adimab

In November 2018, the Company entered into a collaboration agreement with Adimab, LLC (Adimab) (the Adimab Collaboration Agreement). Pursuant to the Adimab Collaboration Agreement, the Company selected a number of biological targets against which Adimab used its proprietary platform technology to discover and/or optimize antibodies based upon mutually agreed upon research plans. Under the Adimab Collaboration Agreement, the Company has the ability to select a specified number of additional biological targets against which Adimab will provide additional antibody discovery and optimization services.

During the research term and evaluation term for a given research program with Adimab, the Company has a non-exclusive worldwide license under Adimab's technology to perform certain research activities and to evaluate the program antibodies to determine whether the Company wants to exercise its option to obtain a royalty-free, fully paid, non-exclusive license to exploit such antibodies and sublicense through multiple tiers.

Under the Adimab Collaboration Agreement, the Company paid a one-time, non-creditable, non-refundable technology access fee. The Company is also required to pay an annual access fee and research funding fees in connection with Adimab's full-time employees' compensation for performance of Adimab's obligations under the Adimab Collaboration Agreement. The Company is also obligated to make certain research delivery, clinical and sales milestone payments to Adimab on a program-by-program basis, subject to certain reductions and discounts.

The Company is obligated to pay certain royalty payments on a product-by-product basis at a low single-digit percentage of annual aggregate worldwide net sales. Such royalty obligations will expire on a country-by-country and product-by-product basis upon the later of (a) a certain low double-digit number of years after the first commercial sale of such product in such country and (b) the expiration of the last issued and not expired, permanently revoked, or invalid claim within a program patent covering such product.

The Company may terminate the Adimab Collaboration Agreement at any time, for any reason, upon a specified period advance written notice. The term of the Adimab Collaboration Agreement expires upon the last research program's evaluation term in the event no Adimab Option is exercised or in the event an Adimab Option is exercised, after the royalty term expires at the later of a specified period or invalid patent coverage of the relevant product.

Amber—Massachusetts Institute of Technology

In December 2019, Amber entered into an Exclusive Patent License Agreement with Massachusetts Institute of Technology (MIT) to develop a cancer immunotherapy product worldwide (the MIT License Agreement). Under the terms of the MIT License Agreement, Amber paid an upfront nonrefundable license fee of less than $0.1 million upon execution. Additionally, Amber issued 200,066 shares of its common stock to MIT and the licensed technology founder upon execution of its Series A Preferred financing in April 2020 as consideration for the licenses granted and incurred $0.2 million of license expenses. In June 2021, Amber issued 153,229 shares of its common stock to MIT as anti-dilution shares upon execution of an additional Series A Preferred financing and incurred less than $0.1 million of license expenses related to the shares issued during 2021.

Amber is also responsible for paying non-refundable, creditable annual license maintenance fees in an increasing amount over a certain number of years and a fixed amount subsequent to this period of time. In addition, MIT granted to Amber an exclusive option to amend the initially determined field to include expansion fields, and such amendment would trigger the payment to MIT of an amendment fee.

Additionally, Amber shall pay certain non-refundable, non-creditable milestone payments up to $7.0 million and $5.5 million to MIT upon the occurrence of certain clinical and regulatory events associated with its first and second indications, respectively, by product, and up to an additional $12.5 million upon the occurrence of cumulative net sales targets. Each milestone payment is paid one time only up to a certain payment amount. No milestones have been achieved to date under the MIT License Agreement.

Under certain conditions upon a change in control of Amber, Amber is required to pay a specified change in control fee and Amber's clinical and regulatory milestone payments shall be increased by 100%.

Furthermore, Amber is required to pay running low single digit royalty percentage on net sales of all licensed products for each reporting period, subject to certain offsets or reductions. The royalties due to MIT for net sales of the licensed product shall not be reduced by more than a mid-double digit percentage. Amber is also required to share any income from sublicensing the licensed products, with the percentage to be determined by the clinical phase of the licensed product, no greater than low-to mid-double digit percentages. Such royalty obligations will expire on a country-by-country and product-by-product basis upon the expiration or abandonment of all issued patents and filed patent applications within the patent rights.

Apollo—The Wistar Institute

In December 2018, Apollo entered into a license agreement with The Wistar Institute (Wistar) to discover and develop a novel Epstein-Barr Nuclear Antigen 1 (EBNA1) inhibitor (the Wistar Agreement). Under the terms of the Wistar Agreement, Apollo paid a nonrefundable up-front option and license fee and issued shares of Apollo common stock to Wistar in exchange for the worldwide, exclusive rights to research and develop Wistar's EBNA1 inhibitor. The Wistar Agreement also provides for Wistar to receive milestone payments upon achievement of patent rights and product development targets and royalties on future sales of licensed products. In December 2018, the Company also entered into a Collaborative Research Agreement with Wistar to continue preclinical research and development with potential product candidate. These studies were budgeted to cost $1.5 million over a three-year timeline.

In May 2020, Apollo terminated the licensing and collaboration agreement with Wistar and decided to discontinue further development of the EBNA1 inhibitor associated with that agreement, VK-2019.

Florentine—Tübingen License Agreement

In August 2020, Florentine entered into an Exclusive License Agreement (the Tübingen License Agreement) with Deutsches Krebsforschungszentrum (DKFZ), Eberhard Karls University of Tübingen, Faculty of Medicine (University of Tübingen) and Universitätsmedizin Gesellschaft für Forschung und Entwicklung mbH, Tübingen (UFE). Pursuant to the Tübingen License Agreement, DKFZ and University of Tübingen, collectively referred to as the Licensor, granted to Florentine an exclusive worldwide, milestone- and royalty-bearing license under certain licensed patent rights, applications, technical information and know-how, with the right to grant sublicenses through multiple tiers to research, develop, commercialize or otherwise exploit licensed products within the field.

Florentine is required to pay to the Licensor an upfront, non-refundable, non-creditable option exercise fee of $0.6 million. As partial consideration for the licenses, Florentine issued to DKFZ and UFE 758,246 and 348,682 shares of Florentine common stock, respectively, who together own five percent (5%) of Florentine's fully diluted shares outstanding as December 31, 2021. DKFZ and UFE were also granted the right to appoint one representative to the board of directors of Florentine.

Additionally, Florentine shall pay certain non-refundable, non-creditable milestone payments to the Licensor upon the occurrence of certain clinical and regulatory events related to a licensed product. Each milestone payment is paid one time only up to a certain payment amount. No milestones have been achieved to date under the Tübingen License Agreement.

Pearl—Taiho Pharmaceuticals, Co. Ltd

In February 2019, Pearl entered into a license and collaboration agreement with Taiho Pharmaceuticals, Co. Ltd (Taiho Pharma) to develop a novel epidermal growth factor receptor (EGFR) inhibitor (the Taiho License Agreement).

As consideration for the license for worldwide exclusive development rights, excluding Japan, Pearl paid an initial, non-refundable, non-creditable license fee of $2.5 million and issued, to Taiho Ventures, LLC (Taiho Ventures) an affiliate of Taiho Pharma, 1,860,000 shares of its common stock in 2019. In addition, Pearl is obligated to pay non-refundable, non-creditable research and development, regulatory and sales milestone payments upon the occurrence of certain milestone events in an aggregate amount of up to $154.5 million for development, regulatory and sales milestones. Each milestone is payable only once. No milestones have been achieved to date under the Taiho License Agreement.

Furthermore, Pearl is required to pay running low single digit to low double digit royalty percentages of annual aggregate net sales worldwide outside Japan on a country-by-country and product-by-product basis during the royalty term, subject to certain offsets, deductions or reductions related to loss or impairment of exclusivity in the territory. The obligation to pay royalties is imposed only once with respect to net sales of the same unit of a licensed product. Such royalty obligations will expire on a country-by-country and product-by-product basis upon the later of (a) the expiration of the last patent which covers a product in such country, (b) the expiration of any exclusivity granted by a regulatory authority and (c) a low double-digit anniversary following the first commercial sale of a product in such country.

In the event (i) Taiho Pharma does not exercise its right of negotiation with respect to a licensed product or (ii) Taiho Pharma does exercise its right of negotiation, but the parties do not consummate a transaction, then at the time Pearl enters into a subsequent transaction with a third party for (a) less than all or less than substantially all of Pearl's rights in a licensed product, Pearl is also obligated to pay Taiho Pharma a mid-single digit percentage of revenue from such transactions or (b) all or substantially all of Pearl's rights in a licensed product, Pearl is obligated to pay Taiho Pharma a low single digit percentage of revenue from such transactions, provided, however, that such payment under (b) shall not be required following the consummation of Pearl's initial public offering.

In parallel with the execution of the Taiho License Agreement, Pearl entered into a Series A Preferred Stock Purchase Agreement with the Company and Taiho Ventures to sell up to 23,000,000 shares of Pearl's Series A Preferred Stock for $1.00 per share for an aggregate purchase price of $23.0 million. The Company and Taiho Ventures invested $14.0 million in the initial closing. The Series A Preferred Stock Purchase Agreement obligated Pearl to sell, and the Company and Taiho Ventures to purchase, at $1.00 per share, the remaining 9,000,000 shares of Pearl's Series A Preferred Stock at a subsequent closing, either upon the approval of Pearl's board of directors or if the cash balance of Pearl is below $1.0 million. Pearl completed the second closing in August 2020. The Company determined that Pearl's second Series A Preferred Stock tranche is separable and therefore a freestanding instrument, but the fair value of the tranche right is not material as of and for the year ended December 31, 2020. See Note 6 for further details.

