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 001-40356

Rain Therapeutics Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**82-1130967**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
8000 Jarvis Avenue, Suite 204 Newark, CA	**94560**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (510) 953-5559

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	RAIN	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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant as of June 30, 2021, the last business day of the Registrant's most recently completed second fiscal quarter, was approximately $120,166,484, based on the closing price of the shares of common stock on The Nasdaq Global Select Market reported for such date. Shares of common stock held by each officer and director and by each person who is known to own 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates of the Registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 17, 2022, the registrant had 26,510,407 shares of common stock, $0.001 par value per share, outstanding, comprised of 18,782,937 shares of common stock, $0.001 par value per share, and 7,727,470 shares non-voting common stock, $0.001 par value per share.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive proxy statement relating to its 2022 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2021 are incorporated herein by reference in Part III of this Annual Report on Form 10-K where indicated.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K includes “forward-looking statements” within the meaning of the federal securities laws, which statements are subject to substantial risks and uncertainties and are based on estimates and assumptions. All statements, other than statements of historical facts included in this Annual Report on Form 10-K, including statements concerning our plans, objectives, goals, strategies, future events, future revenues or performance, financing needs, plans or intentions relating to product candidates and markets and business trends and other information referred to under the sections titled “Business,” “Risk Factors,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” are forward-looking statements. In some cases, you can identify forward looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,”, “design,” “estimate,” “predict,” “potential,” “plan” or the negative of these terms and similar expressions intended to identify forward-looking statements. Forward-looking statements are not historical facts and reflect our current views with respect to future events. Given the significant uncertainties, you should not place undue reliance on these forward-looking statements.

There are a number of risks, uncertainties and other factors that could cause our actual results to differ materially from the forward-looking statements expressed or implied in this Annual Report on Form 10-K. Such risks, uncertainties and other factors include, among others, the risks, uncertainties and factors set forth in “Risk Factors,” and the following risks, uncertainties and factors:

- the ability of our clinical trials to demonstrate safety and efficacy of our product candidates and other positive results;
- the timing and focus of our ongoing and future preclinical studies and clinical trials and the reporting of data from those studies and trials;
- our plans relating to commercializing our product candidates, if approved, including the geographic areas of focus and sales strategy;
- the size of the market opportunity for our product candidates, including our estimates of the number of patients who suffer from the diseases we are targeting;
- our expectations regarding the approval and use of our product candidates as first, second or subsequent lines of therapy or in combination with other drugs;
- the success of competing therapies that are or may become available;
- our estimates of the number of patients that we will enroll in our clinical trials;
- the beneficial characteristics, safety, efficacy and therapeutic effects of our product candidates;
- the timing or likelihood of regulatory filings and approvals, including our expectation to seek an accelerated approval pathway and special designations, such as orphan drug designation, for our product candidates for various diseases;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our plans relating to the further development of our product candidates, including additional indications we may pursue;
- existing regulations and regulatory developments in the United States, Europe and other jurisdictions;
- risks associated with the COVID-19 pandemic, which may adversely impact our business, preclinical studies and clinical trials;
- our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available;
- our continued reliance on third parties to conduct additional clinical trials of our product candidates and for the manufacture of our product candidates for preclinical studies and clinical trials;
- our plans regarding, and our ability to obtain, and negotiate favorable terms of, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- our plans to develop our product candidates in combination with other therapies;
- the need to hire additional personnel and our ability to attract and retain such personnel;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our financial performance;
- the period over which we estimate our existing cash and cash equivalents will be sufficient to fund our future operating expenses and capital expenditure requirements; and
- our expectations regarding the period during which we will qualify as an emerging growth company under the JOBS Act.

There may be other factors that may cause our actual results to differ materially from the forward-looking statements, including factors disclosed in “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” You should evaluate all forward-looking statements made in this Annual Report on Form 10-K in the context of these risks and uncertainties.

We caution you that the risks, uncertainties and other factors referred to above may not contain all of the risks, uncertainties and other factors that are important to you. In addition, we cannot assure you that we will realize the results, benefits or developments that we expect or anticipate or, even if substantially realized, that they will result in the consequences or affect us or our business in the way expected. All forward-looking statements in this Annual Report on Form 10-K apply only as of the date made and are expressly qualified in their entirety by the cautionary statements included in this Annual Report on Form 10-K. We undertake no obligation to publicly update or revise any forward-looking statements to reflect subsequent events or circumstances.

PART I

ITEM 1. BUSINESS.

Company Overview

We are a late-stage precision oncology company developing therapies that target oncogenic drivers for which we are able to genetically select patients we believe will be most likely to benefit. This approach includes using a tumor-agnostic strategy to select patients based on their tumors' underlying genetics rather than histology. We have in-licensed product candidates, each with a differentiated profile relative to available therapies, and we intend to continue strengthening our pipeline through focused business development and internal research efforts.

Our lead product candidate, milademetan (also known as RAIN-32) is a small molecule, oral inhibitor of mouse double minute 2 (MDM2), which may be oncogenic in numerous cancers. We in-licensed milademetan from Daiichi Sankyo Company, Limited (Daiichi Sankyo) in September 2020 based on the results of a Phase 1 clinical trial, which demonstrated meaningful antitumor activity in an MDM2-amplified subtype of liposarcoma (LPS) and other solid tumors. Data from well-differentiated/de-differentiated (WD/DD) LPS patients in the Phase 1 clinical trial of milademetan demonstrated median progression-free survival (mPFS) of approximately seven to eight months. Importantly, this result was accomplished with a rationally designed dosing schedule designed to mitigate safety concerns and widen the therapeutic window of MDM2 inhibition unlocking the potential for milademetan in a broad range of MDM2-dependent cancers. Milademetan is currently being evaluated in an ongoing Phase 3 clinical trial in patients with LPS (MANTRA), as well as a Phase 2 tumor-agnostic basket trial in certain solid tumors (MANTRA-2). We anticipate commencing a Phase 2 clinical trial of milademetan (MANTRA-3), for the treatment of patients with Merkel cell carcinoma who are polyoma virus-positive and refractory to immune checkpoint inhibition (ICI), in the second half of 2022 and a Phase 1 clinical trial to evaluate the safety, tolerability and efficacy of milademetan in combination with atezolizumab in patients with loss of cyclin-dependent kinase inhibitor 2A (CDKN2A) and wildtype p53 advanced solid tumors (MANTRA-4) in the second half of 2022. In addition to milademetan, we are also developing a preclinical program that is focused on inducing synthetic lethality in cancer cells by inhibiting RAD52.

Our Strategy

Our vision is to be a leading precision oncology company that develops and commercializes small molecule therapeutics through leveraging both an acquisition-based business model and internal research efforts. Our strategy to achieve this vision is as follows:

- Rapidly advance our lead product candidate, milademetan, through clinical development toward approval in LPS and subsequently expand across a multitude of MDM2-dependent tumors. As the trials progress, we plan to accelerate efforts to engage with the regulatory authorities and, upon potential receipt of the requisite approvals, will initiate efforts to manufacture and commercially launch milademetan.
- Increase probability of a clinically meaningful benefit for patients for our pipeline programs by utilizing biomarker driven patient selection. We employ widely available, comprehensive next generation sequencing (NGS) diagnostic tests and partner with industry-leading assay developers to identify patients for our clinical trials based on molecular biomarkers indicating oncogene addiction and dependency on specific cellular signaling networks. This pre-selection of patients is designed to target patients most likely to benefit from our therapies.
- Maximize opportunity of commercial success for our pipeline programs by focusing on tumor-agnostic clinical trials. Through our MANTRA-2 open-label basket trial for milademetan, we are employing a tumor-agnostic development approach to the essential biological pathways and molecular machinery of cancer. This strategy leverages existing comprehensive next generation tumor sequencing in cancer patients and we believe will allow for rapid patient enrollment and subsequent collection of data and, as a result, the potential acceleration of clinical trial timelines. We believe our continued focus on this approach will maximize our total addressable patient population and the overall commercial opportunities for our pipeline programs.
- Leverage our business development expertise to expand our pipeline of precision oncology candidates by identifying genetically or biologically defined subsets across solid tumors and hematologic malignancies in patients with limited treatment options. Our team has a diversity of

backgrounds from academia and drug research and development to biopharma industry experience. Our expansive networks in the biopharma landscape coupled with our analytical approach to business development allows us to screen and identify drug candidates and programs with potentially significant commercial opportunities. We are exploring pipeline programs in the following three categories: (1) small molecule programs focusing on novel oncogenic drivers, and with mechanisms of action that are distinct from existing and upcoming therapeutics; (2) programs that improve upon existing therapies with validated oncology targets and clinical efficacy, but which lack clinical utility due to a narrow therapeutic window; and (3) programs targeting emerging classes and/or biological targets of precision oncology, such as synthetic lethality.

- Pursue global clinical and regulatory strategies enabling us to commercialize pipeline programs worldwide. We will pursue a global regulatory approach and take into consideration the differing requirements and criteria of the Food and Drug Administration (FDA), European Medicines Agency (EMA) and other regulatory agencies as our pipeline programs progress in their respective clinical trials. We plan to retain significant economic and commercial rights to our portfolio in the United States and certain other regions. We will evaluate partnership opportunities in regions in which we are unlikely to pursue commercialization on our own.
- Pursue collaborations with leading academic clinical investigators to evaluate new therapeutic indications and combinations of pipeline programs. In addition to building a pipeline of therapies through internal research and business development efforts, we expect to continue to partner with academic and research institutions to expand the scope of our data.

Overview of Precision Oncology and Our Approach

Precision oncology broadly refers to the strategy of harnessing tumor biology to design drugs and clinical trial strategies to treat cancer more effectively in patients. Recent companion diagnostic approvals and reimbursement for multi-gene NGS assays have made it easier to translate and distil cancer biology into tenable biomarkers that can then be readily identified in tumor or blood samples from patients. This approach has accelerated over the last decade and has resulted in numerous targeted therapies for previously difficult to treat cancers such as lung adenocarcinoma, bladder cancer, and cholangiocarcinoma, among others. A recent development within the precision oncology strategy is the strategy of seeking regulatory approval of cancer drugs based solely on tumor biology and biomarkers across cancer types, rather than tumor histology or organ site-specific approvals. Successful examples of this strategy include larotrectinib, developed by Loxo Oncology, Inc., and entrectinib, developed by Ignyta, Inc., both for tumors harboring NTRK gene fusions, and pembrolizumab, developed by Merck, for microsatellite instability-high tumors. As a result, a new era of cancer drug development has emerged, demonstrating an unprecedented degree of insight into the critical drivers of cancer, tumorigenesis and its associated signaling networks.

With a biology-based approach that views a tumor’s biological driver as more important than tumor type for selecting treatment modalities, we believe that understanding the molecular machinery employed by a tumor is paramount to developing cancer therapeutics. We intend to pursue therapeutics that target genetic alterations in cell-signaling pathways that may be oncogenic, including synthetic lethal interactions. By understanding these biological dependencies in cancer cells, we hope to identify new therapies to meaningfully extend patients’ lives.

We seek to build a pipeline of precision oncology therapeutics for genetically-defined patients by discovering or licensing programs in three categories:

- programs focusing on novel oncogenic drivers and small molecules with mechanisms of action that are distinct from existing and upcoming therapeutics;
- programs that improve upon existing therapies with validated oncology targets and clinical efficacy, but which lack clinical utility due to a narrow therapeutic window; and
- programs targeting emerging classes and/or biological targets of precision oncology, such as synthetic lethality.

Programs that capitalize on rational tumor targets are required to exhibit appropriate selectivity with a high degree of target engagement. We view the three key pillars of any successful program as:

- targeting a tumor with unambiguous oncogenic addiction;
- achieving sufficient exposure of therapeutics in plasma and the tumor; and

- strong target engagement during the dosing window.

Our approach leverages currently available tumor genetic testing strategies to enroll and treat patients with advanced cancer. We employ companion diagnostics and partnerships with industry-leading assay developers to identify patients based on molecular biomarkers indicating oncogene addiction and dependency on specific cellular signaling networks. In our MANTRA-2 basket trial of milademetan, we are enrolling patients with advanced or metastatic cancer based on MDM2 gene amplification and p53 mutation status, both of which are widely available on existing commercial NGS assays. The significant expansion of the FDA-approved targeted therapies in non-small cell lung cancer (NSCLC), breast cancer, bladder cancer, melanoma, cholangiocarcinoma and tumor-agnostic indications has led to increasing adoption of multi-gene NGS assays to determine patient eligibility for an ever-expanding number of targeted therapies.

Our Development Pipeline

Our development pipeline is summarized below and is unified by a strategy to target oncogenic drivers through differentiated therapies for which we are able to genetically select the patients we believe will be most likely to benefit from treatment. We currently retain global development and commercialization rights to all of our product candidates.

Our Lead Product Candidate, Milademetan

Milademetan Overview

Our lead product candidate, milademetan, is a small molecule, oral inhibitor of MDM2 and is being developed in patients with MDM2-dependent cancers. Historically, MDM2 inhibition has presented treatment challenges due to dose-limiting, on-target hematologic toxicities. We believe an MDM2-targeted therapy must possess certain pharmacological characteristics related to potency, pharmacokinetics and drug accumulation to allow for the design of an optimized dosing schedule. An optimized dosing schedule is intended to improve peak drug exposure leading to apoptosis and cell cycle arrest during the dosing period, while permitting hematopoietic precursor cell recovery during the dosing break, thereby minimizing hematologic toxicity. Residual drug concentration, due to poor drug clearance or tissue accumulation during the dosing break may otherwise prevent recovery from thrombocytopenia. Milademetan's differentiated profile, as a potent MDM2 inhibitor with rapid plasma clearance and lack of drug accumulation in tissues, has enabled a rationally designed dosing schedule that we believe has the potential to reduce toxicities while preserving activity. We anticipate that this dosing schedule may also be applicable to other MDM2-dependent cancer populations across solid and hematologic tumor types.

Overview of p53 and MDM2

Milademetan reactivates p53, known as the "guardian of the genome," by inhibiting MDM2. p53 is present in every cell and acts as a key regulator of a variety of cellular processes including cell cycle, DNA repair and apoptosis. In a normal cell, the activity of p53 is controlled and regulated by the inhibitory protein MDM2. MDM2

binds to p53, thereby inducing degradation and allowing normal cells to function properly. In response to cell damage and other stress conditions, p53 is activated and prevents the formation of cancerous cells by inducing apoptosis.