Pearl—Zai Lab License Agreement

In December 2020, Pearl entered into a license agreement (Zai License Agreement) with Zai Lab Shanghai Company, Limited (Zai Lab), to grant Zai Lab, an exclusive royalty-bearing license to research, develop, commercialize and manufacture CLN-081 and products which contain CLN-081 in China, Hong Kong, Macau and Taiwan. Zai Lab will be primarily responsible for substantially all the costs related to the operations and control over the significant activities related to the exploitation of the licensed IP of CLN-081.

As partial consideration of the license and rights granted to Zai Lab, Zai Lab paid Pearl a one-time, irrevocable, nonrefundable license fee of $20.0 million. In addition to the upfront fee, Zai Lab is obligated to pay Pearl, research and development, regulatory and sales milestone payments upon the occurrence of certain milestone events in the aggregate amount of up to $211.0 million, and tiered royalty payments based on the annual net sales of the licensed product. The upfront license fee was recognized in revenue. The Company will also recognize the milestone and royalty payments in revenue once they are earned. No milestones have been achieved to date under the Zai License Agreement.

The upfront payment received by Pearl was subject to foreign tax withholdings. When the licensed IP and technology know-how was transferred to Zai Lab in January 2021, Pearl recognized revenue of $18.9 million, which represented the upfront fee less the foreign tax withholdings as Pearl does not expect to recover the amounts relating to the foreign tax withholdings.

In connection with the Taiho License Agreement, Pearl is obligated to pay Taiho Pharma a percentage of future revenue received from Zai Lab, including the upfront payment that was received in January 2021. Upon receipt of the upfront payment, Pearl recognized $3.0 million payable to Taiho Pharma within research and development expenses in the consolidated statements of operations and comprehensive loss.

(5) Cullinan-MICA Asset Acquisition

On May 28, 2020 (the Acquisition Date), in accordance with the Series A Senior Preferred Stock Purchase Agreement (the Purchase Agreement), the Company purchased 5,385,787 shares of Series A Senior Preferred Stock (the Series A Senior Preferred Stock) of PDI Therapeutics, Inc. (PDI Therapeutics), for $7.1 million, and certain existing PDI Therapeutics shareholders purchased approximately 702,495 shares of the Series A Senior Preferred Stock for $0.9 million. Concurrently with the Series A Senior Preferred Stock purchase, PDI Therapeutics was renamed Cullinan MICA Corp. The terms of the Purchase Agreement included two additional closings for total proceeds of up to $26.0 million.

On the Acquisition Date, MICA (formerly PDI Therapeutics) authorized the issuance of 72,890,797 shares, of which 39,000,000 was designated as common stock and 33,890,797 was designated as preferred stock. Of the authorized preferred stock, MICA designated 1,999,998 shares as Series A Junior Preferred Stock, 652,371 shares as Series A-1 Junior Preferred Stock, 11,451,514 shares as Series A-2 Junior Preferred Stock, and 19,786,914 shares as Series A Senior Preferred Stock (collectively the Series Preferred Stock). Following the initial close in May 2020, MICA had 22,829,406 shares outstanding, including 6,088,282 shares of Series A Senior Preferred Stock (of which the LLC held 5,385,787 shares), 602,784 shares of common stock, and 14,103,883 shares of Series A, A-1 and A2 Junior Preferred Stock described above. In addition, there were 2,034,457 shares of common stock underlying options reserved under MICA's equity plan (of which 1,826,402 was reserved for future issuances to MICA’s directors and officers, as well as former employees of PDI Therapeutics).

Other than the Series A-1 Junior Preferred Stock, which shares are non-voting, the Series Preferred Stock of MICA vote equally with the shares of common stock of MICA. In addition to any other vote or consent, the vote or written consent of a majority of the holders of Series A Senior Preferred Stock is required for certain actions, including redemptions, dividends, distributions, dissolutions, creation of new classes of stock, mergers, sale of MICA or its assets, and amendments to the certificate of incorporation, as well as other actions. The other classes of Series Preferred Stock have voting rights pertaining to the increase or decrease in the authorized number of shares of their respective classes.

The Company’s initial purchase represented approximately 24% of MICA’s fully diluted shares outstanding, including shares reserved for future issuance, and 88.5% of the Series A Senior Preferred Stock outstanding. The Company can increase its ownership to approximately 54% of MICA’s fully diluted shares outstanding with the subsequent closings. Additionally, as part of the transaction and as outlined in the Voting Agreement dated May 28, 2020, among the Company and other stockholders of MICA, MICA increased the size of its board of directors from four to five directors, of which three directors are designated by the Company.

The Company also entered into a Services Agreement with MICA under which the Company will perform functions required for MICA's operations, including accounts payable, cash management, record keeping, research and development, and accounting services.

Given the Company's ownership of the Series A Senior Preferred Stock and its majority representation on MICA's board of directors, the Company's obtained a controlling interest in MICA on the Acquisition Date. Further, the Company evaluated the MICA transaction and determined that MICA is not a variable interest entity; however, due to the controlling interest in MICA, the Company will consolidate MICA under the voting interest model.

The Company evaluated the change in control of MICA and concluded that the change in control was an asset acquisition rather than a business combination as substantially all of the value in MICA resided in CLN-619, the IPR&D asset developed by MICA. The cost of the assets was calculated as the sum of the fair value of the Company's investment in MICA, the fair value of the noncontrolling interests in MICA and the Company's transaction costs. This cost was allocated to the assets acquired and liabilities assumed in the transaction based on their relative fair values. The amount allocated to the IPR&D asset acquired was $6.4 million and was charged to research and development expense within the consolidated statements of operations and comprehensive loss during the year ended December 31, 2020 as it had no alternative future use at the time of the acquisition.

In December 2020, the stockholders and the board of directors of MICA approved an amendment to its equity plan that decreased the authorized amount of shares under its equity plan such that no further grants could be made under its equity plan. Any authorized but unissued shares under the equity plan were returned to the status of authorized, unissued shares of common stock.

In June 2021, the MICA board authorized the first additional closing and the Company purchased an additional 5,385,787 shares of Series A Senior Preferred Stock for $7.1 million and certain existing shareholders purchased an additional 702,495 shares of Series A Senior Preferred Stock for $0.9 million pursuant to the MICA Purchase Agreement. Following the first additional closing, the Company's ownership increased to 45% of MICA's fully-diluted shares outstanding and remain as such at December 31, 2021.

(6) Common Stock and Noncontrolling Interest in Subsidiaries

Common Stock

As of December 31, 2021 and 2020, 150,000,000 and 34,900,878 shares of common stock of the Company were authorized, respectively. Each share of common stock entitles the holder to one vote and to receive dividends when and if declared by the board of directors of the Company. No dividends have been declared through December 31, 2021.

The LLC's outstanding Non-Voting Incentive Units have been retroactively adjusted to reflect the effect of the Reorganization and Reverse Stock Split. Refer to Note 3 for additional details relating to the Reorganization and Reverse Stock Split.

Noncontrolling Interest in Subsidiaries

Certain subsidiaries issue common stock in connection with licensing agreements and to employees, directors and consultants pursuant to subsidiary equity incentive plans. The holders of subsidiary common stock are entitled to one vote per share. The holders of subsidiary common stock are entitled to receive dividends when and if declared by the subsidiaries' board of directors and distributions in either case only after the payment of all preferential amounts required to be paid to the holders of shares of preferred stock of the respective subsidiary.

In November 2020, the LLC entered into Restricted Stock Contribution Agreements (Contribution Agreements) with Amber, Florentine and Pearl where the LLC exchanged common units of the LLC for restricted common stock held by LLC employees at each of the subsidiaries. The LLC's outstanding restricted common units have been retroactively adjusted to reflect the effect of the Reorganization and Reverse Stock Split. Refer to Note 3 for additional details relating to the Reorganization and the Reverse Stock Split.

Cullinan Amber Corp.

In April 2020, in connection with its Series A Preferred Stock financing, Amber issued 3,000,000 shares of its Series A Preferred Stock to the Company for gross proceeds of $3.0 million. At any time following the initial closing, upon election of Amber's board of directors, Amber may sell up to an aggregate of 9,000,000 shares of Amber's Series A Preferred Stock at one or more subsequent closings at $1.00 per share.

In April 2020, pursuant to the MIT License Agreement between Amber and MIT, Amber issued 400,132 shares of its common stock, in exchange for no additional consideration as set forth in the MIT License Agreement.

In June 2021, upon election by Amber's board of directors, Amber issued an additional 3,000,000 shares of its Series A Preferred Stock to the Company for gross proceeds of $3.0 million. In connection with the financing, Amber issued 153,229 shares of its common stock to MIT in exchange for no additional consideration, as set forth in the MIT License Agreement.

Under the HLBV method, less than $0.1 and $0.2 million of losses were attributed to the noncontrolling interests for the years ended December 31, 2021 and 2020, respectively.

Cullinan Apollo Corp.

In December 2018, Apollo entered into a Series A Preferred Stock purchase agreement with the Company. The initial closing took place in December and Apollo sold 7,000,000 subsidiary shares of Series A Preferred Stock for gross proceeds of $7.0 million. Pursuant to the Series A Preferred Stock purchase agreement, at any time following the initial closing, upon the election of Apollo's board of directors, Apollo could sell up to an aggregate of 11,000,000 Series A Preferred Stock shares at one or more subsequent closings at $1.00 per share.

The Company dissolved Apollo in August 2021. The Company did not allocate any losses to the noncontrolling interests for the years ended December 30, 2021 and 2020.

Cullinan Florentine Corp.

In August 2020, Florentine entered into a Series A Preferred Stock purchase agreement with the Company. The initial closing took place in August 2020 and Florentine sold 6,000,000 shares of its Series A Preferred Stock to the Company for gross proceeds of $6.0 million. At any time following the initial closing, upon the election of the Florentine's board of directors, Florentine may sell up to an additional 6,000,000 shares of Series A Preferred Stock at one or more subsequent closings at $1.00 per share. Pursuant to the Tübingen License Agreement, Florentine issued 725,118 shares of its common stock, in exchange for no additional consideration as set forth in the Tübingen License Agreement.

In December 2020, Florentine issued 6,000,000 additional shares of its Series A Preferred Stock to the Company for proceeds of $6.0 million under the Florentine Series A Preferred Stock purchase agreement. Florentine issued an additional 381,810 shares of its common stock to DFKZ and UFE as anti-dilution shares, in exchange for no additional consideration as set forth in the Tübingen License Agreement.

In July 2021, Florentine issued 7,500,000 shares of Series B Preferred Stock to the Company for gross proceeds of $8.1 million under the Florentine Series B Preferred Stock purchase agreement. No additional shares of its stock were issued to DFKZ or UFE.

The Company did not allocate any losses to the noncontrolling interests for the year ended December 31, 2021. Under the HLBV method, $0.5 million of losses were attributed to noncontrolling interests for the year ended December 31, 2020.

Cullinan MICA Corp.

In May 2020, MICA issued 6,088,282 million shares of Series A Senior Preferred Stock, including 5,385,787 shares to the Company, at $1.31 per share. See Note 5 for further details.

Using a market-based approach and an option-pricing allocation method, MICA determined the fair market value of MICA's equity at acquisition was $12.8 million, of which $7.1 million was allocated to the Company's Series A Senior Preferred Stock position, and $5.7 million was initially allocated to noncontrolling interests, including the Junior Preferred and Common Stockholders.

In December 2020, the MICA board authorized the issuance of 3,367,804 shares of MICA common stock to the Company, at a purchase price of $0.23 per share for aggregate proceeds to MICA of $0.8 million. As a result of these transactions, the Company's ownership interests in MICA increased to 35% as of December 31, 2020.

In June 2021, pursuant the first additional closing as described in Note 5, the Company's ownership interests in MICA increased to 45%.

Under the HLBV method, $1.1 and $5.4 million of losses were attributed to noncontrolling interests for the years ended December 31, 2021 and 2020, respectively.

Cullinan Pearl Corp.

In February 2019, Pearl entered into a Series A Preferred Stock Purchase Agreement with Taiho Ventures to sell up to 23,000,000 shares of Pearl's Series A Preferred Stock for $1.00 per share. Pearl completed the initial closing of its Series A Preferred Stock where Pearl issued 14,000,000 shares of Series A Preferred Stock for $14.0 million to the Company and Taiho Ventures. In connection with the Taiho License Agreement, Pearl issued 1,860,000 shares of its common stock to Taiho Ventures as anti-dilution shares, in exchange for no cash consideration.

In August 2020, Pearl issued 9,000,000 additional shares of its Series A Preferred Stock for $9.0 million to the Company and Taiho Ventures. In connection with the Taiho License Agreement, Pearl then issued 1,206,000 to Taiho Ventures additional shares of its common stock as anti-dilution shares, in exchange for no additional consideration.

In November 2020, pursuant a subscription agreement between the Company and Pearl, the Company purchased 2,730,227 shares of Pearl's common stock at $0.44 per share, for an aggregate purchase price of $1.2 million.

Under the HLBV method, $0.7 and $1.6 million of losses were attributed to noncontrolling interests for the years ended December 31, 2021 and 2020, respectively.

(7) Equity-Based Compensation

Non-Voting Incentive Units

Prior to the Reorganization, the LLC's 2016 Equity Incentive Plan (the 2016 Plan) provided for the grant of Non-Voting Incentive Units to employees, consultants, advisors and directors, as determined by the board of directors. Vesting was determined by the board of directors. Awards typically provided for vesting of 25% of units at the end of the first year of service with the remaining 75% vesting ratably on a monthly basis over the following three-year period. Unvested Non-Voting Incentive Units may not be sold or transferred by the holder and are subject to repurchase by the LLC if service terminates prior to vesting at a price equal to the amount the recipient paid for the Non-Voting Incentive Units. These restrictions lapse according to the time-based vesting conditions of each award. Non-Voting Incentive Units were granted at a price of not less than the fair value of the Common Unit on the date of grant.

The Non-Voting Incentive Units are subject to ASC 718 and are classified within equity. On the grant date, the fair value of the LLC's Common Units for accounting purposes was determined by the board of directors, with input from management. Compensation expense is recognized on the Non-Voting Incentive Units using the fair value on the date of grant of $0.0001 per unit. Given the early stage nature of the underlying technology and inherent risks associated with obtaining regulatory approval and achieving commercialization, the Company used the current value method to fair value the Non-Voting Incentive Units granted since inception.

In October 2020, the Board of Directors adopted the 2020 Unit Option and Grant Plan and decreased the number of units available for future grants under the 2016 Equity Incentive Plan such that no more Non-Voting Incentive Units could be issued under the plan. The Company did not issue any Non-Voting Incentive Units during the year ended December 31, 2020.

As part of the Reorganization in January 2021, the total outstanding Non-Voting Incentive Units were cancelled and 1,689,949 shares of the Company's common stock were issued in exchange. The amounts presented for Non-Voting Incentive Units included unvested outstanding awards that were exchanged for restricted stock of the Company.

The following table summarizes the Non-Voting Incentive Unit activities for the years ended December 31, 2021 and 2020 as if the Non-Voting Incentive Units were converted to restricted common stock of the Company at the earliest period presented:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
Outstanding unvested as of December 31, 2019	580,334	$ 0.0001
Vested	(407,844)	0.0001
Outstanding unvested as of December 31, 2020	172,490	0.0001
Vested	(172,490)	0.0001
Outstanding unvested as of December 31, 2021	—	0.0001
Outstanding vested as of December 31, 2021	1,689,949	$ 0.0001

For the years ended December 31, 2021 and 2020, compensation expense and unrecognized compensation costs were nominal based on the grant date fair value of $0.0001 per share. All Non-Voting Incentive Units exchanged for restricted common stock were vested as of December 31, 2021.

Restricted Stock and Stock Option Grants of the Subsidiaries

Prior to the Reorganization, the respective boards of directors of certain subsidiaries have authorized equity incentive plans for the grant of stock options and restricted stock awards in the subsidiaries to employees, consultants, advisors and directors. Vesting is determined by each subsidiaries' board of directors. Awards typically provide for vesting of 25% of units at the end of the first year of service with the remaining 75% vesting ratably on a monthly basis over the following three-year period. Unvested restricted shares may not be sold or transferred by the holder and are subject to repurchase by the subsidiaries if service terminates prior to vesting at a price equal to the amount the recipient paid for the restricted stock. These restrictions lapse according to the time-based vesting conditions of each award. Restricted common stocks are granted at a price of not less than the fair value of the common stock on the date of grant.

The restricted stock and stock options are subject to ASC 718 and are classified within equity. The fair values of Pearl common stock in 2018, and of Amber and Florentine common stock in 2019, for accounting purposes was determined by their respective boards of directors, with input from management, at $0.0001 per share.

Contribution and Unit Purchase Agreements with the Subsidiaries

In November 2020, the LLC entered into the Contribution Agreements with each holder of restricted stock of Amber, Florentine and Pearl. Pursuant to the Contribution Agreements, each holder contributed their respective shares of the restricted stock of the subsidiaries and in exchange, received in aggregate 2,231,363 restricted common units of the LLC entity under the 2020 Unit Option and Grant Plan with an aggregate value equal to the value of the restricted stock contributed to the LLC (the Restricted Stock Contribution). The LLC exchanged 368,974 units of the LLC restricted stock for 511,530 units of Amber restricted stock, 513,656 units of the LLC restricted stock for 728,678 units of Florentine restricted stock and 1,348,733 units of the LLC restricted stock for 1,869,834 units of Pearl restricted stock pursuant to the Contribution Agreements.