In contrast to normal cells, in tumor cells, the two primary mechanisms by which p53 can be inactivated in tumor cells are mutations in p53 and activation or overexpression of MDM2. Approximately half of all tumors are characterized by mutations of the p53 gene. The remaining cancer patients have a p53 gene that is not mutated, and is otherwise known as WT p53, but can be functionally suppressed through the activation or overexpression of MDM2. We have identified MDM2 dependence in several solid tumors. This dependence is caused by overexpression of MDM2 through gene amplification or other mechanisms, loss of a negative regulator of MDM2 or other causes. Overexpression of MDM2 promotes the degradation of p53 and also eliminates p53's ability to activate transcription. Milademetan, by binding MDM2 at the p53 interaction site, prevents the formation of the MDM2- p53 complex, allowing p53 reactivation and subsequent transcription of genes, such as MIC-1, that trigger cancer cell cycle arrest or apoptosis, among others.

Phase 1 Clinical Data

Milademetan has been evaluated by Daiichi Sankyo in various solid tumors, including WD/DD LPS, in a Phase 1 trial (U101) for initial assessment of safety, tolerability and preliminary efficacy. The largest population enrolled in the trial were WD/DD LPS patients (approximately 50% of the total patients enrolled). WD/DD LPS tumors have nearly universal MDM2 gene amplification and WT p53, and hence are nearly universally MDM2-dependent. Therefore, we believe these LPS patients represent an appropriate population for MDM2 inhibition therapy. In October 2020, Daiichi Sankyo reported comprehensive results from this Phase 1 trial covering 107 patients. Milademetan has demonstrated meaningful antitumor activity in an MDM2-amplified subtype of LPS and other solid tumors in a Phase 1 clinical trial, validating a rationally-designed dosing schedule to potentially mitigate safety concerns and widen the therapeutic window of MDM2 inhibition.

Clinical Observations to Support Pursuing Milademetan as a Treatment in LPS Patients

Historically, LPS treatment rarely produces tumor responses, regardless of therapy and line of treatment. As a result, efficacy in LPS has been assessed with an endpoint of PFS, and we are using PFS as the primary endpoint in our MANTRA Phase 3 LPS trial. Notwithstanding, tumor responses to milademetan were observed in the Phase 1 trial. Of the 53 patients with WD/DD LPS who received one or more doses of milademetan, two (3.8%) achieved partial response and 34 (64.2%) achieved stable disease.

The trial also identified the disease control rate (DCR) for the LPS population enrolled in the trial, which consisted primarily of patients with MDM2-amplified tumors, as compared to an unselected non-LPS population. The DCR in the LPS population was nearly double the DCR in the non-LPS population, 58.5% versus 32.4%, respectively, supporting our plan to select patients with MDM2 amplification in future clinical trials.

In July 2021, we provided an update on patients who received milademetan monotherapy from the concluded Phase 1 dose escalation and expansion study. As of July 1, 2021, three WD/DD LPS patients received therapy with milademetan monotherapy for greater than 51 months. Two of these patients received therapy with durations of 51 and 57 months without disease progression, and an additional patient received therapy for greater than 59 months before discontinuation in the second quarter of 2021. We believe this highlights the potential for milademetan to have a favorable long-term tolerability and safety profile.

Based on the Phase 1 data, we initiated a pivotal Phase 3 trial in WD/DD LPS patients (MANTRA) in July 2021.

Clinical Observations in Non-LPS Patients to Support Pursuing Milademetan as a Tumor-agnostic Treatment for Patients with MDM2-amplified Tumors

In contrast to LPS patients who rarely have tumor responses to treatment, certain non-LPS patients enrolled in the Phase 1 trial exhibited tumor responses when treated with milademetan. Of the ten non-LPS patients receiving milademetan in Schedule D of the completed Phase 1 clinical trial, three patients were characterized for MDM2 gene amplification. Patients characterized for MDM2 gene amplification included patients with breast cancer (copy number of 16.8), synovial sarcoma (copy number of 25.9) and small cell lung cancer

(SCLC) (copy number of 36.6). The first patient exhibited a confirmed tumor volume reduction. The latter two patients exhibited partial responses, one of which was a confirmed partial response.

Based on the available data from patients with non-LPS MDM2-amplified tumors, we initiated a Phase 2 tumor agnostic basket clinical trial (MANTRA-2) in November 2021.

Clinical Development Plan

Phase 3 Trial in WD/DD LPS Patients (MANTRA)

In July 2021, we initiated a randomized, multicenter, open-label, Phase 3 registrational trial (MANTRA) for patients with unresectable or metastatic DD LPS with or without a WD LPS component that has progressed on one or more prior systemic therapies, including at least one anthracycline-based therapy. This trial is an open label, 1:1 randomized trial comparing milademetan to trabectedin, an SOC therapeutic, in approximately 160 WD/DD LPS patients with at least one prior anthracycline-based therapy. The dosing schedule for the Phase 3 trial will be identical to the Schedule D dose of 260 mg (qd 3/14x2) employed in the Phase 1 trial. The primary objective of the trial is to compare PFS evaluated by Response Evaluation Criteria in Solid Tumors (RECIST) criteria in blinded independent review between the milademetan treatment arm and the trabectedin control arm. Secondary endpoints include overall survival, PFS by investigator assessment, objective response rate, duration of response, disease control rate, safety and patient reported outcomes. We anticipate top-line data from this trial in 2023. Our commencement of a Phase 3 trial following the Phase 1 trial referenced above is based on the data observed in the Phase 1 trial and FDA feedback with respect to our development plan.

The PFS assumptions for statistical powering are based on a PFS assumption for the control arm of 3.0 months and 6.0 months for milademetan. The doubling of PFS corresponds to a hazard ratio of 0.5.

Phase 2 MDM2-amplified Tumor-agnostic Basket Trial (MANTRA-2)

In November 2021, the first patient was dosed in the multicenter, single arm, open-label, Phase 2 basket trial evaluating Milademetan for the treatment of MDM2-amplified advanced solid (MANTRA-2). The MANTRA-2 trial is designed to evaluate the safety and efficacy of milademetan in patients with advanced or metastatic solid tumors refractory or intolerant to standard-of-care therapy and that exhibit wild-type p53 and a prespecified minimum MDM2 gene copy number. Approximately 65 patients are anticipated to be enrolled to receive milademetan. The primary endpoint of the trial is objective response rate as measured by RECIST criteria. Secondary endpoints include duration of response, disease control rate progression-free survival by investigator assessment, overall survival, and growth modulation index. An interim analysis from MANTRA-2 is anticipated in the second half of 2022.

We are enrolling patients that have received and progressed on standard of care (SOC) therapy and will be unlikely to tolerate or derive clinically meaningful benefit from SOC therapy. Patients with MDM2 amplification will be selected using a commercially-available NGS-based diagnostic assay. Milademetan will be administered in doses of 260 mg using the Schedule D dosing schedule from the Phase 1 trial (qd 3/14x2). The primary endpoint of this trial will be ORR by RECIST, with secondary endpoints of PFS, Duration of Response (DOR), OS and growth-modulation index (GMI). We believe the basket trial is supported by data in the Phase 1 clinical trial, in which non-LPS patients with MDM2-amplified tumors exhibited tumor volume reductions and confirmed partial responses under RECIST criteria.

Phase 2 Trial for Milademetan in Merkel Cell Carcinoma (MANTRA-3)

An oncogenic Merkel cell polyoma virus (MCV) presents in approximately 80% of MCC tumors. MCV-positive MCC typically contains mutant retinoblastoma and WT p53. Inactivating mutations in p53 have rarely been found in MCC. MCV small T antigen functions as a transcriptional activator to increase levels of MDM2 and downregulate p53 levels. Notably, other MDM2 programs have demonstrated proof-of-concept in MCC with clinical responses. Other MDM2 inhibitors have demonstrated potent activity in virus-positive, WT p53 MCC cancer models, albeit with high toxicity due to a narrow therapeutic window.

Based on recent non-clinical data from the Dana-Farber Cancer Institute presented at the Triple Cancer Conference, we announced a plan to commence a Phase 2 clinical trial, named MANTRA-3, evaluating the efficacy of milademetan, an oral MDM2 inhibitor, as a monotherapy for the treatment of patients with MCC refractory to ICI. The MANTRA-3 trial is designed to evaluate the efficacy of milademetan, as a monotherapy in patients with MCC that have progressed on immune checkpoint inhibitors. Approximately 34 patients are expected to be enrolled to receive milademetan. The primary endpoint of the trial is objective response rate as

measured by RECIST criteria. Secondary endpoints include duration of response, disease control rate, progression free survival by investigator assessment, growth modulation index, overall survival and safety.

Phase 1 Trial for Milademetan in Combination with Atezolizumab in Patients with CDKN2A Loss and Wildtype p53 advanced solid tumors.

Cyclin-dependent kinase inhibitor 2A (CDKN2A) encodes for the tumor suppressor p14ARF, an inhibitor of MDM2, and the loss of CDKN2A may lead to MDM2-dependent cancers. This concept of MDM2 dependency is supported by nonclinical data demonstrating *in vitro* sensitivity to milademetan of cancer cell lines harboring CDKN2A loss and WT p53 as well as several in vivo models with CDKN2A loss showing anti-tumor activity of milademetan. Loss of p53 activity via MDM2 and/or CDKN2A loss has also been associated with poor clinical outcomes for patients treated with immune checkpoint inhibitors (ICI). Nonclinical data in an immune competent mouse model of colorectal cancer with CDKN2A loss demonstrated enhanced combinatorial activity of milademetan plus an anti-PD1 antibody compared to either agent alone.

In January 2022, we announced a clinical supply agreement with Roche for the supply of the anti-Programmed Death Ligand-1 (PD-L1) monoclonal antibody, atezolizumab. Clinical trials are planned to evaluate milademetan in combination with atezolizumab for the treatment of patients in genetically selected populations. Under this agreement, we are the sponsor of the anticipated clinical trials, and Roche will supply atezolizumab.

An initial Phase 1 clinical trial is planned to evaluate the safety, tolerability and efficacy of milademetan in combination with atezolizumab in patients with loss of CDKN2A and wildtype p53 advanced solid tumors who have previously progressed on ICI. We anticipate the start of the Phase 1 clinical trial in the second half of 2022. Subsequent Phase 2 clinical trials evaluating the combination of milademetan and atezolizumab may span various additional tumor types.

Preclinical RAD52 Program

We are also developing a preclinical program focused on targeting RAD52 in the DNA damage repair pathway. While our RAD52 program is in an early stage of development, we expect to develop this program for patients with a molecularly diagnosed HRD+, such as mutations and loss-of-function in BRCA1/2 or others that utilize RAD52 as an alternative DNA repair pathway, as well as for patients that may have relapsed to poly (ADP ribose) polymerase (PARP) inhibitor therapy. There are currently no approved therapies or clinical programs in development targeting RAD52.

Targeting RAD52 represents a novel strategy for tumors exhibiting tumor HRD+ or a loss of function, of several pathway constituents, including BRCA1/2 or others in tumor types frequently characterized by these deficiencies. These tumors include breast, prostate, pancreatic, ovarian and possibly other cancers. Developmental paths for RAD52 inhibitors include as a monotherapy in HRD+ patients relapsing on PARP inhibitor therapy, or in front-line combinations with PARP inhibitors in HRD+ tumors.

Our RAD52 program is currently in lead optimization stage. We anticipate evaluating identified RAD52 inhibitor candidates in animal models of patient tumors with HRD+ that have relapsed on PARP inhibitors and in HRD+ tumors with a loss-of-function mutation of BRCA1/2 in combination with PARP inhibitors.

Collaboration and License Agreements

Daiichi Sankyo License Agreement

On September 2, 2020, we entered into a license agreement with Daiichi Sankyo, a Japanese corporation (the Daiichi Sankyo License Agreement). Pursuant to the Daiichi Sankyo License Agreement, we obtained a worldwide, sublicensable (through multiple tiers), royalty-bearing, exclusive right and license under Daiichi Sankyo's know how and seven families of patents and patent applications to make, have made, use, import and export milademetan (also known as RAIN-32) (the Licensed Compound) for all human prophylactic or therapeutic uses that derive therapeutic effect by binding to MDM2 for the prevention and treatment of any indication for the purpose of making, having made, using, offering for sale, selling, marketing, distributing, importing, and exporting products containing milademetan as an active pharmaceutical ingredient (the Products). See the section titled "Intellectual Property."

While we are solely responsible under the Daiichi Sankyo License Agreement for the research, development and registration of the Licensed Compound and Products, Daiichi Sankyo will continue to conduct three ongoing clinical trials and prepare final reports with respect to these clinical trials. We have agreed to reimburse Daiichi Sankyo certain third-party expenses incurred by Daiichi Sankyo while conducting such trials.

We are obligated to use commercially reasonable efforts to develop, commercialize and manufacture the Products and to commercially launch the Products as soon as reasonably practicable after receiving the requisite marketing approvals from the authorities in any given country. We are also obligated to use commercially reasonable efforts to receive at least three full approvals for use in each of the following countries: France, Germany, Italy, Spain, the United Kingdom, the United States and one country outside of the United States and the European Union.

In accordance with the terms of the Daiichi Sankyo License Agreement, we have paid Daiichi Sankyo an initial upfront payment of $5.0 million. We are required to make aggregate future milestone payments of up to $222.5 million, contingent on the attainment of certain development, regulatory and sales milestones. In July 2021, we announced that the first patient has been randomized in the multicenter, open-label, Phase 3 registrational trial (MANTRA) evaluating milademetan for the treatment of DD LPS. Accordingly, pursuant to the Daiichi Sankyo License Agreement, we recorded $5.5 million in milestone fees as research and development expense in the statement of operations. Of the $5.5 million milestone fees, $2.5 million was paid in the third quarter of 2021 and $3.0 million was accrued as part of accrued research and development in the balance sheet as of December 31, 2021.

Pursuant to the Daiichi Sankyo License Agreement, Daiichi Sankyo had the right to continue to conduct three clinical trials and prepare final reports with respect to these clinical trials, and such right expires upon all subjects completing the study treatment. We have agreed to reimburse Daiichi Sankyo certain third-party expenses incurred while conducting such trials.

Additionally, we are required to pay Daiichi Sankyo a high single digit royalty based on the annual net sales of the Products, subject to reduction at an agreed rate upon the expiration of the licensed patent in the particular country where the Products are sold. To date, no royalty payments have been made to Daiichi Sankyo under the Daiichi Sankyo License Agreement. The royalty obligation terminates on a country-by-country and Product-by-Product basis on the later of: (i) loss of all market exclusivity for such Product in such country, (ii) the last-to-expire patent that covers the Licensed Compound or the Product in such country and (iii) twelve years from launch of the first Product sold by us in such country.

Unless sooner terminated, the Daiichi Sankyo License Agreement will remain in full force and effect until we, our affiliates and our sublicensees cease all development and commercial activity related to the Licensed Compound and Products. Either party may terminate the Daiichi Sankyo License Agreement for cause in the event of the other party's uncured material breach after a certain cure period. With respect to Daiichi Sankyo's uncured material breach, however, we may only terminate the Daiichi Sankyo License Agreement with respect to the countries affected by such uncured material breach. Daiichi Sankyo may also terminate the Daiichi Sankyo License Agreement in the event of our bankruptcy or insolvency. Additionally, Daiichi Sankyo may terminate the Daiichi Sankyo License Agreement immediately upon written notice if we, our affiliates or our sublicensors initiate or join any challenge to the validity or enforceability of a licensed patent, subject to certain exclusions. Furthermore, we may terminate the Daiichi Sankyo License Agreement in its entirety or on a country-by-country basis for bona fide material concerns regarding the (i) lack of safety for human use arising from toxicity of the Licensed Compound or Product(s), (ii) lack of efficacy of the Licensed Compound or Product(s) or (iii) adverse economic impact to us in connection with our continued development of the Products, in each case, upon six months' prior written notice to Daiichi Sankyo. In addition, if we are acquired by a third party that is developing and commercializing a competing compound and the acquiring party decides not to discontinue the development or commercialization of such competing compound, such third party must terminate the Daiichi Sankyo License Agreement within 30 days of such acquisition if it does not discontinue such development or commercialization. Upon termination of the Daiichi Sankyo License Agreement by Daiichi Sankyo for our uncured material breach or by us for our bona fide material concerns regarding the safety, efficacy or adverse economic impacts relating to the Licensed Compound or Products, or our development thereof, we are required to, among other actions, if requested by Daiichi Sankyo (i) transfer to Daiichi Sankyo ongoing clinical trials, data, reports, records and materials, (ii) grant to Daiichi Sankyo an exclusive, irrevocable, sublicensable, fully paid-up license under any patents and know-how that are controlled and actually used by us at the time of termination in connection with the Products to allow Daiichi Sankyo exploit the Licensed Compound or Products in countries that are affected by the termination, (iii) grant to Daiichi Sankyo an exclusive, irrevocable, sublicensable, fully paid up license to use trademarks that are specific to the Products and (iv) assign any applicable sublicenses.

Agreement with Drexel University

On July 30, 2020, we entered into an intellectual property license agreement with Drexel University (Drexel) (the Drexel License Agreement). Pursuant to the Drexel License Agreement, Drexel granted to us (i) a

non-transferable (with certain exceptions), worldwide, exclusive, sublicensable (after the first anniversary, subject to certain conditions) license under Drexel's patent rights relating to RAD52 inhibitors for the treatment of cancer to make, have made, use, import, offer for sale and sell licensed products in all fields of use covered by the licensed patent rights, and (ii) a non-transferable (with certain exceptions), worldwide, nonexclusive, sublicensable (after the first anniversary, subject to certain conditions) license under certain technical information and know-how related to the licensed patent rights to make, have made, use, import, offer for sale and sell products in all fields of use covered by the licensed patent rights. The foregoing license grant is subject to (i) Drexel's retained rights to use, and to permit other non-commercial entities to use, the licensed patent rights for educational and research purposes, but excluding research sponsored by a commercial entity and the use of the licensed products in clinical trials, except for investigator-initiated clinical trials, and (ii) United States government rights, including but not limited to, any applicable requirement that the licensed products that are sold in the United States must be substantially manufactured in the United States.

We are obligated to use commercially reasonable efforts to (i) develop, commercialize, market and sell licensed products in a manner consistent with a development plan and (ii) achieve certain development, regulatory and clinical milestone events, including, among other things, receiving IND approval for a licensed product by the fourth anniversary of the effective date. Under the Drexel License Agreement, for a period of five years from the effective date and to the extent that there are no third-party obligations, we are granted the first option to license Drexel's rights in certain improvements, developments or inventions developed by Drexel (or jointly by the parties) during the five-year period that are directly related to the licensed products or to RAD52 or compounds that have been generated to specifically target RAD52.

In addition to a one-time, non-refundable initiation fee of $20,000, the Drexel License Agreement requires us to make milestone payments to Drexel of up to $6.25 million in aggregate, for the achievement of specified development and regulatory milestones for each licensed product. We are also required to reimburse Drexel (i) after the filing of the first IND for the first licensed product, for all costs related to the filing, prosecution and maintenance of the licensed patent rights accumulated prior to the effective date, and (ii) for all reasonable costs related to the filing, prosecution and maintenance of the licensed patent rights after the effective date. In addition, we are also required to pay Drexel, on a quarterly basis, a low single digit royalty on net sales by us, our affiliates, and sublicensees of the licensed products, subject to specified reductions and a minimum quarterly royalty payment of $6,250. Lastly, we are also obligated to pay Drexel (i) an annual license maintenance fee of $15,000 commencing upon filing of the first IND for a licensed product until the first sale of the first licensed product, (ii) a sublicense fee of low double digits percentage on all consideration received by us from our sublicensees, subject to certain reductions and (iii) a one-time transaction fee equal to the actual amount of Drexel's licensing and legal expenses in connection with the Drexel License Agreement and the Sponsored Research Agreement the parties simultaneously entered into with the Drexel License Agreement (the Sponsored Research Agreement).

Unless earlier terminated or extended, the term of the Drexel License Agreement with respect to any licensed product and country continues until the later of (i) the expiration or abandonment of the last-to-expire valid claim of the licensed patent rights that covers the sale of such licensed product in such country, (ii) the expiration of any granted statutory period of marketing and/or data exclusivity for such licensed product pursuant to which we have exclusive commercialization rights, (iii) the month of the first sale of a generic equivalent of such licensed product in such country and (iv) ten years after the first sale of the first licensed product.

We may terminate the Drexel License Agreement at any time by providing 60 days' prior written notice to Drexel, in which case we will be required to cease exploitation of all licensed products, terminate all permitted sublicenses and pay all amounts owed to Drexel under the Drexel License Agreement and the Sponsored Research Agreement through the effective date of termination. Drexel may terminate the Drexel License Agreement for our uncured material breach (with 30-135 day cure periods), for our bankruptcy or insolvency, for our uncured material default under the Sponsored Research Agreement, or if we challenge the validity or enforceability of the licensed patent rights.

Manufacturing and Supply

We do not own or operate, and currently have no plans to establish any manufacturing facilities. We currently rely and expect to continue to rely for the foreseeable future, on third parties for the manufacture of our drug candidates for preclinical and clinical testing, as well as for commercial manufacture of any drugs that we may commercialize.

Clinical drug product supplies and active pharmaceutical ingredients (API) for the milademetan program were produced and supplied to us by Daiichi Sankyo. Clinical drug product manufactured in Daiichi Sankyo's GMP production facilities was supplied to us as brite stock and is being used in our ongoing LPS trial and basket

trial. For the milademetan program, we have selected and transferred Daiichi Sankyo processes to suitable commercial contract manufacturing organizations to supply API and clinical drug product for our clinical trials and in preparation for submission of marketing applications and potential future commercial supplies.

We obtain our supplies from contract manufacturers on a purchase order basis. We do not currently have arrangements in place for redundant supply for APIs and drug product. We intend to identify and qualify additional manufacturers to provide the APIs and drug product for our future development plan for milademetan. All our drug candidates are compounds of low molecular weight, generally called small molecules. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities.

Manufacturing clinical products is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance. Our contract manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with Current Good Manufacturing Practice (cGMP) requirements which impose certain production, manufacturing, procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements 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 requirements and other aspects of regulatory compliance.

Intellectual Property

We strive to protect the proprietary technologies, inventions and improvements that we believe are important to our business, including pursuing, obtaining, maintaining, defending and enforcing patent rights, whether developed internally or licensed from third parties, intended to cover the composition of matter of our product candidates, including milademetan, their methods of use, related technologies, such as biomarkers, solid state forms, formulations, etc. and other inventions that are important to our business. In addition to patent protection, we also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in our field.

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

The patent positions for biotechnology companies like us are generally uncertain and can involve complex legal, scientific and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. We also cannot ensure that patents will be issued with respect to any patent applications that we or our licensors may file in the future, nor can we ensure that any of our owned or licensed patents or future patents will be commercially useful in protecting our product candidates and methods of manufacturing the same. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. As a result, we cannot guarantee that any of our drug candidates will be protected or remain protectable by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented or invalidated by third parties. For more information regarding the risks related to our intellectual property, please see “Risk Factors—Risks Related to Our Intellectual Property.”

We generally file patent applications directed to our key programs in an effort to secure our intellectual property positions vis-a-vis these programs. As of December 31, 2021, we owned or in-licensed eighteen U.S. patents, one allowed U.S. patent application, one hundred and fifteen foreign patents, two allowed foreign patent applications, six U.S. pending non-provisional patent applications, fifty-three foreign pending patent applications, and five pending Patent Cooperation Treaty (PCT) applications.

The intellectual property portfolio for our most advanced programs as of December 31, 2021, is summarized below. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office and foreign patent offices may be significantly narrowed before issuance, if issued at all. We expect this may be the case with respect to some of our pending patent applications referred to below.

Milademetan

With regard to milademetan, as of December 31, 2021, our patent portfolio contained fourteen issued U.S. patents, three pending U.S. non-provisional patent applications, ninety-seven issued foreign patents, and thirty-four pending foreign patent applications, all exclusively licensed from Daiichi Sankyo. One patent family in the milademetan portfolio is directed to the composition of matter of milademetan where we have issued patents in various jurisdictions including the United States, Japan, thirty-seven countries in Europe, Australia, Canada, China, Colombia, Indonesia, India, Israel, Korea, Malaysia, Mexico, New Zealand, Philippines, Russia, South Africa, Taiwan, Singapore, and Vietnam and pending patent applications in various jurisdictions including the United States, Brazil, Egypt, and Thailand, all of which are expected to expire in March 2032, excluding potential patent term adjustments or patent term extensions, where applicable. Another patent family supporting milademetan pertains to crystal-forms of milademetan. Under this patent family, we have eight issued U.S. patents and thirteen issued foreign patents in various jurisdictions including Japan, certain countries in Europe, Canada, China, Hong Kong, Korea, Russia and Taiwan, and pending patent applications in Brazil and India all of which are expected to expire in 2033, excluding potential patent term adjustments or patent term extensions, where applicable.

Furthermore, we exclusively licensed from Daiichi Sankyo five patent families directed to combination therapies with milademetan, methods of synthesis of milademetan, and dosing regimens of Milademetan within these five patent families, we have five issued U.S. patents, two pending U.S. patent applications, twenty-three issued foreign patents and twenty-six pending foreign patent applications, including in Japan, Europe, Canada, China, Hong Kong, Korea, India, Brazil and Taiwan, all of which are expected to expire between September 2034 and October 2037, excluding potential patent term adjustments or patent term extensions, where applicable. These combination therapy, method of synthesis, and method of use (dosing regimen) patents and patent applications will not present barriers to our competitors with respect to any unclaimed therapies or methods of synthesis or use involving milademetan.

We intend to pursue additional patent protection for milademetan and other development candidates relating to milademetan, its methods of use and related technologies that we consider important to our business.

RAD52

With regard to our RAD52 program, as of December 31, 2021, we exclusively licensed from Drexel two patent families directed to compositions of matter RAD52 inhibitors and their use in the treatment of cancer. One of the patent families comprises two issued U.S. patents and one pending U.S. non-provisional patent application, all of which are expected to expire in June 2036, excluding potential patent term adjustments or patent term extensions, where applicable. The second patent family comprises one PCT application. Patents that issue, if any, and claim priority to this PCT application will be expected to expire in October 2040, excluding potential patent term adjustments or patent term extensions. We intend to pursue additional patent protection for our RAD52 program and other development candidates relating to our RAD52 inhibitor, its methods of use and related technologies that we consider important to our business.

Patent Terms

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the term of a patent covering an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act) as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent applicable to an approved drug is eligible for extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering milademetan, RAD52 or our

preclinical programs, if issued, and products from our intellectual property may or will be entitled to patent term extensions. If our drug candidates receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved use or the drug candidates. We also intend to seek patent term extensions in any jurisdictions where they are available; however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

Protection of Proprietary Information

In addition to patent protection, we also rely on trade secret protection and confidential know-how for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, including certain aspects of our manufacturing processes. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our confidential information, as well as entering into non-disclosure and confidentiality agreements with our employees, consultants, independent contractors, advisors, contract manufacturers, contract research organizations (CROs), hospitals, independent treatment centers, suppliers, collaborators and other third parties, such parties may breach such agreements and disclose our proprietary information including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Furthermore, these agreements may not provide meaningful protection. Third parties may also independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or to obtain or use information that we regard as proprietary. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. For more information regarding the risks related to our intellectual property please see “Risk Factors—Risks Related to Our Intellectual Property.”

Government Regulations

Government authorities in the United States, at the federal, state, local levels, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, product approval, manufacture, quality control, manufacturing changes, packaging, storage, recordkeeping, labeling, promotion, advertising, sales, distribution, marketing, and import and export of drugs and biologic products. All of our foreseeable product candidates are expected to be regulated as drugs. The processes for obtaining regulatory approval in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities both pre- and post-commercialization, are a significant factor in the production and marketing of our products and our research and development activities and require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA and other government entities regulate drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and its implementing regulations, as well as other federal and state statutes and regulations. Failure to comply with applicable legal and regulatory requirements in the United States at any time during the product development process, approval process, or after approval, may subject us to a variety of administrative or judicial sanctions, such as a delay in approving or refusal by the FDA to approve pending applications, withdrawal of approvals, delay or suspension of clinical trials, issuance of warning letters and other types of regulatory letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil monetary penalties, refusals of or debarment from government contracts, exclusion from the federal healthcare programs, restitution, disgorgement of profits, civil or criminal investigations by the FDA, U.S. Department of Justice, State Attorneys General, and/or other agencies, False Claims Act suits and/or other litigation, and/or criminal prosecutions.

An applicant seeking approval to market and distribute a new drug in the United States must typically undertake the following:

(1) completion of pre-clinical laboratory tests, animal studies, and formulation studies in compliance with the FDA’s good laboratory practice (GLP) regulations or other applicable regulations;

(2) submission to the FDA of an IND Application for human clinical testing, which must become effective without FDA objection before human clinical trials may begin;

(3) approval by an independent institutional review board (IRB) or ethics committee representing each clinical site before each clinical trial may be initiated;

(4) performance of adequate and well-controlled human clinical trials in accordance with good clinical practice (GCP) regulations, to establish the safety and effectiveness of the proposed drug product for each indication for which approval is sought;

(5) preparation and submission to the FDA of a New Drug Application (NDA);

(6) satisfactory review of the NDA by an FDA advisory committee, where appropriate or if applicable,

(7) satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practice (cGMP) regulations and to assure that the facilities, methods, and controls are adequate to ensure the product's identity, strength, quality, and purity, and of selected clinical investigation sites to assess compliance with GCP; and

(8) payment of user fees, as applicable, and securing FDA review approval of the NDA.