Simultaneous with the Restricted Stock Contribution, the board of directors of each of Amber, Florentine and Pearl accelerated the vesting of the unvested restricted stock immediately prior to the Restricted Stock Contribution. The acceleration facilitated the exchange of the units between the subsidiaries and the LLC. Subsequent to the exchange, all restricted common units of the LLC reverted to the original vesting schedule of the respective awards at the subsidiaries. Lastly, the board of directors of each of Amber, Florentine and Pearl terminated their respective stock option and grant plans. The remaining shares reserved for issuance under each respective stock option and grant plan for Amber and Florentine were retired to the status of authorized and unissued shares and in the case of Pearl, issued to the LLC in exchange for their fair value.

The Contribution Agreement is determined to be a cancellation of the restricted stock issued at the subsidiaries with a concurrent grant of a replacement award at the LLC and is accounted for as a modification.

Unit Purchase Agreement with Cullinan Pearl

In November 2020, the board of directors of Cullinan Pearl authorized the entry into a Common Unit Purchase Agreement (Unit Purchase Agreement) with the LLC pursuant to which Pearl purchased 22,868 common units of the LLC for a purchase price of $0.61 per common unit, for an aggregate purchase price of less than $0.1 million. Pearl then transferred those common units to two directors of Pearl in exchange for the cancellation of an aggregate 93,000 subsidiary stock options issued to those directors.

The common unit purchase between Pearl and the LLC and the subsequent exchange of the purchased units for the stock options issued to the directors is determined to be a cancellation of the stock options issued at Pearl with a concurrent grant of a replacement award at the LLC. The cancellation and concurrent grant of a replacement is accounted for as a modification.

Pursuant to the Contribution and Unit Purchase Agreements, the LLC exchanged 2,254,231 units of the LLC for restricted stocks and stock options held by employees, consultants, advisors and directors of the subsidiaries. The exchange provided for $1.2 million in excess fair value and on the effective date of the exchange, the Company recognized $0.2 million and $0.1 million of modification expense within research and development expense and general and administrative expense, respectively, in the consolidated statements of operations and comprehensive loss. The remaining excess fair value will be recognized over the vesting terms.

As part of the Reorganization in January 2021, all of the LLC units exchanged for restricted stock or stock options of the Subsidiaries were cancelled and 320,228 shares of the Company's common stock were issued in exchange. The amounts presented for the exchange number of shares included unvested outstanding awards that were exchanged for restricted stock of the Company.

For the years ended December 31, 2021 and 2020, the Company recognized $0.4 million and $0.2 million of equity-based compensation expense relating to the excess fair value within research and development expense and general and administrative expense categories, respectively, in the consolidated statements of operations and comprehensive loss.

As of December 31, 2021 and 2020, there were $0.3 million and $0.7 million in unrecognized compensation cost expected to be recognized over estimated weighted-average amortization periods of 1.48 and 2.41 years, respectively.

The following table summarizes the restricted common unit activities for the years ended December 31, 2021 and 2020 as if the restricted common units were converted to restricted common stock of the Company at the earliest period presented:

	Number of Shares	Incremental Fair Value Per Share
Total units exchanged as of November 4, 2020	320,228	$ 3.87
Vested	(128,358)	3.87
Outstanding unvested as of December 31, 2020	191,870	$ 3.87
Vested	(102,987)	3.87
Outstanding unvested as of December 31, 2021	88,883	$ 3.87
Outstanding vested as of December 31, 2021	231,345	$ 3.87

2021 Stock Option and Incentive Plan

The Company's 2021 Stock Option and Incentive Plan (the 2021 Stock Plan) was adopted by the board of directors in December 2020 and the stockholders approved the plan in January 2021, prior to the completion of the Company's IPO. The 2021 Stock Plan became effective on the day immediately prior to the effectiveness of the Company's registration statement. The purpose of the 2021 Stock Plan is to encourage and enable the officers, employees, directors, consultants and other key persons of the Company whose judgment, initiative and efforts the Company largely depends on for the successful conduct of its business, to acquire a proprietary interest in the Company. The term of the options may be up to 10 years, and options are exercisable in cash or is net exercised. The exercise price of the options are determined based on the fair market value of the Company's common stock on the date of grant with 25% of the awards issued vesting on the first anniversary of the vesting commencement date, with the remaining portion of the awards vesting over the following 36 months in equal monthly installments.

The 2020 Unit Option and Grant Plan (2020 Plan) was terminated once the 2021 Stock Plan was effective. As part of the Reorganization, all common unit options granted under the 2020 Unit Option and Grant Plan were cancelled and exchanged for stock options under the 2021 Stock Plan with the same vesting terms and conditions. This was considered a modification

of the common unit options previously issued with no incremental fair value as there were no changes to the terms and conditions of the awards.

The Company initially reserved 12,546,386 shares of common stock for issuance of awards under the 2021 Stock Plan, which included (i) split-adjusted 320,228 shares of restricted stock issued in exchange for restricted stock and stock options granted at the Subsidiaries, as referenced above, and (ii) split-adjusted equity awards comprised of 4,616,187 shares of common stock issuable upon the exercise of stock options at a weighted average exercise price of $4.30 that were issued in exchange for common unit options cancelled under the 2020 Unit Option and Grant Plan.

The 2021 Stock Plan provides that the number of shares reserved and available for issuance under the 2021 Stock Plan will automatically increase each January 1, beginning on January 1, 2022, by 5% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31 or such lesser number of shares as determined by the Company's board or compensation committee. This number is subject to adjustment in the event of a stock split, stock dividend or other change in capitalization.

The following table summarizes the activity related to stock option grants to employees and non-employees for the years ended December 31, 2021 and 2020 under the 2021 Stock Plan. This also includes the common unit options issued under the 2020 Plan that were cancelled and exchanged into stock options under the 2021 Stock Plan with the number of options issued and weighted average exercise price presented as if the Reorganization occurred at the earliest period presented:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)
Outstanding as of December 31, 2019	—	$ —	—
Granted	4,616,187	4.30	—
Exercised	(13,050)	4.30	—
Outstanding as of December 31, 2020	4,603,137	$ 4.30	9.84
Granted	5,481,816	23.82	—
Exercised	(763,000)	4.30	—
Forfeited	(63,214)	17.23	—
Outstanding as of December 31, 2021	9,258,739	$ 15.77	9.22
Options exercisable as of December 31, 2021	3,271,196	$ 7.65	8.90
Options unvested as of December 31, 2021	5,987,543	$ 20.20	9.39

As of December 31, 2021 and 2020, there were $75.8 million and $14.2 million, respectively, in unrecognized compensation cost that are expected to be recognized over an estimated weighted-average amortization period of 3.15 and 2.68 years, respectively. As of December 31, 2021, the aggregate intrinsic value of options outstanding and options exercisable based on a fair value per share of $15.43 was $42.5 million and $29.1 million, respectively. As of December 31, 2020, the aggregate intrinsic value of options outstanding and options exercisable based on a fair value per share of $18.02 was $63.1 million and $28.6 million, respectively.

The fair value of options is estimated using the Black-Scholes option pricing model, which takes into account inputs such as the exercise price, the value of the underlying common stock at the grant date, expected term, expected volatility, risk-free interest rate and dividend yield. The fair value of each grant of options during the years ended December 31, 2021 and 2020 were determined using the methods and assumptions discussed below:

- The expected term of employee options is determined using the "simplified" method, as prescribed in the SEC Staff Accounting Bulletin (SAB) No. 107, whereby the expected life equals the arithmetic average of the vesting term and the original contractual term of the option due to the Company's lack of sufficient historical data. The Company also elected to use the simplified method to determine the expected term of non-employee options.
- The risk free interest rate is based on the treasury constant maturity rate published on the Federal Reserve website.

- The expected volatility is based on historical volatilities of similar entities within the Company's industry which were commensurate with the expected term assumption as described in SAB No. 107.
- The estimated annual dividend yield is 0% because the Company has not historically paid, and does not expect for the foreseeable future to pay, a dividend on its common stock.
- The Company considered numerous objective and subjective factors in estimating the fair value of its common stock prior to the IPO, including the concluded equity value based on IPO and liquidation scenarios and their related timing and probabilities of occurrence.

For the years ended December 31, 2021 and 2020, the weighted average grant date fair value of the options granted were $15.73 and $6.19 per share, respectively. The grant date fair value was estimated at the time of grant using the Black-Scholes option-pricing model using the following weighted average assumptions:

	Year Ended December 31, 2021	Year Ended December 31, 2020
Weighted average risk-free interest rate	1.02%	0.51%
Expected term (in years)	6.00	5.98
Expected volatility	76.22%	77.40%
Expected dividend yield	0.00%	0.00%

For the year ended December 31, 2021, the Company recorded $8.7 million and $15.2 million of equity-based compensation expense within the research and development and general and administrative expense categories, respectively. For the year ended December 31, 2020, the Company recorded $5.6 million and $8.8 million of equity-based compensation expense within the research and development and general and administrative expense categories, respectively. These amounts are included in the consolidated statements of operations and comprehensive loss.

2021 Employee Stock Purchase Plan

The 2021 Employee Stock Purchase Plan (the ESPP) was adopted by our board of directors in December 2020 and the stockholders approved the plan in January 2021, prior to the completion of the Company's IPO. The ESPP became effective on the day immediately prior to the effectiveness of the Company's IPO. The Company has initially reserved 416,665 shares of common stock for issuance to participating employees.

The ESPP provides that the number of shares reserved and available for issuance under the ESPP will automatically increase each January 1, beginning on January 1, 2022, by the lesser of 833,330 shares of our common stock, 1% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31, or such lesser number of shares as determined by the Company's compensation committee. This number is subject to adjustment in the event of a stock split, stock dividend or other change in capitalization.

For the twelve months ended December 31, 2021, the Company issued 12,977 shares of its common stock and recorded less than $0.1 million of equity-based compensation expense pursuant the ESPP.

Equity-based compensation expense

The Company recorded equity-based compensation in the following expense categories in the consolidated statements of operations and comprehensive loss:

	Year ended December 31,	
	2021	2020
	(in thousands)	
Research and development	$ 8,914	$ 5,912
General and administrative	15,461	8,998
Total equity-based compensation	$ 24,375	$ 14,910

(8) Related Party Transactions

MPM Capital is a significant investor in the Company through one of its managed funds. In October 2016, the Company also began receiving consulting and management services pursuant to agreements with a managing director at MPM Capital and a principal at F2 Ventures, also a significant investor in the Company. No expenses were incurred for the year ended December 31, 2021. For the year ended December 31, 2020, the Company incurred $0.2 million for management and advisory services, inclusive of their director compensation, in connection with those agreements.

For each of the years ended December 31, 2021 and 2020, the Company paid MPM Capital less than $0.1 million for other operational support. These expenses were recorded as general and administrative expense.

In April 2020, the Company entered into a consulting agreement (the Globeways Agreement) with Globeways Holdings Limited, or Globeways. Globeways and entities affiliated with F2 Ventures beneficially own in the aggregate greater than five percent of the Company's outstanding shares and Globeways is beneficially owned by a member of the Company's board of directors. Pursuant to the Globeways Agreement, the board member provides leadership and advice regarding the Company's scientific, clinical, product development and related activities and operations. Pursuant to the Globeways Agreement, the Company pays Globeways a consulting fee at a monthly rate of $25,000. As the sole beneficial owner of Globeways, this board member receives all of the compensation paid to Globeways under the Globeways Agreements.

For the years ended December 31, 2021 and 2020, the Company incurred less than $0.1 million and $0.2 million in costs related to this agreement, respectively. The agreement expired as of March 31, 2021.

Royalty Transfer Agreements

Between October 2019 and May 2020, each of the Asset Subsidiaries entered into royalty transfer agreements with MPM Oncology Charitable Foundation, Inc. and UBS Optimus Foundation (together, the Foundations). Under each of these respective agreements, each Foundation is entitled to receive a royalty equal to 0.5% (1.0% in aggregate) of all global net sales of any products developed by the applicable subsidiary, subject to limitations after patent expirations and on intellectual property developed after a change of control. The Company has deemed these royalty transfer agreements to be freestanding financial instruments that should be accounted for at fair value. Management of the Company has concluded that these instruments had no value at the inception of the agreements and at December 31, 2021 and 2020.

Given the early-stage nature of the underlying technologies and inherent technical, regulatory and competitive risks associated with achieving approval and commercialization, the Company ascribed no value to the royalty transfer agreements as of December 31, 2021 and 2020. The Company currently does not have any applicable net sales from its products and as a result, has paid no royalties under these obligation as of December 31, 2021 and 2020 nor has the Company accrued any liability as of such dates. The Company will monitor these instruments for changes in fair value at each reporting date

(9) Income Taxes

For the years ended December 31, 2021 and December 31, 2020, the Company did not record a current or deferred income tax expense or benefit due to current and historical losses incurred by the Company.

A reconciliation of the Company's statutory income tax rate to the Company's effective income tax rate is as follows:

	Year ended December 31,	
	2021	2020
Federal statutory rate	21.00%	21.00%
State taxes, net of federal benefit	9.96%	(1.83)%
Permanent differences	0.01%	(0.01)%
Equity-based compensation	0.39%	—
Tax credits	(0.25)%	0.77%
Valuation allowance	(32.12%)	(12.65%)
Non-taxable income	—	(5.01)%
IPR&D	—	(2.28%)
Change in tax status	1.76%	—
Return to provision	1.15%	—
Other	(1.90)%	—
	0.00%	0.00%

The net deferred income tax asset balance related to the following:

	December 31,	
	2021	2020
	(in thousands)	
Deferred tax assets:		
Net operating loss	$ 31,414	$ 18,563
Capitalized organizational and start-up expenses	140	148
Licenses	1,875	1,601
Accrued expenses	968	467
Research and development credit	1,563	1,859
Equity-based compensation	8,584	8
Gross deferred tax assets	44,544	22,646
Valuation allowance	(44,552)	(22,642)
Net deferred tax asset	(8)	4
Deferred tax liability		
Depreciation and amortization	8	(4)
Net deferred tax asset	$ —	$ —

As of December 31, 2021, the Company had federal and state net operating loss (NOL) carryforwards of $117.4 million and $119.0 million, respectively. The Company generated federal NOLs of $5.8 million prior to 2018, which begin to expire in 2036. State losses also begin to expire in 2036. The Company generated combined federal NOLs of $111.6 million, which can be carried forward indefinitely. As of December 31, 2021, the Company had federal and state research and development tax credit carryforwards of $1.3 million and $0.1 million, respectively, which begin to expire in 2037 and 2033, respectively. The Company has state research and development tax credit carryforwards of $0.3 million which can be carried forward indefinitely.

Utilization of the net operating loss carryforwards and research and development tax credits may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 (Section 382) due to ownership change limitations that have occurred previously or that could occur in the future in accordance with Section 382, as well as similar state provisions. These ownership changes may limit the amount of NOL carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change as defined by Section 382 results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets, which are comprised principally of net operating loss carryforwards, licenses, equity-based compensation and research and development credit carryforwards. Management has considered the Company's history of net losses since inception and its lack of commercialization of any products and has concluded that it is more likely than not the Company will not realize the benefits of the deferred tax assets. The Company's valuation allowance increased during the years ended December 31, 2021 and 2020 due primarily to the generation of net operating losses, as follows:

	Year ended December 31,	
	2021	2020
	(in thousands)	
Valuation allowance at beginning of year	$ 22,642	$ 10,653
Increases recorded to income tax provision	21,674	11,989
Increases recorded to OCI/Equity	236	—
Valuation allowance at end of year	$ 44,552	$ 22,642

The calculation of the Company's tax liabilities involves dealing with uncertainties in the application of complex tax laws and regulations for both federal taxes and the states in which the Company operates or does business in. ASC 740 states that a tax benefit from an uncertain tax position may be recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, on the basis of the technical merits.

The Company records uncertain tax positions as liabilities in accordance with ASC 740 and adjusts these liabilities when its judgment changes as a result of the evaluation of new information not previously available. Due to the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from the Company's current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to income tax expense in the period in which new information is available. As of December 31, 2021 and 2020, the Company has not recorded any uncertain tax positions in its consolidated financial statements.

The Company recognizes interest and penalties related to unrecognized tax benefits on the income tax expense line in the accompanying consolidated statements of operations and comprehensive loss. As of December 31, 2021 and 2020, no accrued interest or penalties are included in the consolidated balance sheet.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions in the United States. There are currently no pending tax examinations. The Company thus is still open under the U.S. statute from 2016 to the present. To the extent that the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service and the state tax authorities to the extent utilized in a future period. The Company had not, as yet, conducted a study of research and development tax credit carryforwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheets or statements of operations and comprehensive loss if an adjustment was required.

(10) Commitments and Contingencies

Operating Lease

Rent expense for each of the years ended December 31, 2021 and 2020 was $0.6 million.

In December 2017, the Company signed an operating lease for 7,531 rentable square feet of office space in Cambridge, Massachusetts which commenced on February 1, 2018. The lease expires on June 30, 2024. Rent expense will be recorded ratably over the lease period. The lease includes escalating rental payments, which are also being charged to rent expense ratably over the lease period.

The following table summarizes future minimum payments due under the operating lease as of December 31, 2021:

Years Ending December 31,	(in thousands)
2022	$ 608
2023	618
2024	313
	$ 1,539

(11) Employee Benefit Plan

The Company maintains a defined contribution 401(k) plan (the 401(k) Plan) in which employees may contribute a portion of their compensation, subject to statutory maximum contribution amounts. The Company assumes all administrative costs of the 401(k) Plan. For each of the years ended December 31, 2021 and 2020, the expense relating to the matching contribution was $0.3 million and $0.1 million, respectively.

(12) Net Loss per Share

The following table sets forth the calculation of basic and diluted net loss per share as if the Reorganization occurred at the earliest period presented:

	Year ended December 31,	
	2021	2020[1]
	(in thousands, except share and per share data)	
Numerator:		
Net loss attributable to common stockholders of Cullinan	$ (65,570)	$ (51,799)
Denominator		
Total weighted-average shares used in computing net loss per share, basic and diluted	43,077,330	19,887,307
Net Loss per share:	$ (1.52)	$ (2.60)

(1) The shares and per share amounts for the year ended December 31, 2020 were derived from the consolidated financial statements as of that date and were retroactively adjusted as a result of the Reorganization and Reverse Stock Split. See Note 3 to the for additional details.