Preclinical Studies and an IND

Preclinical studies can include in vitro and animal studies to assess the potential for adverse events and, in some cases, to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. Other studies include laboratory evaluation of the purity, stability and physical form of the manufactured drug substance or active pharmaceutical ingredient and the physical properties, stability and reproducibility of the formulated drug or drug product. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. Some preclinical testing, such as longer-term toxicity testing, animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Following commencement of a clinical trial under an IND, the FDA may place a clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND, such as restrictions on dosing or patient enrollment. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume in full or in part, as applicable, after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with Current Good Clinical Practices (cGCP) requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB or ethics committee representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Some studies also include oversight by an independent group of qualified experts organized by the clinical trial 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. Information about certain clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

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

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently $3,117,218 for fiscal year 2022, for applications requiring clinical data, and the sponsor of an approved NDA is also subject to an annual program fee, currently $369,413 for fiscal year 2022. These fees are adjusted annually.

Under certain circumstances, the FDA will waive the application fee for the first human drug application that a small business, defined as a company with less than 500 employees, including employees of affiliates, submits for review. An affiliate is defined as a business entity that has a relationship with a second business entity if one business entity controls, or has the power to control, the other business entity, or a third-party controls, or has the power to control, both entities. In addition, an application to market a prescription drug product that has received orphan designation is not subject to a prescription drug user fee unless the application includes an indication for other than the rare disease or condition for which the drug was designated.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also 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. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act (PDUFA), the FDA has agreed to specified performance goals in the review process of NDAs. Specifically, the FDA has a goal of reviewing most NDAs for new molecular entities within ten months from the date of filing, and of reviewing most "priority review" NDAs within six months of the filing date. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant.

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

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The FDA also may require submission of a risk evaluation and mitigation strategy (REMS) plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities and clinical sites, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter indicates that the review cycle is complete, and the application will not be approved in its present form. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional clinical or nonclinical testing or other information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months of receipt depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. After approval, the FDA may seek to prevent or limit further marketing of a product based on the

results of post-market studies or surveillance programs. 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

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation entitles the applicant to incentives such as grant funding towards clinical trial costs, tax advantages, and waivers of FDA user fees. Orphan drug designation must be requested before submitting an NDA, and both the drug and the disease or condition must meet certain criteria specified in the Orphan Drug Act and FDA's implementing regulations at 21 C.F.R. Part 316. The granting of an orphan drug designation does not alter the standard regulatory requirements and process for obtaining marketing approval.

After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. If a product that has orphan drug designation subsequently receives the first FDA approval 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 application to market the same drug for the same indication for seven years, except in very 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 for the same disease or condition, or the same drug for a different disease or condition.

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 orphan designation. 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, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Review and Accelerated Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate the FDA's review and approval of NDAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition and data demonstrate its potential to address unmet medical needs for the disease or condition. Fast Track Designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. A Fast Track product may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. .

In addition, the Food and Drug Administration Safety and Innovation Act of 2012 established the Breakthrough Therapy Designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a Fast Track Designation and/or Breakthrough Therapy Designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated

approval. NDAs for drugs intended to treat serious or life-threatening conditions may be eligible for priority review where there is evidence that the product candidate, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition.

The FDA may grant accelerated approval for an NDA if the drug treats a serious or life-threatening condition, provides a meaningful advantage over available therapies, and demonstrates an effect on either (1) a surrogate endpoint that is reasonably likely to predict clinical benefit, or (2) on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. 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.

Post-approval Requirements

Drugs 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, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fee requirements for any marketed products.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- clinical holds on ongoing or planned clinical trials;
- product seizure or detention, or refusal to permit the import or export of products; or
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of

the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA), which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Marketing Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application (ANDA), or an NDA submitted under Section 505(b)(2) (505(b)(2) NDA), submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

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

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

FDA Approval and Regulation of Companion Diagnostics

If safe and effective use of a drug candidate depends on an in vitro diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and in vitro companion diagnostics. According to the guidance, if FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the drug or new indication if the companion diagnostic device is not approved or cleared for that indication. 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. The review of in vitro companion diagnostics in conjunction with the review of our product candidates will, therefore, likely involve coordination of review by the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics and Radiological Health.

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 two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval (PMA).

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. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation (QSR), which imposes elaborate testing, control, documentation, and other quality assurance requirements.

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

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

Review and Approval of Drug Products in the European Union

In order to market any pharmaceutical product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions governing, among other things, research and development, testing, manufacturing, quality control, safety, efficacy, clinical trials, marketing authorization, packaging, storage, record keeping, reporting, export and import, advertising and other promotional practices involving pharmaceutical products, as well as commercial sales, distribution and post-approval monitoring and reporting of our products. Whether or not it obtains FDA approval for a pharmaceutical product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the pharmaceutical product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods, as evidenced by the preliminary feedback from the EMA on the design of our planned Phase 3 liposarcoma trial. The time required to obtain approval in other countries and jurisdictions might differ from and be longer and far more difficult than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

The United Kingdom (UK) formally left the European Union (EU) on January 31, 2020 and the transition period, during which EU laws continued to apply to the UK, expired on December 31, 2020. This means EU laws now only apply to the UK in respect of Northern Ireland as laid out in the Protocol on Ireland and Northern Ireland. Following the end of the transition period, the EU and the UK concluded a trade and cooperation agreement (TCA), which applied provisionally from January 1, 2021 and entered into force on May 1, 2021.

The TCA includes provisions affecting the life sciences sector (including on customs and tariffs) but areas for further discussion between the EU and the UK remain. In addition, there are some specific provisions concerning pharmaceuticals. These include the mutual recognition of Good Manufacturing Practice (GMP) and issued GMP documents. The TCA does not, however, contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards.

Since January 1, 2021, the EU laws which have been transposed into UK law through secondary legislation continue to be applicable in the UK as “retained EU law”. As there is no general power to amend these regulations, the UK government has enacted the Medicines and Medical Devices Act 2021. The purpose of the act is to enable the existing regulatory frameworks in relation to human medicines, clinical trials of human medicines, veterinary medicines and medical devices to be updated. The powers under the act may only be exercised in relation to specified matters and must safeguard public health.

Specified provisions of the Medicines and Medical Devices Act 2021 entered into force on February 11, 2021. The remaining provisions came into effect within two months of February 11, 2021 or will otherwise come into effect as stipulated in subsequent statutory instruments. The Medicines and Medical Devices Act 2021 supplements the UK Medical Devices Regulations 2002 (UK Regulations), which are based on the EU Medical Devices Directive as amended to reflect the UK’s post-Brexit regulatory regime. Notably, the UK Regulations do not include any of the revisions that have been made by the EU Medical Devices Regulation (EU) 2017/745, which, since May 26, 2021, now applies in all EU Member States.

The UK’s Medicines and Healthcare products Regulatory Agency (MHRA) conducted a comprehensive consultation between September and November 2021 on proposals to develop a new UK regime for medical devices in the UK. The proposals include more closely aligning definitions for medical devices and in vitro medical devices with internationally recognized definitions and changing the classification of medical devices according to levels or risk. The proposals are intended to improve patient and public safety and increase the appeal of the UK market. The new regime is planned to come into force on July 1, 2023, which will align with the date from which the UK is due to stop accepting CE marked medical devices and require UKCA (UK Conformity Assessed) marking. It is envisaged that, in Northern Ireland, the amended regime could run in parallel with any existing or future EU rules in accordance with the Protocol on Ireland and Northern Ireland.

Drug Development Process

The conduct of clinical trials is currently governed by the EU Clinical Trials Directive 2001/20/EC (Clinical Trials Directive), and will be gradually replaced by the EU Clinical Trials Regulation (EU) No. 536/2014 (CTR). The CTR introduces a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU. It entered into force on January 31, 2022.

Under the current regime, which will expire after a transition period of one or three years, respectively, as outlined below in more detail, before a clinical trial can be initiated, it must be approved in each EU Member State in which the clinical trial is to be conducted. The approval must be obtained from two separate entities: the National Competent Authority (NCA) and one or more Ethics Committees. The NCA of the EU Member States in which the clinical trial will be conducted must authorize the conduct of the trial, and the independent Ethics Committee must grant a positive opinion in relation to the conduct of the clinical trial in the relevant EU Member State before the commencement of the trial. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be submitted to or approved by the relevant NCA and Ethics Committees. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial must be reported to the NCA and to the Ethics Committees of the EU Member State where they occur.

A more unified procedure applies under the new CTR. A sponsor is able to submit a single application for approval of a clinical trial through a centralized EU clinical trials portal. One national regulatory authority (the reporting EU Member State proposed by the applicant) takes the lead in validating and evaluating the application consult and coordinate with the other concerned Member States. If an application is rejected, it may be amended and resubmitted through the EU clinical trials portal. If an approval is issued, the sponsor may start the clinical trial in all concerned Member States. However, a concerned EU Member State may in limited circumstances

declare an “opt-out” from an approval and prevent the clinical trial form being conducted in such Member State. The CTR also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU Database. After several postponements of the coming into effect of the CTR due to technical difficulties with the underlying IT systems, the “go live” of these systems and, accordingly, the coming into force of the regulation, took place on January 31, 2022. While Member States will work in CTIS immediately after the system has gone live, the CTR provides for two transition periods for sponsors: For one year, until 31 January 2023, clinical trial sponsors can still choose whether to submit an initial clinical trial application in line with the current system (Clinical Trials Directive) or via CTIS. From 31 January 2023, submission of initial clinical trial applications via CTIS becomes mandatory, and by 31 January 2025, all ongoing trials approved under the current Clinical Trials Directive will be governed by the new Regulation and have to be transitioned to CTIS.

Under both the current regime and the new CTR, national laws, regulations, and the applicable Good Clinical Practice and Good Laboratory Practice standards must also be respected during the conduct of the trials, including the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines on Good Clinical Practice (GCP) and the ethical principles that have their origin in the Declaration of Helsinki.

During the development of a pharmaceutical product, the European Medicines Agency (EMA) and national regulators within the EU provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Committee for Medicinal Products for Human Use (CHMP) on the recommendation of the Scientific Advice Working Party (SAWP). A fee is incurred with each scientific advice procedure, but is significantly reduced for designated orphan medicines. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application of the product concerned.

Marketing Authorization Procedures

In the EU and in Iceland, Norway, and Liechtenstein (together, the European Economic Area or EEA), pharmaceutical products may only be placed on the market after obtaining a Marketing Authorization (MA).

Marketing Authorizations have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Applications for renewal must be made to the EMA at least nine months before the five-year period expires.

Data and Market Exclusivity in the European Union

As in the United States, it may be possible to obtain a period of market and/or data exclusivity in the European Union that would have the effect of postponing the entry into the marketplace of a competitor’s generic, hybrid or biosimilar product (even if the pharmaceutical product has already received an MA) and prohibiting another applicant from relying on the MA holder’s pharmacological, toxicological and clinical data in support of another MA for the purposes of submitting an application, obtaining MA or placing the product on the market.

New medicinal products authorized in the European Union, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The overall ten-year period of market exclusivity can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

The data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference medicinal product when applying for a generic or biosimilar marketing authorization in the European Union during a period of eight years from the date on which the reference product was first authorized in the European Union. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the European Union until 10 years have elapsed from the initial authorization of the reference product in the European Union.

Orphan Drug Designation and Exclusivity

The criteria for designating an orphan medicinal product in the European Union are similar in principle to those in the United States. The EMA grants Orphan Drug Designation if the medicinal product is intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating, affecting not more than five in 10,000 people in the European Union and for which no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorized, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition (prevalence criterion). In addition, Orphan Drug Designation can be granted if, for economic reasons, the medicinal product would be unlikely to be developed without incentives and if there is no other satisfactory method approved in the European Union of diagnosing, preventing, or treating the condition, or if such a method exists, the proposed medicinal product is a significant benefit to patients affected by the condition. An application for orphan drug designation (which is not a marketing authorization, as not all orphan-designated medicines reach the authorization application stage) must be submitted first before an application for marketing authorization of the medicinal product is submitted. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted, and sponsors must submit an annual report to EMA summarizing the status of development of the medicine. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Designated orphan medicines are eligible for conditional marketing authorization.

The EMA's Committee for Orphan Medicinal Products (COMP) reassesses the Orphan Drug Designation of a product in parallel with the review for a marketing authorization; for a product to benefit from market exclusivity it must maintain its Orphan Drug Designation at the time of marketing authorization review by the EMA and approval by the EC. Additionally, any marketing authorization granted for an orphan medicinal product must only cover the therapeutic indication(s) that are covered by the Orphan Drug Designation. Upon the grant of a marketing authorization, Orphan Drug Designation provides up to ten years of market exclusivity in the orphan indication. During this ten-year period, with a limited number of exceptions, the regulatory authorities of the EU Member States and the EMA may not accept applications for marketing authorization, accept an application to extend an existing marketing authorization or grant marketing authorization for other similar medicinal products for the same therapeutic indication. Conversely, the ten-year market exclusivity period may be reduced to six years if at the end of the fifth year, it is established that the product no longer fulfils the criteria for an Orphan Drug Designation.

Pediatric Development

In the EU, companies developing a new pharmaceutical product are obligated to study their product in children and must therefore submit a Pediatric Investigation Plan (PIP) together with a request for agreement to the EMA. Pharmaceutical products that are granted a marketing authorization on the basis of the pediatric clinical trials conducted in accordance with the approved PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the approved PIP are developed and submitted. An approved PIP is also required when a marketing authorization holder wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized and covered by intellectual property rights.

Approval and Regulation of Companion Diagnostics

In Europe, in vitro diagnostic medical devices are currently regulated by Directive 98/79/EC which regulates the placing on the market, the CE-marking, the essential requirements, the conformity assessment procedures, the registration obligations for manufactures and devices as well as the vigilance procedure. In vitro diagnostic medical devices must comply with the requirements provided for in the Directive, and with further requirements implemented at national level (as the case may be). The Directive 98/79/EC will be replaced by the Regulation on In-Vitro Diagnostic Devices (No. 2017/746), which will apply from 26 May 2022, following a five-year transition period. In the meantime, manufacturers can opt to place in-vitro diagnostic devices on the market under Directive 98/79/EC or under the new Regulation if they fully comply with it.

Companion diagnostics can also be considered "combination products" which are governed by a different regulatory pathway depending on the mode of action of the products. A combination medicine/device product could either be regulated as a medicinal product or a medical device based on its primary mode of action. In principle, if a medical device incorporates a substance which, if used separately, is likely to be considered as a

medicinal product and act on the human body by an action ancillary to that of the device, the device must be evaluated and authorized in accordance with the medical device regulations. However, if the medicinal substance constitutes the main function of the product, then the product is considered as a medicinal product. Currently, for such combination products, the manufacturer will have to consult, prior to obtaining the CE marking of the device, the EMA or NCA to obtain scientific advice on the quality and safety of the medicinal substance, including the benefit/risk profile of its incorporation into the device.

The regulation of companion diagnostics will be subject to further requirements as of the entry into force of the in-vitro diagnostic devices Regulation (No 2017/746) which introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue a CE certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a NCA or the EMA.

Post-approval Regulation

Similar to the United States, both marketing authorization holders and manufacturers of pharmaceutical products are subject to comprehensive regulatory oversight by the EMA, the EC and/or the competent regulatory authorities of the EU Member States.

The holder of an EU marketing authorization for a pharmaceutical product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of pharmaceutical products.

Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU laws and the EU Member State laws implementing Directive 2001/83/EC on pharmaceutical products for human use and other core legislation relating to pharmaceutical products, and other EU Member State laws that apply to the conduct of clinical trials, manufacturing approval, marketing authorization of pharmaceutical products and marketing of such products, both before and after grant of marketing authorization, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal, or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Advertising and Promotion

In the EU, the advertising and promotion of our products is subject to EU regulation. This includes but is not limited to the promotion of pharmaceutical products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. Laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct both at EU level and in the individual EU Member States may apply. These laws may limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on its promotional activities with healthcare professionals. For instance, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of pharmaceutical products is prohibited in the EU. Relationships with healthcare professionals and associations are subject to stringent anti-gift statutes and anti-bribery laws, the scope of which differs across the EU. In addition, payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her regulatory professional organization, and/or the authorities of the individual EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Pricing and Reimbursement Environment

Even if a pharmaceutical product obtains a marketing authorization in the European Union, there can be no assurance that reimbursement for such product will be secured on a timely basis or at all. The EU Member

States are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. An EU Member State may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms.

To obtain reimbursement or pricing approval in some countries, including the EU Member States, we may be required to conduct studies that compare the cost-effectiveness of our product candidates to other therapies that are considered the local SOC. There can be no assurance that any country will allow favorable pricing, reimbursement and market access conditions for any of our products, or that we will be feasible to conduct additional cost-effectiveness studies, if required.

European Union Data Laws

The collection and use of personal health data and other personal information in the European Union is governed by the provisions of the European General Data Protection Regulation (EU) 2016/679 (GDPR), which came into force in May 2018, and related implementing laws in individual EU Member States.

The GDPR imposes a number of strict obligations and restrictions on the ability to process (processing includes collection, analysis and transfer of) personal data of individuals within the European Union and in the EEA, including health data from clinical trials and adverse event reporting. The GDPR also includes requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals prior to processing their personal data or personal health data, notification of data processing obligations to the national data protection authorities and the security and confidentiality of the personal data. EU Member States may also impose additional requirements in relation to health, genetic and biometric data through their national implementing legislation.

Under the GDPR, personal data can only be transferred within the EU Member States and the three additional European Economic Area countries (Norway, Iceland and Liechtenstein) that have adopted a national law implementing the GDPR. Appropriate safeguards are required to enable cross-border transfers of personal data from the EU and EEA Member States to a “third country” (a country outside the EU or EEA). This status has a number of significant practical consequences, in particular for international data transfers, competent supervisory authorities and enforcement of the GDPR.

In conclusion, the GDPR prohibits the transfer of personal data to countries outside of the European Union /EEA (including the United States) that are not considered by the European Commission to provide an adequate level of data protection, except if the data controller meets very specific requirements such as the use of standard contractual clauses (“SCCs”), issued by the European Commission. In this respect recent legal developments in Europe have created complexity and compliance uncertainty regarding certain transfers of personal data from the EU/EEA. For example, following the Schrems II decision of the Court of Justice of the European Union on July 16, 2020, in which the Court invalidated the Privacy Shield under which personal data could be transferred from the EU/EEA to United States entities who had self-certified under the Privacy Shield scheme, there is uncertainty as to the general permissibility of international data transfers under the GDPR. The Court did not invalidate the then current SCCs, but ruled that data exporters relying on these SCCs are required to verify, on a case-by-case basis, if the law of the third country ensures an adequate level of data protection that is essentially equivalent to that guaranteed in the EU/EEA. In light of the implications of this decision we may face difficulties regarding the transfer of personal data from the European Union/EEA to third countries. However, on June 4, 2021 the EU Commission issued a new set of SCCs for data transfers from controllers or processors in the EU/EEA to controllers or processors established outside the EU/EEA. These SCCs replace the old sets of SCCs that were adopted under the previous European Data Protection Directive 95/46. Since September 27, 2021, it is no longer possible to conclude contracts incorporating these previous versions of the SCCs. In addition, for contracts concluded before September 27, 2021, it is still possible to rely on the previous SCCs until the end of an additional 15 months transitional period (until December 27, 2022), provided that the processing operations which are the subject matter of the contract remain unchanged and reliance on previous SCCs ensures that the transfer is subject to appropriate safeguards. On November 11, 2021, the European Data Protection Board has adopted recommendations on such appropriate safeguards that supplement transfer mechanisms. These recommendations aim to assist data exporters with their duty to identify and implement appropriate supplementary measures where they are needed to ensure an essentially equivalent level of protection to the personal data they transfer to third countries.

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States may result in significant monetary fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater, other administrative penalties and a number of criminal offenses (punishable by uncapped fines) for organizations and in certain cases their directors and officers as well as civil liability claims from individuals whose personal data was processed. Data protection authorities from the different EU Member States may still implement certain variations, enforce the GDPR and national data protection laws differently, and introduce additional national regulations and guidelines, which adds to the complexity of processing personal data in the European Union. Guidance developed at both EU level and at the national level in individual EU Member States concerning implementation and compliance practices are often updated or otherwise revised.

There is, moreover, a growing trend towards required public disclosure of clinical trial data in the European Union which adds to the complexity of obligations relating to processing health data from clinical trials. Such public disclosure obligations are provided in the new EU Clinical Trials Regulation, EMA disclosure initiatives and voluntary commitments by industry. Failing to comply with these obligations could lead to government enforcement actions and significant penalties against us, harm to our reputation, and adversely impact our business and operating results. The uncertainty regarding the interplay between different regulatory frameworks, such as the Clinical Trials Regulation and the GDPR, further adds to the complexity that we face with regard to data protection regulation.

With regard to the transfer of data from the European Union to the United Kingdom, the TCA provided for a transition period of up to six months as of January 1, 2021 to enable the European Commission to complete its adequacy assessment of the UK's data protection laws. On June 28, 2021 the European Commission adopted two adequacy decisions for the United Kingdom – one under the GDPR and the other for the Law Enforcement Directive. Personal data may now freely flow from the European Union to the United Kingdom since the United Kingdom is deemed to have an adequate data protection level. Additionally, following the UK's withdrawal from the European Union and the EEA, companies also have to comply with the UK's data protection laws (including the UK GDPR, which is based on the EU GDPR), the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The adequacy decisions include a 'sunset clause' which entails that the decisions will automatically expire four years after their entry into force.

New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in the European Union, its Member States and other states of Europe that could significantly change the statutory provisions governing the testing, approval, manufacturing, marketing, coverage and reimbursement of pharmaceutical products. In addition to new legislation, pharmaceutical regulations and policies are often revised or interpreted by the EMA and national agencies in ways that may significantly affect our business and our products.

U.S. Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as, in the United States, Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or 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. A payor's decision to provide coverage for a drug product does not necessarily imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider a product to be cost effective compared to other available therapies, they may not cover the product after approval

as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. Even if favorable coverage and reimbursement status is attained for one or more products that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

The U.S. government and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, risk sharing, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals. As a result, the marketability of any product which receives regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement.

U.S. Healthcare Reform

In the United States, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time.

In particular, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA, was signed into law and contained provisions that may reduce the profitability of drug products, including, for example, increasing rebates for drugs sold to Medicaid programs, extending Medicaid rebates to Medicaid managed care plans, requiring mandatory discounts for certain Medicare Part D beneficiaries and imposing annual fees based on pharmaceutical companies' share of sales to federal health care programs. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. For example, in 2017, Congress enacted the Tax Cuts and Jobs Act, or the TCJA, which eliminated the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit affirmed the District Court's decision that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard the case, but overturned the decision on the basis that the plaintiffs lacked standing and did not address the constitutionality. The Supreme Court's decision left open the opportunity for additional challenges to the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year and reduced payments to several types of Medicare providers, which will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021 absent additional congressional action. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. Individual states in the United States have also become increasingly active in implementing 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, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

Healthcare Laws and Regulations

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with healthcare providers, physicians, third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships

through which we market, sell and distribute products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal healthcare Anti-Kickback Statute prohibits, among other things, persons from soliciting, offering, receiving or providing any remuneration (in cash or in kind), directly or indirectly, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any item, facility or service for which payment may be made in whole or in part under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- the federal Foreign Corrupt Practices Act, or FCPA, prohibits, among other things, U.S. corporations and persons acting on their behalf from offering, promising, authorizing or making payments to any foreign government official (including certain healthcare professionals in many countries), political party, or political candidate in an attempt to obtain or retain business or otherwise seek preferential treatment abroad;
- the federal False Claims Act, which may be enforced by the U.S. Department of Justice or private whistleblowers to bring civil actions (qui tam actions) on behalf of the federal government, imposes civil penalties, as well as liability for treble damages and for attorneys' fees and costs, on individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent, making a false statement material to a false or fraudulent claim, or improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the Department of Health and Human Services' Civil Monetary Penalties authorities, which imposes administrative sanctions for, among other things, presenting or causing to be presented false claims for government payment and providing remuneration to government health program beneficiaries to influence them to order or receive healthcare items or services;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other conduct, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA 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 and its implementing regulations, also imposes criminal and civil liability and penalties on those who violate requirements, including mandatory contractual terms, intended to safeguard the privacy, security, transmission and use of individually identifiable health information;
- the federal false statements statute relating to healthcare matters prohibits falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal Physician Payment Sunshine Act requires manufacturers of drugs (among other products) to report to the Centers for Medicare and Medicaid Services within the U.S. Department of Health and Human Services, or HHS, information related to payments and other transfers of value to physicians (as defined by statute), certain other healthcare providers beginning in 2022, and teaching hospitals, as well as physician ownership and investment interests in the reporting manufacturers;
- similar state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers;
- certain state laws require pharmaceutical companies to comply with voluntary compliance guidelines promulgated by a pharmaceutical industry association and relevant compliance guidance issues by HHS Office of Inspector General; bar drug manufacturers from offering or providing certain types of payments or gifts to physicians and other health care providers; and/or require disclosure of gifts or payments to physicians and other healthcare providers; and

- Various state and foreign laws also govern the privacy and security of health information in some circumstances; many of these laws differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, civil and criminal penalties, damages, fines, additional reporting obligations, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

Competition

The biotechnology industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including pharmaceutical and biotechnology companies, ranging in size from early stage to major global companies, academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for the research, development, manufacturing and commercialization of cancer therapies. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop cancer therapies. We focus on the development of precision small molecule therapies for patients with cancers where there is a high unmet medical need. There are numerous other companies that have commercialized or are developing cancer therapies for the same or similar targets.

With respect to our lead product candidate, milademetan, there are no approved drugs targeting MDM2. There are multiple companies testing MDM2 inhibitors and degraders in various stages of development and various indications, including, Kartos (navtemadlin), Ascentage (alrizomadlin), Boehringer Ingelheim (BI-907828), Aileron (ALRN-6924), Kymera (KT-253), and others.

With respect to our RAD52 program, there are currently no other approved or clinical-stage therapeutics that inhibit RAD52. We are aware of academic groups working on discovery-stage RAD52 programs; however, we believe that our RAD52 program is currently the most advanced program for this target.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and commercializing and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and enrolling subjects for our clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We could see a reduction or elimination of our commercial opportunities if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or obtain more favorable reimbursement than any products that we or our collaborators may develop. Our competitors also may obtain FDA or foreign 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 or our collaborators are able to enter the market. The key competitive factors affecting the success of all our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics, if required, the level of biosimilar or generic competition, and the availability of reimbursement from government and other third-party payors.

Employees and Human Capital Resources

As of December 31, 2021, we had 44 full-time employees, of whom 31 were engaged in research and development activities and 13 were engaged in general and administrative activities. 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. Recruiting and retaining experienced and qualified scientific personnel to perform research and development work now and in the future will be critical to our business success. We may not be able to attract and retain personnel on acceptable terms given the competition among pharmaceutical and

biotechnology companies, academic and research institutions and government agencies for experienced scientists.

Our values—relentless, energetic, and committed to excellence—guide how we make decisions, and treat each other. All employees are responsible for upholding these values, the Rain Code of Conduct, and Employee Handbook form the foundation of our policies and practices and ethical business culture.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees.

Inclusion

Diversity and inclusion are instrumental in driving innovation and delivering stronger business growth. Among our 44 full-time employees, 48% are women. Over 21 languages are spoken by our employees and they hail from many countries around the world.

Compensation and Benefits

We strive to provide pay, benefits, and services that help meet the varying needs of our employees. Our total rewards package includes market-competitive pay, broad-based stock grants and bonuses, an employee stock purchase plan, healthcare and retirement benefits, paid time off and family leave, and flexible work schedules.

Growth and Development

We are dedicated to helping each employee take charge to lead, and to grow professionally and personally. Through our regular self-evaluation, goal setting and performance review, employees can voice learning and development experiences.

Health and Safety

We are committed to providing a safe and healthy work environment for our employees, and all other individuals working on our behalf.

Throughout our response to COVID-19, our priority has remained protecting the health and safety of our employees and other parties. Most of our employees are working remotely. We will continue to monitor the evolving situation related to the COVID-19 pandemic and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. In response to COVID-19, we continue to take the following safety measures to ensure the health and safety of our employees as well as the communities in which we operate:

- allow employees to work remotely where feasible; and
- restrict company travel to essential business travel that requires prior multi-level approvals

Environmental Matters

We are committed to operating our business in a manner that protects the environment as much as possible, and are further committed to compliance with all applicable environmental laws, regulations, and industry best practices, such as those that affect hazardous waste disposal, emissions, and water purity.

Corporate Information

We were incorporated in the State of Delaware on April 6, 2017. Our corporate offices are located at 8000 Jarvis Avenue, Suite 204, Newark, California 94560 and our telephone number is (510) 953-5559. Our website address is www.rainthera.com. Information contained on or accessible through our website is not a part of this Annual Report on Form 10-K, and the inclusion of our website address in this Annual Report on Form 10-K is an inactive textual reference only.