The following table sets forth equity instruments were excluded from the computation of the diluted net loss per share for the periods presented because their effect would have been anti-dilutive as if the Reorganization occurred at the earliest period presented:

	Year ended December 31,	
	2021	2020
Stock options	9,258,739	4,603,137
Restricted stock awards	88,883	364,360
Total	9,347,622	4,967,497

EXHIBIT INDEX

Exhibit Number	Description
3.1	Second Amended and Restated Certificate of Incorporation of the Registrant, as amended by the Certificate of Amendment, effective as of February 25, 2021 (incorporated by reference to Exhibit 3.1 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on March 30, 2021).
3.2	Second Amended and Restated Bylaws of the Registrant, effective as of February 25, 2021 (incorporated by reference to Exhibit 3.2 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on March 30, 2021).
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 28, 2020).
4.2	Registration Rights Agreement, dated January 7, 2021, among the Registrant and certain of its stockholders (incorporated by reference to Exhibit 4.2 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on March 30, 2021).
4.3	Description of Securities (incorporated by reference to Exhibit 4.3 of the Registrant's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on March 30, 2021).
10.1#	2021 Stock Option and Incentive Plan and form of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on January 4, 2021).
10.2#	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on January 4, 2021).
10.3#	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.4#	Form of Indemnification Agreement, between the Registrant and each of its directors (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.5#	Form of Indemnification Agreement, between the Registrant and each of its executive officers (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.6†	Exclusive Patent License Agreement, dated December 12, 2019, as amended on April 3, 2020, by and between Massachusetts Institute of Technology and Cullinan Amber Corp. (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.7†	Collaboration Agreement, dated November 28, 2018, by and between Adimab, LLC and the Registrant (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.8†	License and Collaboration Agreement, dated February 4, 2019, by and among Taiho Pharmaceutical, Co., Ltd. and Cullinan Pearl Corp. (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed on December 18, 2020).

10.9†	Exclusive License Agreement, dated August 31, 2020, by and among Deutches Krebsforschungszentrum, Eberhard Karls University of Tuebingen, Faculty of Medicine, Universitatsmedizin Gesellschaft fur Forschung und Entwicklung mbH, Tubingen and Cullinan Florentine Corp. (incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.10#	Form of Executive Employment Agreement (incorporated by reference to Exhibit 10.13 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.11#	Consulting Agreement, dated January 1, 2019, by and between the Registrant and Corinne Savill (incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.12#	Consulting Agreement, dated January 1, 2019, by and between the Registrant and Globeways Holdings Limited (incorporated by reference to Exhibit 10.16 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.13	Sublease, effective as of December 14, 2017, by and between Teva Pharmaceuticals USA, Inc. and the Registrant (incorporated by reference to Exhibit 10.17 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.14	Form of Voting Agreement (incorporated by reference to Exhibit 10.18 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.15	Form of Investors Rights Agreement (incorporated by reference to Exhibit 10.19 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.16	Form of Services Agreement (incorporated by reference to Exhibit 10.20 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.17	Form of Royalty Transfer Agreements (incorporated by reference to Exhibit 10.21 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.18	Form of Contribution Agreement (incorporated by reference to Exhibit 10.22 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on January 4, 2021).
10.19#	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.23 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 18, 2020).
10.20†	License Agreement, dated December 24, 2020, by and between Cullinan Pearl Corp. and Zai Lab (Shanghai) Co., Ltd. (incorporated by reference to Exhibit 10.24 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on December 28, 2020).
10.21#	Services Agreement, by and between the Registrant and Patrick Baeuerle (incorporated by reference to Exhibit 10.25 of the Registrant's Registration Statement on Form S-1 (File No. 333-251512) filed with the SEC on January 4, 2021).
10.22#	Consulting Agreement, dated May 20, 2021, by and between the Registrant and Jon Wigginton, M.D. (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed with the SEC on August 10, 2021).
10.23#*	Separation Agreement, effective as of October 18, 2021, by and between the Registrant and Owen Hughes.
10.24#	Employment Agreement, effective as of October 18, 2021, by and between the Registrant and Nadim Ahmed (incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed with the SEC on October 18, 2021).

21.1*	List of Subsidiaries of the Registrant.
23.1*	Consent of KPMG LLP, the Company's independent registered public accounting firm.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

---

* Filed herewith.

** The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Annual Report on Form 10-K and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

# Indicates a management contract or compensatory plan, contract or arrangement.

† Non-material schedules and exhibits have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Company hereby undertakes to furnish supplementally copies of any of the omitted schedules and exhibits upon request by the Securities and Exchange Commission.

SIGNATURES

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

Cullinan Oncology, Inc.

Date: March 17, 2022

By: /s/ Nadim Ahmed
Name: Nadim Ahmed
Title President and Chief Executive Officer

POWER OF ATTORNEY

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

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

Name	Title	Date
/s/ Nadim Ahmed **Nadim Ahmed**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 17, 2022
/s/ Jeffrey Trigilio **Jeffrey Trigilio**	Chief Financial Officer (Principal Financial and Accounting Officer)	March 17, 2022
/s/ Thomas Ebeling **Thomas Ebeling**	Director	March 17, 2022
/s/ Ansbert Gadicke, M.D. **Ansbert Gadicke, M.D.**	Director	March 17, 2022
/s/ Anne-Marie Martin **Anne-Marie Martin**	Director	March 17, 2022
/s/ Anthony Rosenberg **Anthony Rosenberg**	Director	March 17, 2022
/s/ Stephen Webster **Stephen Webster**	Director	March 17, 2022

Exhibit 10.23

SEPARATION AGREEMENT

This Separation Agreement (this "Agreement") is made between Cullinan Oncology, Inc., a Delaware corporation (the "Company"), and Owen Hughes (the "Executive"). The Company together with the Executive shall be referred to as the "Parties".

WHEREAS, the Parties entered into an Employment Agreement dated January 12, 2021 (the "Employment Agreement"), which superseded in all respects the prior employment agreement between the Parties dated May 1, 2017 (the "Prior Agreement");

WHEREAS, pursuant to the Employment Agreement, the Company and the Executive each retained the right to terminate the Executive's employment by the Company without any breach of the Employment Agreement under the circumstances set forth in Section 3 of the Employment Agreement;

WHEREAS, the Executive's employment will end on October 18, 2021 (the "Date of Termination") pursuant to Section 3(d) of the Employment Agreement;

WHEREAS, if the Executive enters into, does not revoke and complies with this Agreement, the Executive will be eligible to receive the severance pay and benefits as described in this Agreement, as well as to continue his service relationship with the Company for a period of time after which his unvested equity awards will vest, all subject to the terms and conditions set forth in this Agreement;

WHEREAS, this Agreement is the "Separation Agreement" referred to in the Employment Agreement; and

WHEREAS, the Parties agree that this Agreement was enclosed with a "Notice of Termination", and that such notice satisfies the Company's obligations related to a Notice of Termination under Section 4(a) of the Employment Agreement.

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties hereby agree as follows:

1.**Ending of Employment**. The Executive's employment with the Company will end on the Date of Termination. To the extent applicable, the Executive shall be deemed to have resigned from all officer and board member positions that the Executive holds with the Company or any of its respective subsidiaries and affiliates upon the Date of Termination. The Executive shall execute any documents in reasonable form as may be requested to confirm or effectuate any such resignations. By entering into this Agreement, the Executive acknowledges and agrees that the payments and benefits set forth in this Agreement are the exclusive payments and benefits to be paid to the Executive in connection with the ending of his employment and that he is not entitled to any other severance pay, benefits or equity rights, including without limitation pursuant to any severance plan, program or arrangement.

DOCPROPERTY DOCXDOCID DMS=InterwovenIManage Format=<<NUM>>_<<VER>> PRESERVELOCATION * MERGEFORMAT 119911237_2

2.**Accrued Obligations**. The Executive acknowledges and agrees that in connection with the ending of his employment, and regardless of whether this Agreement becomes effective, the Company shall pay or provide to the Executive the following "Accrued Obligations": (i) any Base Salary (as defined in the Employment Agreement) and any accrued but unused vacation, if applicable earned through the Date of Termination; (ii) unpaid expense reimbursements (subject to, and in accordance with, Section 2(c) of the Employment Agreement); and (iii) any vested benefits the Executive may have under any employee benefit plan of the Company through the Date of Termination, which vested benefits shall be paid and/or provided in accordance with the terms of such employee benefit plans.

In addition, regardless of whether this Agreement becomes effective, the Executive will be provided with information regarding the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA") under separate cover, including payment obligations.