We file electronically with the SEC our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act). We make available on our website at www.rainthera.com, under “Investors,” free of charge, copies of these reports as soon

as reasonably practicable after filing or furnishing these reports with the SEC. The reports that we file or furnished to SEC can be obtained electronically by means of the SEC's website at www.sec.gov.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We are an emerging growth company, as defined in Section 2(a) of the Securities Act of 1933, as amended (the Securities Act), as modified by the Jumpstart Our Business Startups Act of 2012 (the JOBS Act), and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including relief from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, less extensive disclosure obligations regarding executive compensation in our registration statements, periodic reports and proxy statements, exemptions from the requirements to hold a nonbinding advisory vote on executive compensation, and exemptions from stockholder approval of any golden parachute payments not previously approved. We may also elect to take advantage of other reduced reporting requirements in future filings. As a result, our stockholders may not have access to certain information that they may deem important and the information that we provide to our stockholders may be different than, and not comparable to, information presented by other public reporting companies. We could remain an emerging growth company until the earlier of (1) the last day of the year following the fifth anniversary of the completion of our initial public offering (IPO), (2) the last day of the year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

In addition, the JOBS Act also provides that an emerging growth company may take advantage of the extended transition period provided in the Securities Act for complying with new or revised accounting standards. An emerging growth company may therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, as a result, will not be subject to the same implementation timing for new or revised accounting standards as are required of other public companies that are not emerging growth companies, which may make comparison of our financial information to those of other public companies more difficult.

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

Item 1A. RISK FACTORS.

Investing in our common stock involves significant risks. You should carefully consider the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our audited financial statements and related notes, and other filings we have made and make in the future with the Securities and Exchange Commission. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In such case, the trading price of our common stock would likely decline, and you may lose all or part of your investment. Below is a summary of some of the risks we face. We caution you that the risks, uncertainties and other factors referred to below and elsewhere in this Annual Report on Form 10-K may not contain all of the risks, uncertainties and other factors that may affect our future results and operations. Moreover, new risks will emerge from time to time. It is not possible for our management to predict all risks.

Risk Factor Summary

An investment in our common stock involves significant risks. You should carefully consider the risks and uncertainties described below before making a decision to invest in our common stock. If we are unable to successfully address these risks and uncertainties, our business, financial condition, results of operations, or prospects could be materially adversely affected. In such case, the trading price of our common stock would likely decline, and you may lose all or part of your investment. Below is a summary of some of the risks we face.

- We have a limited operating history, have not initiated, conducted or completed any clinical trials, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and viability.
- We have incurred significant losses since inception, and we expect to incur significant losses for the foreseeable future and may not be able to achieve or sustain profitability in the future. We have not generated any revenue from our product candidates and may never generate revenue or become profitable.
- If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of development programs or future commercialization efforts.
- Our future growth depends on our ability to identify and acquire or in-license products.
- We are substantially dependent on the success of our lead product candidate, milademetan, and our anticipated clinical trials of milademetan may not be successful.
- We may find it difficult to enroll patients in our clinical trials given the relatively small patient populations with the indications for which our product candidates are being developed.
- The results of our preclinical testing and early clinical trials may not be predictive of the success of our later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA or other comparable foreign regulatory authorities.
- We face substantial competition, which may result in others discovering, developing, licensing or commercializing products before or more successfully than we do.
- The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable.
- We currently rely, and plan to rely in the future, on third parties to conduct and support our preclinical studies and clinical trials.
- We currently rely and expect to rely in the future on the use of manufacturing suites in third-party facilities or on third parties to manufacture our product candidates, and we may rely on third parties to produce and process our products, if approved.
- We may, in the future, form or seek collaborations or strategic alliances or enter into licensing arrangements, and we may not realize the benefits of such collaborations, alliances or licensing arrangements.

- Our ability to protect our patents and other proprietary rights is uncertain, exposing us to the possible loss of competitive advantage.
- We may be subject to patent infringement claims or may need to file claims to protect our intellectual property, which could result in substantial costs and liability and prevent us from commercializing our potential products.
- We license patent rights from third-party owners and we rely on such owners to obtain, maintain and enforce the patents underlying such licenses.

Risks Related to Our Limited Operating History, Business, Financial Condition, Results of Operations and Need for Additional Capital

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

We are a clinical-stage company with limited operating history. Since our inception in 2017, we have incurred significant operating losses and have utilized substantially all of our resources to date in-licensing and developing our product candidates, organizing and staffing our Company and providing other general and administrative support for our operations. We have no significant experience as a company in initiating, conducting or completing clinical trials, including global late-stage clinical trials. In particular, Daiichi Sankyo conducted the Phase 1 trial for our lead product candidate, RAIN-32, prior to our in-license of milademetan in September 2020. In part because of this lack of experience, we cannot be certain that our planned clinical trials will begin or be completed on time, if at all. In addition, we have not yet demonstrated an ability to 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. Further, we may encounter unexpected expenses, challenges and complications from known and unknown factors such as the COVID-19 pandemic.

We have incurred significant losses since inception, and we expect to incur significant losses for the foreseeable future and may not be able to achieve or sustain profitability in the future. We have not generated any revenue from our product candidates and may never generate revenue or become profitable.

Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risks that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale, we 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 do not expect to generate product revenue unless or until we successfully complete preclinical and clinical development and obtain regulatory approval of, and then successfully commercialize, at least one product candidate. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. If we are unable to generate sufficient revenue through the sale of our current product candidates or any future product candidates, we may be unable to continue operations without additional funding.

We have incurred significant net losses in each period since we commenced operations in April 2017. Our net losses were $51.4 million and $21.1 million for the years ended December 31, 2021 and 2020, respectively. We expect to continue to incur significant losses for the foreseeable future. Our failure to become profitable would decrease the value of our Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business and/or continue our operations. A decline in the value of our Company could also cause you to lose all or part of your investment.

We will require substantial additional capital to finance our operations in the future. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of development programs or future commercialization efforts.

Developing biopharmaceutical products is a very long, time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials of, and seek marketing approval for milademetan, and advance our other

product candidates and future product candidates. Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing and distribution activities to launch any such product. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies to perform preclinical studies or clinical trials in addition to those that we currently anticipate. Because the design and outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of funding that will be necessary to successfully complete the development and commercialization of any product candidate we develop. Our future capital requirements depend on many factors, including factors that are not within our control. We will also incur additional costs associated with operating as a public company. Accordingly, we will require substantial additional funding to continue our operations. Based on our current operating plan, we believe that our existing cash, cash equivalents and short-term marketable securities, will be sufficient to fund our operations for at least the next twelve months following the date of this Annual Report on Form 10-K. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

We do not have any committed external sources of funds and adequate additional financing may not be available to us on acceptable terms, or at all. We may be required to seek additional funds sooner than planned through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Such financing may dilute our stockholders or the failure to obtain such financing may restrict our operating activities. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect your rights as a stockholder. Debt financing may result in imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through upfront payments or milestone payments pursuant to future collaborations with third parties, we may have to relinquish valuable rights to our product candidates or grant licenses on terms that are not favorable to us. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research-stage programs, clinical trials or future commercialization efforts.

Our future growth depends on our ability to identify and acquire or in-license products.

We have in-licensed the rights to all of our current product candidates from third parties who conducted the initial development of each product candidate. An important part of our business strategy is to continue to develop a pipeline of product candidates by acquiring or in-licensing products, businesses or technologies. Future in-licenses or acquisitions, however, may entail numerous operational and financial risks. In addition, we may compete with competitors in pursuing these in-licensing opportunities and such competitors may have access to greater financial resources than us and may have greater experience in identifying and evaluating new opportunities.

If we breach any of the agreements under which we license rights to our product candidates from others, we could lose the ability to develop and commercialize our product candidates.

In September 2020, we entered into a worldwide, exclusive license agreement with Daiichi Sankyo relating to milademetan for all human prophylactic or therapeutic uses and in July 2020 we entered into a license agreement with Drexel University relating to our RAD52 research program. Because we have in-licensed the rights to all of our product candidates from third parties, if there is any dispute between us and our licensors regarding our rights under these license agreements, our ability to develop and commercialize these product candidates may be adversely affected. Any uncured, material breach under these license agreements could result in our loss of exclusive rights to the related product candidate and may lead to a complete termination of our product development efforts for such product candidate.

Due to the significant resources required for the development of our product candidates, we must prioritize development of certain product candidates and/or the pursuit of treatments for certain indications. 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.

We are developing therapies for patients with genetically defined cancers with unmet needs. We apply a tumor-agnostic development approach to the essential biological pathways and molecular machinery of cancer. Our lead product candidate, milademetan, is a small molecule, oral inhibitor of MDM2, may be oncogenic in numerous cancers. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or indications may not lead to the development of any viable commercial product and may divert resources away from better opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. For example, even if milademetan receives marketing approval, it may not achieve commercial success, including as a result of the gravity of the patients' illnesses in our target market. The primary endpoint for the pivotal Phase 3 trial for milademetan that we commenced in WD/DD LPS is progression-free survival (PFS) evaluated by Response Evaluation Criteria in Solid Tumors. Even if the primary endpoint of such trial is met and milademetan demonstrates meaningful increases in PFS, there is no guarantee that such increases in PFS will lead to the market acceptance or commercial success of milademetan, if approved. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights. We may make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in our industry.

Risks Related to Product Development

We are substantially dependent on the success of our lead product candidate, milademetan, and our anticipated clinical trials of milademetan may not be successful.

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, milademetan, our lead product candidate. We are investing a majority of our efforts and financial resources into the research and development of milademetan. Our other product candidates are in earlier stages of development. We commenced a pivotal Phase 3 trial for milademetan in WD/DD LPS in the July 2021. We commenced an open-label Phase 2 MDM2-amplified tumor-agnostic basket trial for milademetan across solid tumors in patients with pre-specified MDM2 amplification levels and WT p53 in November 2021.

Miladametan will require additional clinical development, evaluation of clinical, preclinical and manufacturing activities, marketing approval in multiple jurisdictions, substantial investment and significant marketing efforts before we generate any revenues from product sales. We are not permitted to market or promote milademetan, or any other product candidates, before we receive marketing approval from the FDA and comparable foreign regulatory authorities, and we may never receive such marketing approvals.

The success of miladametan will depend on a variety of factors. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of milademetan, even if approved. If we are not successful in commercializing milademetan, or are significantly delayed in doing so, our business will be materially harmed.

We may find it difficult to enroll patients in our clinical trials given the relatively small patient populations with the indications for which our product candidates are being developed. If we experience delays or difficulties in the enrollment of patients in clinical trials, including failure to develop or use existing companion diagnostic tests, our successful completion of clinical trials or receipt of marketing approvals could be delayed or prevented.

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. Because our product candidates are focused on indications with relatively small patient populations, our ability to enroll eligible patients in our clinical trials may be limited or may result in slower enrollment than we anticipate. Moreover, because specific genetic mutations will be used to identify the appropriate patients for our programs and our current or future product candidates, successful enrollment of eligible patients to these trials may depend, in part, on our

ability to use existing companion diagnostic tests and genetic sequencing, or to develop novel companion diagnostics in collaboration with partners. Patient enrollment may be affected by various factors, including if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and patients instead enroll in such other clinical trials. In addition, we have clinical trial sites in Russia, Georgia and surrounding countries, which may be impacted by the current situation with Ukraine and Russia and could result in difficulties enrolling or completing our clinical trials on schedule. Our inability to enroll a sufficient number of patients or a delay in enrolling such patients, could result in significant delays in completing clinical trials, increased development costs, or a delay or inability to receive marketing approvals and may require us to abandon one or more clinical trials altogether.

The results of our preclinical testing and early clinical trials may not be predictive of the success of our later clinical trials, and the results of any of our clinical trials may not satisfy the requirements of the FDA or other comparable foreign regulatory authorities.

We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective before we can seek marketing approvals for their commercial sale. Demonstrations of efficacy or an acceptable safety profile in our prior preclinical studies does not mean that future clinical trials will yield the same results. For instance, we do not know whether milademetan will perform in future clinical trials as milademetan has performed in preclinical studies and early clinical trials conducted by Daiichi Sankyo, and, despite decades of research on p53 as a target for precision medicines, prior product development efforts have been unsuccessful. Product candidates, including milademetan, may fail to demonstrate in later-stage clinical trials sufficient safety and efficacy to the satisfaction of the FDA and other comparable foreign regulatory authorities despite having progressed through preclinical studies and earlier stage clinical trials. Regulatory authorities may also limit the scope of later-stage trials until we have demonstrated satisfactory safety or efficacy results in preclinical studies or earlier-stage trials, which could prevent us from conducting the clinical trials we currently anticipate. For example, our open-label Phase 2 basket trial evaluating milademetan across solid tumors in patients with pre-specified MDM2 amplification levels may not meet the primary endpoint of an objective response rate as measured by RECIST criteria. We may not meet the secondary endpoints, including duration of response, disease control rate progression-free survival by investigator assessment, overall survival, and growth modulation index. Even if we are able to initiate our planned clinical trials on schedule, there is no guarantee that we will be able to complete such trials on the timelines we anticipate, that such trials will produce positive results, or that positive results will result in FDA approval or the commercial sale of any product candidate. Any limitation on our ability to conduct clinical trials could delay or prevent regulatory approval or limit the size of the patient population to which we may market our product candidates, if approved.

Preclinical and clinical development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future 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 candidates.

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. Our clinical trials may not be conducted as planned or completed on schedule, if at all, and a failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. In particular, we initiated a pivotal Phase 3 trial for milademetan in WD/DD LPS patients in July 2021. Although data from WD/DD LPS patients in our Phase 1 clinical trial demonstrated median PFS approximately three to four times greater than the current SOC, the efficacy of the SOC in prior preclinical studies does not mean that future clinical trials will yield the same results. Unexpectedly favorable results of the SOC in our Phase 3 trial could lead to unfavorable comparisons to milademetan. 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.

We cannot guarantee that any clinical trials will be initiated or conducted as planned or completed on schedule, if at all. We also cannot be sure that submission of an investigational new drug application (IND) or similar application will result in the FDA or other regulatory authority, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory

authorities to suspend or terminate such clinical trials. Events that may prevent successful or timely initiation or completion of clinical trials include: inability to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials; delays in reaching a consensus with regulatory authorities on study design or implementation of the clinical trials; delays or failure in obtaining regulatory authorization to commence a trial; delays in reaching agreement on acceptable terms with prospective 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; delays in identifying, recruiting and training suitable clinical investigators; delays in obtaining required institutional review board (IRB) approval at each clinical trial site; delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing; failure by our CROs, other third parties or us to adhere to clinical trial protocols; failure to perform in accordance with the FDA's or any other regulatory authority's good clinical practice requirements (GCPs) or applicable regulatory guidelines in other countries; changes to the clinical trial protocols; clinical sites deviating from trial protocol or dropping out of a trial; changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data; transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization (CMO) and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and third parties being unwilling or unable to satisfy their contractual obligations to us. In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs 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 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 resulting in the imposition of a clinical hold, 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. If we are required to conduct additional 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, if the results of these trials 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.

Preliminary, "top-line" or interim data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures.

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which are 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. We also make assumptions, estimations, calculations and conclusions as part of our analyses of these data without the opportunity to fully and carefully evaluate complete data. As a result, the preliminary or top-line 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 or subsequently made subject to audit and verification procedures. Any preliminary or top-line data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and our Company in general. In addition, the information we choose to publicly disclose regarding a particular preclinical study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the preliminary, top-line or interim data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Public health crises such as pandemics or similar outbreaks have affected and could continue to seriously and adversely affect our preclinical studies and anticipated clinical trials, business, financial condition and results of operations.

The ongoing COVID-19 pandemic continues to rapidly evolve, and we will continue to monitor the COVID-19 situation closely. The extent of the impact of the COVID-19 pandemic on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, clinical trial sites, contract research organizations (CROs), third-party manufacturers and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. To the extent possible, we are conducting business as usual, with necessary or advisable modifications, and most of our employees are working remotely. We will continue to monitor the evolving situation related to the COVID-19 pandemic and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay or otherwise seriously harm our business.

As a result of the COVID-19 pandemic, or similar pandemics, and related “shelter in place” orders and other public health guidance measures, we have, and may in the future, experience disruptions that could seriously harm our business. Potential disruptions include but are not limited to: delays or difficulties in enrolling patients in, initiating or expanding our clinical trials, including delays or difficulties with clinical site initiation and recruiting clinical site investigators and clinical site staff; increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19 or other health conditions or being forced to quarantine; interruption of key clinical trial activities, such as clinical trial site data monitoring and efficacy, safety and translational data collection, processing and analyses, due to limitations on travel imposed; recommendations by federal, state or local governments, employers and others or interruptions of clinical trial subject visits, which may impact the collection and integrity of subject data and clinical trial endpoints; 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; delays or disruptions in preclinical experiments and IND-enabling studies due to restrictions of on-site staff and unforeseen circumstances at CROs and vendors; interruption or delays in the operations of the FDA and comparable foreign regulatory authorities including delays in receiving approval from local regulatory authorities to initiate our planned clinical trials; interruption of, or delays in receiving, supplies of our product candidates from our CMOs due to staffing shortages, raw materials shortages, production slowdowns or stoppages and disruptions in delivery systems; and limitations on employee or other resources that would otherwise be focused on the conduct of our clinical trials and preclinical work, including because of sickness of employees or their families, the desire of employees to avoid travel or contact with large groups of people, an increased reliance on working from home, school closures or mass transit disruptions.

The COVID-19 pandemic may also affect the ability of the FDA and other regulatory authorities to perform routine functions. If global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the COVID-19 pandemic may affect our clinical trials, business, financial condition and results of operations will depend on future developments, which are highly uncertain and cannot be predicted at this time, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs 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. Future developments in these and other areas present material uncertainty and risk with respect to our clinical trials, business, financial condition and results of operations.

A variety of risks associated with marketing our product candidates internationally may materially adversely affect our business.

We plan to eventually seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries and

meeting differing regulatory requirements in foreign countries. Risks associated with international operations may materially adversely affect our business, financial condition and results of operations.

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

We face substantial competition from major pharmaceutical companies and biotechnology companies worldwide. Many of our competitors have significantly greater financial, technical and human resources. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

In particular, we are aware of molecules that also are being explored for p53 upregulation and activation in various stages of clinical development by Actavalon, Aprea Therapeutics, CDG Therapeutics, Cotinga Pharmaceuticals, Innovation Pharmaceuticals, PMV Pharmaceuticals and Senhwa Biosciences, among others. We are also aware of selective small molecule inhibitors that are designed to target WT p53 containing tumors through the p53-MDM2 interaction, which are in various stages of clinical development by Aileron Therapeutics, Ascentage Pharma, Boehringer Ingelheim, Kartos Therapeutics, Novartis, and Roche, including testing MDM2 inhibitors in combination with a variety of other anti-cancer agents.

We face competition with respect to our current product candidates and will face competition with respect to any future product candidates from segments of the pharmaceutical, biotechnology and other related industries that pursue targeted therapies for patients with genetically defined cancers. If milademetan or our future product candidates do not offer sustainable advantages over competing products, we may otherwise not be able to successfully compete against current and future competitors.

Our competitors may obtain regulatory approval of their products more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products. In addition, we will likely need to develop our product candidates in collaboration with companion diagnostic companies, and we will face competition from other companies in establishing these future collaborations.

Furthermore, we also face competition more broadly across the market for existing cost-effective and reimbursable cancer treatments. Our product candidates, if any are approved, may compete with these existing drug and other therapies but may not be competitive with them in price. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic, including branded generic, products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our product candidates that we successfully introduce to the market will pose challenges.

Our product candidates may cause significant adverse events, toxicities or other undesirable side effects that may result in a safety profile that could prevent regulatory approval, marketing approval or market acceptance, or limit their commercial potential.

If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or INDs, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may adversely affect our business, financial condition and prospects significantly.

In general, the anticipated clinical trials of milademetan will include cancer patients who are very sick and whose health is deteriorating, and we expect that additional clinical trials of milademetan and our other product candidates will include similar patients with deteriorating health. A number of patients in milademetan trials have experienced adverse events, including blood and lymphatic disorders and gastrointestinal disorders.

The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such

patients' illnesses. For example, it is expected that many of the patients enrolled in our milademetan clinical trials will die or experience major clinical events either during the course of our clinical trials or after participating in such trials. Such outcomes may make it more difficult for us to identify a clinical benefit in our targeted patient populations, and could ultimately prevent us from obtaining regulatory approval for milademetan in such critically ill populations, including WD/DD LPS. Additionally, such adverse events or deaths in clinical trials involving our product candidates, even if not ultimately attributable to our product or product candidates, could result in increased government regulation, unfavorable public perception and publicity, potential regulatory delays in the testing or licensing of our product candidates, stricter labeling requirements for those product candidates that are licensed and a decrease in demand for any such product candidates.

Additionally, if one or more of our product candidates receives marketing approval and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result. For example, regulatory authorities may suspend, limit or withdraw approvals of such product or seek an injunction against its manufacture or distribution, require additional warnings on the label, including "boxed" warnings, or issue safety alerts, require press releases or other communications containing warnings or other safety information about the product, require us to change the way the product is administered or conduct additional clinical trials or post-approval studies, require us to create a risk evaluation and mitigation strategy (REMS) which could include a medication guide outlining the risks of such side effects for distribution to patients, impose fines, injunctions or criminal penalties. We could also be sued and held liable for harm caused to patients, and our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could seriously harm our business.

Risks Related to Regulatory Process and Other Legal Compliance Matters

The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. If we are not able to obtain, or if there are delays 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.

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, 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. We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including our lead product candidate milademetan, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for each targeted indication. Securing regulatory approval also requires the submission of information about the drug 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. The FDA and comparable foreign regulatory authorities 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 data. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including: the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; 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; the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; 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 acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials; the FDA or the applicable foreign regulatory authority may disagree regarding the formulation, labeling and/or the specifications of our product

candidates; the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; 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. Thus, the approval requirements for our product candidates are likely to vary by jurisdiction such that success in one jurisdiction is not necessarily predicative of success elsewhere.

Of the large number of drugs 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.

If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, including failing to approve the most commercially promising indications, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. If we are not able to obtain, or if there are delays 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.

If we are required by the FDA to obtain approval of a companion diagnostic test in connection with approval of any of our product candidates and we fail to obtain or face delays in obtaining FDA approval of a diagnostic device, we could be delayed or may not be able to commercialize such product candidate and our ability to generate revenue will be materially impaired.

If safe and effective use of any of our product candidates depends on an *in vitro* diagnostic that is not otherwise commercially available, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves our product candidates, if at all. Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical devices by the FDA and comparable regulatory authorities, and, to date, the FDA has required premarket approval of all companion diagnostics for cancer therapies, such as those we are developing. The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express the specific genetic alteration that the companion diagnostic was developed to detect.

According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. If a satisfactory companion diagnostic is not commercially available, we may be required to develop or obtain one that would be subject to regulatory approval requirements. The process of obtaining or creating such diagnostics is time-consuming and costly. If the FDA or a comparable foreign regulatory authority requires approval of a companion diagnostic for any of our product candidates, whether before or after it obtains marketing approval, we, and/or future collaborators, may encounter difficulties in developing and obtaining approval for such product candidate. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval of a companion diagnostic could delay or prevent approval or continued marketing of such product candidate. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process for the companion diagnostic or in transferring that process to commercial partners or negotiating insurance reimbursement plans, all of which may prevent us from completing our clinical trials or commercializing our product candidates, if approved, on a timely or profitable basis, if at all.

We may seek orphan drug designation for our product candidates, but we may be unable to obtain such designation or to obtain or maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our product revenue, if any, to be reduced.

We have obtained orphan drug designation in the United States for milademetan for the treatment of LPS and we may seek additional orphan drug designations for milademetan or our other product candidates; however,

we may never receive such designations. See the section titled “Business—Government Regulation—Review and Approval of Drugs in the United States—Orphan Drug Designation” in this Annual Report on Form 10-K.

Exclusive marketing rights in the United States may be unavailable if we or our collaborators 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. Even if we obtain orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is safer, is more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Even if we receive regulatory approval of our product candidates, we will be subject to extensive 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 regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or comparable foreign regulatory authorities approve our product candidates, 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 will be subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with current good manufacturing practices (cGMPs) and GCPs for any clinical trials that we conduct following approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMPs.

If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials, restrictions on the manufacturing process, warning or untitled letters, civil and criminal penalties, injunctions, product seizures, detentions or import bans, voluntary or mandatory publicity requirements and imposition of restrictions on operations, including costly new manufacturing requirements. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

Even if we are able to commercialize any product candidates, due to unfavorable pricing regulations and/or third-party coverage and reimbursement policies, we may not be able to offer such products at competitive prices which would seriously harm our business.

Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which 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. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. See the sections titled “Business—Government Regulation—Review and Approval of Drug Products

in the European Union," "Business—Government Regulation—Review and Approval of Drug Products in the United States—New Legislation and Regulations," "Business—Government Regulation—U.S. Pharmaceutical Coverage, Pricing and Reimbursement" and "Business—Government Regulation—U.S. Healthcare Reform" in this Annual Report on Form 10-K.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and any infraction could subject us to liability.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. See the section titled "Business—Government Regulation—Review and Approval of Drugs in the United States—Post-approval Requirements" in this Annual Report on Form 10-K. If we do not appropriately manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

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

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors acting for or on our behalf may engage in misconduct or other improper activities. We have adopted a code of conduct, but it is not always possible to identify and deter misconduct by these parties and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. See the section titled "Business—Government Regulation—Healthcare Laws and Regulations" in this Annual Report on Form 10-K for a more detailed description of the laws that may affect our ability to operate.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. If our operations, including certain arrangements we have with physicians who are compensated in the form of stock or stock options for services provided to us, are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly and time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

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 may involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may

impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters, Managing Our Growth and Other Risks Related to Our Business

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 managerial, scientific and medical personnel, including our Chief Executive Officer and our Chief Scientific Officer. If we do not succeed in attracting and retaining qualified personnel, it could materially adversely affect our business, financial condition and results of operations. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts.

In order to successfully implement our plans and strategies, we will need to grow the size of our organization and we may experience difficulties in managing this growth.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical operations, regulatory affairs and, potentially, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. We are dependent on our limited financial resources and the experience of our management team in managing a company with such anticipated growth, and we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel.

Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems and those of our third-party CROs, other contractors (including sites performing our clinical trials) and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties, which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. To the extent that any disruption or security breach were to result in a loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our product candidates could be delayed. Further, our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in, or failure or security breach of, our systems or third-party systems where information important to our business operations or commercial development is stored.

Risks Related to Reliance on Third Parties

We currently rely, and plan to rely in the future, on third parties to conduct and support 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 have utilized and plan to continue to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs and strategic partners, to conduct and support our

preclinical studies and clinical trials under agreements with us. We will 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 will have less direct control over the conduct, timing and completion of these preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we were relying 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, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCP regulations, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our products candidates in clinical development. If we or any of these third parties fail to comply with applicable GCP 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 by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. 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 will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our 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.

We currently rely and expect to rely in the future on the use of manufacturing suites in third-party facilities or on third parties to manufacture our product candidates, and we may rely on third parties to produce and process our products, if approved. Our business could be adversely affected 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 CMOs to manufacture our product candidates. 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, if approved. We received a batch of our product candidate that we believe is representative of our anticipated early commercial batch requirements. However, as a clinical-stage company with no prior history of product sales or commercialization of products, representative batches of our product candidate received to date may not represent what will be required to meet our future commercial requirements or be manufactured at scale. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or other regulatory authorities for the manufacture of our product candidates. Beyond periodic audits, we have no control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs and materially adversely affect our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Similarly, our failure, or the failure of our CMOs, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

Moreover, if any CMOs on which we will rely fail to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a

cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected. Our business could be materially adversely affected by business disruptions to our third-party providers that could materially adversely affect our potential future revenue and financial condition and increase our costs and expenses. 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.

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

We may, in the future, form or seek strategic alliances, create joint ventures or collaborations, or enter into 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 increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

Risks Related to Our Intellectual Property

Our ability to protect our patents and other proprietary rights is uncertain, exposing us to the possible loss of competitive advantage.

We rely upon a combination of patents, trademarks, trade secret protection and confidentiality agreements to protect the intellectual property related to our products and technologies and to prevent third parties from copying and surpassing our achievements, thus eroding our competitive position in our market. Our success depends in large part on our ability to obtain and maintain patent protection for our platform technologies, product candidates and their uses, as well as our ability to operate without infringing on or violating the proprietary rights of others. We own and have licensed rights to pending patent applications and expect to continue to file patent applications in the United States and abroad related to our novel discoveries and technologies that are important to our business. However, we may not be able to protect our intellectual property rights throughout the world and the legal systems in certain countries may not favor enforcement or protection of patents, trade secrets and other intellectual property. Filing, prosecuting and defending patents on product candidates worldwide would be prohibitively expensive and our intellectual property rights in some foreign jurisdictions can be less extensive than those in the United States. As such, we do not have patents in all countries or all major markets and may not be able to obtain patents in all jurisdictions even if we apply for them. Our competitors may operate in countries where we do not have patent protection and can freely use our technologies and discoveries in such countries to the extent such technologies and discoveries are publicly known or disclosed in countries where we do have patent protection or pending patent applications. Our pending and future patent applications may not result in patents being issued. Any issued patents may not afford sufficient protection of our product candidates or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive technologies, products or product candidates. Further, even if these patents are granted, they may be difficult to enforce. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated if we fail to comply with these requirements. Further, any issued patents that we may license or own covering our product candidates could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad, including the United States Patent and Trademark Office (USPTO). Also, patent terms, including any extensions or adjustments that may or may not be available to us, may be inadequate to protect our competitive position on our product candidates for an adequate amount of time, and we may be subject to claims challenging the inventorship, validity, enforceability of our patents and/or other intellectual property. Finally, changes in U.S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our product candidates. Further, if we encounter delays in our clinical trials or delays in obtaining regulatory approval, the period of time during which we could market our product candidates under patent protection would be reduced. Thus, the patents that we own, and license may not afford us any meaningful competitive advantage.