3.**Severance Pay and Benefits and Accelerated Vesting** In exchange for the Executive entering into, not revoking and complying with this Agreement, the Executive will be entitled to the following:

a. the Company shall pay the Executive an amount equal to the sum of (A) twelve (12) months of the Executive's Base Salary plus (B) $216,507, which is a pro-rata portion of the Target Bonus based on the Date of Termination;

b. subject to the Executive's copayment of premium amounts at the applicable active employees' rate and the Executive's proper election to receive benefits under COBRA, the Company shall pay to the group health plan provider or the COBRA provider a monthly payment equal to the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company until the earliest of (A) the twelve (12) month anniversary of the Date of Termination; (B) the date that the Executive becomes eligible for group medical plan benefits under any other employer's group medical plan; or (C) the cessation of the Executive's health continuation rights under COBRA; provided, however, that if the Company determines that it cannot pay such amounts to the group health plan provider or the COBRA provider (if applicable) without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), then the Company shall convert such payments to payroll payments directly to the Executive for the time period specified above. Such payments to the Executive shall be subject to tax-related deductions and withholdings and paid on the Company's regular payroll dates;

c. acceleration of Executive's outstanding unvested equity interests as of the Effective Date (the "Accelerated Vesting"); and

(d) [***] proceeds (up to a maximum of [***] in proceeds) arising from the Subsidiary Monetization Event (as defined in the Company's Cash Phantom Pool, as approved by the Board), related to [***]; provided the Subsidiary Monetization Event must occur on or prior to the one year anniversary of the Date of Termination.

The amounts payable under this Section 3, to the extent taxable, shall be paid out in substantially equal installments in accordance with the Company's payroll practice over twelve (12) months

commencing on the first practicable payroll date following the Effective Date of this Agreement (as defined below); provided that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination.

4.**Continued Service as a Senior Advisor**. If the Executive enters into, does not revoke and complies with this Agreement and notwithstanding the terms of the Employment Agreement, the Executive will have the option of continuing as a senior advisor until the earlier of: (i) the one year anniversary of the Date of Termination; or (ii) a date determined by the Company's then CEO. While serving as a senior advisor, the Executive will continue to have a Service Relationship with the Company as defined in, and in accordance with, the terms of the applicable equity award agreements and equity incentive plan(s) (the "Equity Documents"). The Executive may exercise any vested stock options within the time period set forth in the Equity Documents during and following the ending of the Service Relationship. The Executive hereby resigns as an officer and/or director of all of the Company's subsidiaries and affiliates and agrees to execute requested documentation associated with such resignations.

5.**General Release**. In consideration for, among other terms, the Severance Pay and Benefits and Accelerated Vesting and the opportunity to continue his Service Relationship pursuant to Section 4, to which the Executive acknowledges that he would otherwise not be entitled, the Executive irrevocably and unconditionally releases and forever discharges the Company, all of its affiliated and related entities, its and their respective predecessors, successors and assigns, its and their respective employee benefit plans and the fiduciaries of such plans, and the current and former officers, directors, stockholders, employees, attorneys, accountants, and agents of each of the foregoing in their official and personal capacities (collectively referred to as the "Releasees") generally from all claims, demands, debts, damages and liabilities of every name and nature, known or unknown ("Claims") that, as of the date when the Executive signs this Agreement, he has, ever had, now claims to have or ever claimed to have had against any or all of the Releasees. This release includes, without limitation, the complete waiver and release of all Claims: related to the Executive's employment by the Company or termination of employment; arising out of or relating to the Employment Agreement, the Prior Agreement or any other agreement between the Executive and any of the Releasees; of breach of express or implied contract; of wrongful termination of employment whether in contract or tort; of violation of public policy; of intentional, reckless, or negligent infliction of emotional distress; of breach of any express or implied covenant of employment, including the covenant of good faith and fair dealing; of interference with contractual or advantageous relations, whether prospective or existing; of deceit or misrepresentation; of discrimination or retaliation under state, federal or municipal law, including, without limitation, Title VII of the Civil Rights Act of 1964, the Americans with Disabilities Act, the Age Discrimination in Employment Act, and the Massachusetts Fair Employment Practices Act; of whistleblower retaliation; of fraud; under any other federal, state or local statute, rule, ordinance or regulation; of promissory estoppel or detrimental reliance; for wages, bonuses, incentive compensation, stock, stock options, vacation pay, severance allowances or entitlements, and any other compensation or benefits, either under the Massachusetts Wage Act, or otherwise; of slander, libel, defamation, disparagement, intentional infliction of emotional distress, personal injury, negligence or other torts; for damages or other remedies of any sort, including, without limitation, compensatory damages, punitive damages, injunctive relief, attorneys' fees, experts' fees, medical fees or expenses, costs and disbursements. The Executive understands that this general release of Claims includes, without

DOCPROPERTY DOCXDOCID DMS=InterwovenIManage Format=<<NUM>>_<<VER>> PRESERVELOCATION * MERGEFORMAT 119911237_2

limitation, any and all Claims against the Company in respect of any stock-based awards of any kind, and all Claims in his capacity as a Company stockholder arising up to and through the date that the Executive enters into this Agreement. The Executive understands that this general release does not extend to any rights or Claims that may arise out of acts or events that occur after the date on which the Executive signs this Agreement, to Claims that cannot be released as a matter of law or to any rights to any indemnification and defense that the Executive has with the Company. This release does not affect the Executive's rights or obligations under this Agreement, nor shall it affect the Executive's rights, if any, to unemployment compensation benefits or to workers' compensation. The Executive agrees not to accept damages of any nature, other equitable or legal remedies for the Executive's own benefit or attorney's fees or costs from any of the Releasees with respect to any Claim released by this Agreement. The Executive represents that he has not assigned to any third party and has not filed with any agency or court any Claim released by this Agreement.

6.**Return of Property**. The Executive acknowledges and agrees that he is required to return all Company property to the Company pursuant to the Employee Confidentiality, Assignment and Nonsolicitation Agreement between the Executive and the Company (the "Restrictive Covenants Agreement") upon the ending of his employment. By entering into this Agreement, the Executive confirms that he has returned to the Company all Company property, including, without limitation, any Company laptop, computer equipment, software, keys and access cards, credit cards, files and any documents (including computerized data and any copies made of any computerized data or software) containing information concerning the Company, its business or its business relationships, without deletion or alteration. After returning all Company property, the Executive agrees to delete and finally purge any duplicates of files or documents that may contain Company or customer information from any non-Company computer or other device that remains the Executive's property after the Date of Termination. The obligations under this Section 6 are supplemental to, and not in lieu of, the Executive's obligations under the Restrictive Covenants Agreement.

7.**Communications; Non-Disparagement**.

a. The Executive agrees that he will not communicate about his departure with anyone until after the Company has made a formal announcement about the Executive's departure through a company-wide communication (together, the "Company Announcement"); provided that the Executive may communicate with his tax advisors, attorneys and spouse about his departure before the Company Announcement, provided further that the Executive first advises such persons not to reveal information about the Executive's departure and each such person agrees. Once the Company has made the Company Announcement, the Executive agrees to limit any communications regarding his departure to statements consistent with the Company Announcement.

b. Subject to Section 12, the Executive agrees not to make any disparaging statements (whether written, oral, through social or electronic media or otherwise) concerning the Company or any of the Releasees. The Executive further agrees not to take any actions or conduct himself in any way that would reasonably be expected to affect adversely the reputation or goodwill of the Company or any of the Releasees. The Executive agrees that he shall not communicate in any way with the Company's investors regarding the Company other than as is

explicitly authorized by the Board or the Company's new Chief Executive Officer.

8.**Noncompetition**. In connection with the Executive's separation from employment, and in order to protect the Company's Proprietary Information (as defined in the Restrictive Covenants Agreement) and goodwill, the Executive agrees that for a period of one year following the Date of Termination, the Executive shall not, directly or indirectly, whether as owner, partner, shareholder, director, manager, consultant, agent, employee, co-venturer or otherwise, anywhere in the world, engage or otherwise participate in any Restricted Business. For purposes of this Agreement, "Restricted Business" shall mean (i) any business that has any compound in preclinical or clinical development with the same or similar mode of action to any clinical program that is in development at the Company or (ii) any business that, during the Executive's employment, has engaged or is engaging in business development discussions with the Company on any mode of action between such business and the Company that have progressed to the non-binding term sheet stage. The Executive acknowledges that this covenant is necessary because the Company's legitimate business interests cannot be adequately protected solely by the other covenants in this Agreement.

9.**Cooperation**. The Executive shall cooperate fully with the Company, including in (i) the defense or prosecution of any claims or actions now in existence or which may be brought in the future against or on behalf of the Company which relate to events or occurrences that transpired while the Executive was employed by the Company, and (ii) the investigation, whether internal or external, of any matters about which the Company believes the Executive may have knowledge or information. The Executive's full cooperation in connection with such claims, actions or investigations shall include, but not be limited to, being available to meet with counsel to answer questions or to prepare for discovery or trial and to act as a witness on behalf of the Company at mutually convenient times. The Executive also shall cooperate fully with the Company in connection with any investigation or review of any federal, state or local regulatory authority as any such investigation or review relates to events or occurrences that transpired while the Executive was employed by the Company. The Company shall reimburse the Executive for any reasonable out-of-pocket expenses incurred in connection with the Executive's performance of obligations pursuant to this Section 9.

10.**Continuing Obligations; Termination of Payments; Injunctive Relief**. The Executive acknowledges that his right to the Severance Pay and Benefits is conditioned on his full compliance with Sections 6 through 9 of this Agreement and the Restrictive Covenants Agreement. The Restrictive Covenants Agreement is incorporated by reference into this Agreement, and, together with Sections 6 through 9 of this Agreement, shall be referred to as the "Continuing Obligations". In the event that the Executive fails to comply with any of the Continuing Obligations, in addition to any other legal or equitable remedies it may have for such breach, the Company shall have the right to terminate payments provided under this Agreement other than the Accrued Obligations. Such termination in the event of a breach by the Executive of the Continuing Obligations shall not affect the general release in Section 5 of this Agreement or the Executive's obligation to comply with the Continuing Obligations and shall be in addition to, and not in lieu of, the Company's rights to other legal and equitable remedies that the Company may have. Further, the Executive agrees that it would be difficult to measure any harm caused to the Company that might result from any breach by the Executive of any of the Continuing Obligations and that, in any event, money damages would be an inadequate remedy

for any such breach. Accordingly, the Executive agrees that if he breaches, or proposes to breach, any portion of the Continuing Obligations, then the Company shall be entitled, in addition to all other remedies it may have, to an injunction or other appropriate equitable relief to restrain any such breach, without showing or proving any actual damage to the Company and without the necessity of posting a bond, and to recover the Company's attorneys' fees and costs associated with any such breach by the Executive.

11.**Absence of Reliance**. This Agreement is a legally binding document and the Executive's signature will commit the Executive to its terms. In signing this Agreement, the Executive agrees that he is not relying upon any promise or representations made by anyone at or on behalf of the Company.

12.**Protected Disclosures**. Nothing in this Agreement or otherwise limits the Executive's: (i) obligation to testify truthfully in any legal proceeding; (ii) right to file a charge, claim or complaint with any federal agency (such as the Equal Employment Opportunity Commission) or any state or local governmental agency or commission (together, a "Government Agency"), provided that the Executive waives any right to monetary or other individualized relief (either individually or as part of any collective or class action); provided further that nothing in this Agreement limits any right that the Executive may have to receive a whistleblower award or bounty for information provided to the Securities and Exchange Commission; or (iii) ability to communicate with any Government Agency or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency.

13.**Time for Consideration; Effective Date**. The Company advises the Executive to consult with an attorney before entering into this Agreement. The Executive acknowledges that he has carefully read and fully understands all of the provisions of this Agreement and that the Executive is voluntarily and knowingly entering into this Agreement. The Executive acknowledges that he has been given the opportunity to consider this Agreement for twenty-one (21) days before executing it (the "Consideration Period"). To accept this Agreement, the Executive must return a signed, unmodified original or PDF copy of this Agreement so that it is received by the undersigned at or before the expiration of the Consideration Period. If the Executive signs this Agreement before the end of the Consideration Period, the Executive acknowledges that such decision was entirely voluntary and that the Executive had the opportunity to consider this Agreement for the entire Consideration Period. For the period of seven (7) business days from the date when the Executive signs this Agreement, the Executive has the right to revoke this Agreement by written notice to the undersigned, provided that such notice is delivered so that it is received at or before the expiration of the seven (7) business day revocation period. This Agreement shall not become effective or enforceable during the revocation period. This Agreement shall become effective on the first business day following the expiration of the revocation period (the "Effective Date").

14.**Enforceability**. The Executive acknowledges that, if any portion or provision of this Agreement or the Continuing Obligations shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision shall be valid and enforceable to the fullest extent permitted by law.

DOCPROPERTY DOCXDOCID DMS=InterwovenIManage Format=<<NUM>>_<<VER>> PRESERVELOCATION * MERGEFORMAT 119911237_2

15.**Entire Agreement**. This Agreement, together with the Restrictive Covenants Agreement, constitutes the entire agreement between the Executive and the Company concerning the Executive's relationship with the Company, and supersedes and replaces any and all prior agreements and understandings between the Parties concerning the Executive's relationship with the Company including, without limitation, the Employment Agreement and the Prior Agreement, provided that the Equity Documents shall continue to be in full force and effect.

16.**Waiver; Amendment**. No waiver of any provision of this Agreement, including the Continuing Obligations, shall be effective unless made in writing and signed by the waiving party. The failure of either Party to require the performance of any term or obligation of this Agreement or the Continuing Obligations, or the waiver by either Party of any breach of this Agreement or the Continuing Obligations shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach. This Agreement may not be modified or amended except in a writing signed by both the Executive and a duly authorized officer of the Company.

17.**Taxes**. All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law. Nothing in this Agreement shall be construed to require the Company to make any payments to compensate the Executive for any adverse tax effect associated with any payments or benefits or for any deduction or withholding from any payment or benefit.

18.**Section 409A**. The Parties intend that this Agreement will be administered in accordance with Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"). To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2). The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

19.**Acknowledgment of Wage and Other Payments**. The Executive acknowledges and represents that, except as expressly provided in this Agreement, the Executive has been paid all wages, bonuses, compensation, benefits and other amounts that any of the Releasees has ever owed to the Executive. The Executive is not entitled to any bonus, incentive compensation or other compensation except as specifically set forth in this Agreement.

20.**Governing Law; Interpretation**. This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles thereof. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit. In the event of any dispute, this Agreement is intended by the Parties to be construed as a whole, to be interpreted in accordance with its fair meaning, and not to be construed strictly for or against either Party or the "drafter" of all or any portion of this Agreement.

DOCPROPERTY DOCXDOCID DMS=InterwovenIManage Format=<<NUM>>_<<VER>> PRESERVELOCATION * MERGEFORMAT 119911237_2

21.**Consent to Jurisdiction**. The parties hereby consent to the exclusive jurisdiction of the state and federal courts of the Commonwealth of Massachusetts. Accordingly, with respect to any such court action, the Executive (a) submits to the exclusive personal jurisdiction of such courts; (b) consents to service of process; and (c) waives any other requirement (whether imposed by statute, rule of court, or otherwise) with respect to personal jurisdiction or service of process.

22.**Assignment; Successors and Assigns**. Neither the Executive nor the Company may make any assignment of this Agreement or any interest in it, by operation of law or otherwise, without the prior written consent of the other; provided, however, that the Company may assign its rights and obligations under this Agreement (including the Restrictive Covenants Agreement) without the Executive's consent to any affiliate or to any person or entity with whom the Company shall hereafter effect a reorganization or consolidation, into which the Company merges or to whom it transfers all or substantially all of its properties or assets. This Agreement shall inure to the benefit of and be binding upon the Executive and the Company, and each of the Executive's and the Company's respective successors, executors, administrators, heirs and permitted assigns. In the event of the Executive's death after the Date of Termination but prior to the completion by the Company of all payments due to the Executive under this Agreement, the Company shall continue such payments to the Executive's beneficiary designated in writing to the Company prior to the Executive's death (or to the Executive's estate, if the Executive fails to make such designation).

23.**Counterparts**. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original, but all of which together shall constitute one and the same document. Electronic and pdf signatures shall be deemed to be of equal force and effect as originals.

[Remainder of page intentionally left blank]

DOCPROPERTY DOCXDOCID DMS=InterwovenIManage Format=<<NUM>>_<<VER>> PRESERVELOCATION * MERGEFORMAT 119911237_2

IN WITNESS WHEREOF, the Parties, intending to be legally bound, have executed this Agreement on the date(s) indicated below.

COMPANY:

CULLINAN ONCOLOGY, INC.

By: /s/ Anthony Rosenberg
Name: Anthony Rosenberg
Title: Chairman, Board of Directors

Date: 11/1/21

EXECUTIVE:

/s/ Owen Hughes
Owen Hughes

Date: 10/17/21

Exhibit 21.1

SUBSIDIARIES

Subsidiary	Jurisdiction of Organization
Cullinan Amber Corp.	Delaware
Cullinan Florentine Corp.	Delaware
Cullinan Mica Corp.	Delaware
Cullinan Pearl Corp.	Delaware
Cullinan Securities Corp.	Massachusetts

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements (No. 333-251943 and 333-263428) on Form S-8 of our report dated March 17, 2022, with respect to the consolidated financial statements of Cullinan Oncology, Inc.

/s/ KPMG LLP

Boston, Massachusetts
March 17, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Nadim Ahmed, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2021 of Cullinan Oncology, Inc. (the "registrant");

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 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)) 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) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (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 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 17, 2022

By: /s/ Nadim Ahmed
Nadim Ahmed
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jeffrey Trigilio, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2021 of Cullinan Oncology, Inc. (the "registrant");

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 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)) 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) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (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 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 17, 2022

By: /s/ Jeffrey Trigilio
Jeffrey Trigilio
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER 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 of Cullinan Oncology, Inc. (the "Company") on Form 10-K for the period ending December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of their knowledge:

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

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

Date: March 17, 2022 By: /s/ Nadim Ahmed
Nadim Ahmed
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 17, 2022 By: /s/ Jeffrey Trigilio
Jeffrey Trigilio
Chief Financial Officer
(Principal Financial and Accounting Officer)