Moreover, we or our licensors may be subject to a third-party preissuance submission of prior art to the USPTO or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant

review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. In addition to seeking patents for some of our technology and product candidates, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors and those affiliated with or controlled by state actors. In addition, while we undertake efforts to protect our trade secrets and other confidential information from disclosure, others may independently discover trade secrets and proprietary information, and in such cases, we may not be able to assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

As is common in the biotechnology and pharmaceutical industries, we employ individuals and engage the services of consultants who previously worked for other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that our consultants have used or disclosed trade secrets or other proprietary information of their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. 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.

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

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

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. 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. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for any product candidates we may develop, our business may be materially harmed.

In the United States, the patent term of a patent that covers an FDA-approved drug may be eligible for limited patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and certain other non-United States jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We may not be granted patent term extension either in the United States or in any foreign country 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 term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering any of our product candidates that we may identify even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for our licensed patents, we may not have the right to control prosecution, including filing with the USPTO, a petition for patent term extension under the Hatch-Waxman Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed, or obtained, from the USPTO.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book). We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application filed with the FDA to obtain permission to sell a generic version of such product candidate.

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

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act (the Leahy-Smith Act) could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation

could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

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

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect. For example, we may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

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 for technology covered by our issued patents or our pending applications, or that we were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our patent applications or patents, which could require us to obtain rights to issued patents covering such technologies.

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be subject to patent infringement claims or may need to file claims to protect our intellectual property, which could result in substantial costs and liability and prevent us from commercializing our potential products.

Because the intellectual property landscape in the biotechnology industry is rapidly evolving and interdisciplinary, it is difficult to conclusively assess our freedom to operate without infringing on or violating third

party rights. However, if certain of our product candidates are ultimately granted regulatory approval, we are currently aware of certain patent rights held by third parties that, if found to be valid and enforceable, could be alleged to render one or more of our product candidates infringing. If a third party successfully brings a claim against us, we may be required to pay substantial damages, be forced to abandon any affected product and/or seek a license from the patent holder. In addition, any intellectual property claims (e.g., patent infringement or trade secret theft) brought against us, whether or not successful, may cause us to incur significant legal expenses and divert the attention of our management and key personnel from other business concerns. We cannot be certain that patents owned or licensed by us will not be challenged by others in the course of litigation. Some of our competitors may be able to sustain the costs of complex intellectual property 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 funds and on the market price of our common stock.

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time-consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court or administrative body may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court or administrative body may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable.

Further, we may be required to protect our patents through procedures created to attack the validity of a patent at the USPTO. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

In addition, if our product candidates are found to infringe the intellectual property rights of third parties, these third parties may assert infringement claims against our future licensees and other parties with whom we have business relationships and we may be required to indemnify those parties for any damages they suffer as a result of these claims, which may require us to initiate or defend protracted and costly litigation on behalf of licensees and other parties regardless of the merits of such claims. If any of these claims succeed, we may be forced to pay damages on behalf of those parties or may be required to obtain licenses for the products they use.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings.

We license patent rights from third-party owners, and we rely on such owners to obtain, maintain and enforce the patents underlying such licenses.

We are a party to certain licenses, including with our licensors Daiichi Sankyo and Drexel University, that provide us rights to intellectual property that are necessary or useful for our product candidates, milademetan and RAD52, and their respective components, formulations, methods of manufacturing and methods of treatment. These license agreements require us to satisfy certain obligations and, if these agreements are terminated (e.g., as a result of our failure to satisfy such obligations), our technology and our business could be adversely affected. We also expect to enter into additional licenses to third-party intellectual property in the future; however, we may not be able to obtain such licenses on economically feasible terms or other reasonable terms and conditions, or at all.

Our licensors may not successfully prosecute the patent applications that we are licensed. Even if patents are issued in respect of these patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. Without protection for the intellectual property we license, other companies

might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects.

Additionally, we may sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may 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.

We have limited, if any, control over the amount or timing of resources that our licensors devote on our behalf or the priority they place on maintaining these patent rights and prosecuting these patent applications to our advantage. For example, should Daiichi Sankyo decide it no longer wants to maintain any of the patents licensed to us, Daiichi Sankyo is required to afford us the opportunity to do so at our expense. However, we cannot be sure that Daiichi Sankyo will perform as required. If Daiichi Sankyo does not perform, and if we do not assume the maintenance of the licensed patents in sufficient time to make required payments or filings with the appropriate governmental agencies, we risk losing the benefit of all or some of those patent rights. In the event our licensors fail to adequately pursue and maintain patent protection for patents and applications they control, and to timely cede control of such prosecution to us, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Our technology licensed from various third parties may be subject to retained rights.

Our licensors often retain certain rights under their agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse. Further, the U.S. government may retain certain rights under the Bayh-Dole Act for research funded by the Federal Government.

We may not be able to effectively secure first-tier technologies when competing against other companies or investors.

Our future success may require that we acquire patent rights and know-how to new or complimentary technologies. However, we compete with a substantial number of other companies that may also compete for technologies we desire. In addition, many venture capital firms and other institutional investors, as well as other biotechnology companies, invest in companies seeking to commercialize various types of emerging technologies. Many of these companies have greater financial, scientific and commercial resources than us. Therefore, we may not be able to secure the technologies we desire. Furthermore, should any commercial undertaking by us prove to be successful, there can be no assurance competitors with greater financial resources will not offer competitive products and/or technologies.

Risks Related to 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 the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K. The realization of any of these factors could have a dramatic and adverse impact on the market price of our common stock.

In addition, the stock market in general, and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In particular, the trading prices for biotechnology companies have been highly volatile as a result of the COVID-19 pandemic. In addition, 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 materially adversely affect our business, financial condition and results of operation.

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.

As of December 31, 2021, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned a significant portion of our outstanding voting common stock. These stockholders, acting together, may be able to impact matters requiring stockholder approval. For example, they may be able to impact 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. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

General Risk Factors

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our 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. In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL) prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Any provision of our amended and restated certificate of incorporation, amended and restated bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another State court in Delaware or the federal district court for the District of Delaware) is the exclusive forum for certain actions, in all cases subject to the court's having jurisdiction over indispensable parties named as defendants. In addition, our amended and restated certificate of incorporation provides that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act but that the forum selection provision will not apply to claims brought to enforce a duty or liability created by the Exchange Act. These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes, which may discourage lawsuits. There is uncertainty as to whether a court would enforce such provisions. If a court were to find these types of provisions to be inapplicable or unenforceable, and if a court were to find the exclusive forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could materially adversely affect our business.

The dual class structure of our common stock may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.

The dual class structure of our common stock may limit your ability to influence corporate matters. Holders of our common stock are entitled to one vote per share, while holders of our non-voting common stock are not entitled to any votes. Nonetheless, each share of our non-voting common stock may be converted at any time into one share of our common stock at the option of its holder by providing written notice to us, subject to the limitations provided for in our amended and restated certificate of incorporation. Consequently, if holders of our non-voting common stock exercise their option to make this conversion, this will have the effect of increasing the

relative voting power of those prior holders of our non-voting common stock, and correspondingly decreasing the voting power of the holders of our common stock, which may limit your ability to influence corporate matters. Additionally, stockholders who hold, in the aggregate, more than 10% of our common stock and non-voting common stock, but 10% or less of our common stock, and are not otherwise an insider, may not be required to report changes in their ownership due to transactions in our non-voting common stock pursuant to Section 16(a) of the Exchange Act, and may not be subject to the short-swing profit provisions of Section 16(b) of the Exchange Act.

Item 1B. UNRESOLVED STAFF COMMENTS.

None

Item 2. PROPERTIES.

Our corporate headquarters are located in Newark, California where we occupy approximately 3,900 square feet of office space under a lease that expires on September 30, 2024. We use this facility for administrative purposes. We believe that our facility is sufficient to meet our current needs. We also believe we will be able to obtain additional space, as needed, on commercially reasonable terms.

Item 3. LEGAL PROCEEDINGS.

We are currently not a party to any material legal proceedings. From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity, reputational harm and other factors, and there can be no assurances that favorable outcomes will be obtained.

Item 4. MINE SAFETY DISCLOSURES.

Not applicable.

PART II

Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Market Information

Our common stock is traded on The Nasdaq Global Select Market under the symbol "RAIN."

Holders

As of February 17, 2022, we had 32 holders of record of our common stock.

Dividend Policy

We have never declared or paid dividends on our capital stock. We currently intend to retain any future earnings and do not anticipate paying dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our Board of Directors and will be dependent on a number of factors, including our financial condition, results of operations, capital requirements, contractual restrictions, general business conditions, and any other factors that our board may deem relevant.

Use of Proceeds from our Initial Public Offering

On April 27, 2021, we completed our IPO, in which we issued and sold 7,352,941 shares of our common stock, $0.001 par value per share, at the public offering price of $17.00 per share. On May 7, 2021, the underwriters exercised their option to purchase 492,070 additional shares our common stock at the public offering price (the Overallotment) and the Overallotment closed on May 11, 2021.

The offer and sale of all of the shares of our common stock in the IPO were registered under the Securities Act pursuant to our Registration Statement on Form S-1, as amended (File No. 333-254998), which was declared effective on April 22, 2021. Goldman Sachs & Co. LLC, Citigroup, Global Markets, Inc., Piper, Sandler & Co., and Guggenheim Securities LLC acted as joint book-running managers for the IPO.

We received net proceeds from our IPO of approximately $121.5 million, after deducting underwriting discounts and commissions, and other offering fees, inclusive of the Overallotment. None of the underwriting discounts and commissions or other offering expenses were incurred or paid, directly or indirectly, to any of our directors or officers or their associates or to persons owning 10% or more of our common stock or to any of our affiliates.

The net proceeds from the IPO (including the Overallotment) have been used and will be used, to fund a pivotal Phase 3 trial in LPS, a Phase 2 tumor-agnostic basket trial in certain solid tumors and a Phase 2 trial in Merkel cell carcinoma, in each case, for our lead product candidate, milademetan, to fund the purchase of raw materials and drug substance and drug product manufacturing for our milademetan program and to fund various clinical pharmacology, biomarker and translational studies for our milademetan program, and for working capital, including continuing to advance our pipeline through preclinical studies and clinical trials, and general corporate purposes. This use of proceeds represents a change from our intended use of proceeds from our IPO as described in the prospectus filed with the SEC pursuant to Rule 424(b)(4) on April 23, 2021, as the Phase 2 clinical trial of milademetan in Merkel cell carcinoma will replace the previously planned Phase 2 clinical trial of milademetan in intimal sarcoma.

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 financial statements and the related notes and other financial information included elsewhere in this *Annual Report on Form 10-K*. This discussion and analysis contain forward-looking statements based upon our current plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and beliefs. Our actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under the section titled "Risk Factors" and included elsewhere in this *Annual Report on Form 10-K*. You should carefully read the sections titled "Note Regarding Forward-Looking Statements" and "Risk Factors" to gain an understanding of the important factors that could cause actual results to differ materially from the results described below.

Overview

We are a late-stage precision oncology company developing therapies that target oncogenic drivers for which we are able to genetically select patients we believe will be most likely to benefit. This approach includes using a tumor-agnostic strategy to select patients based on their tumors' underlying genetics rather than histology. We have in-licensed product candidates, each with a differentiated profile relative to available therapies, and we intend to continue strengthening our pipeline through focused business development and internal research efforts.

Our lead product candidate, milademetan (also known as RAIN-32) is a small molecule, oral inhibitor of mouse double minute 2 (MDM2), which may be oncogenic in numerous cancers. We in-licensed milademetan from Daiichi Sankyo in September 2020 based on the results of a Phase 1 clinical trial, which demonstrated meaningful antitumor activity in an MDM2-amplified subtype of liposarcoma (LPS) and other solid tumors. Data from well-differentiated/de-differentiated (WD/DD) liposarcoma LPS patients in the Phase 1 clinical trial of milademetan demonstrated median progression-free survival (mPFS) of approximately seven to eight months. Importantly, this result was accomplished with a rationally designed dosing schedule designed to mitigate safety concerns and widen the therapeutic window of MDM2 inhibition unlocking the potential for milademetan in a broad range of MDM2-dependent cancers. Based on these data, we commenced a pivotal Phase 3 trial in LPS (MANTRA) in July 2021. We also commenced a Phase 2 tumor-agnostic basket trial in certain solid tumors (MANTRA-2) in November 2021. We anticipate commencing a Phase 2 clinical trial in Merkel cell carcinoma (MCC) (MANTRA-3) in the second half of 2022 and a Phase 1 clinical trial to evaluate the safety, tolerability and efficacy of milademetan in combination with atezolizumab in patients with loss of cyclin-dependent kinase inhibitor 2A (CDKN2A) and wildtype p53 advanced solid tumors (MANTRA-4) in the second half of 2022. In addition to milademetan, we are also developing a preclinical program that is focused on inducing synthetic lethality in cancer cells by inhibiting RAD52.

Since our inception in 2017, we have incurred significant operating losses and have utilized substantially all of our resources to date in-licensing and developing our product candidates, organizing and staffing our Company and providing other general and administrative support for our operations. As of December 31, 2021, we had an accumulated deficit of $90.0 million and we incurred net losses of approximately $51.4 million and $21.1 million for the years ended December 31, 2021 and 2020, respectively. Our operations to date have been funded primarily through the issuance of convertible promissory notes, the issuance of convertible preferred stock, as well as issuance and sale of common stock through our initial public offering (IPO). From our inception through December 31, 2021, we have raised aggregate gross proceeds of $9.9 million from the issuance of convertible promissory notes and $81.9 million from the issuance of convertible preferred stock. On April 27, 2021, we completed our IPO in which we issued and sold 7,352,941 shares of common stock at a public offering price of $17.00 per share. On May 11, 2021, we issued an additional 492,070 shares of common stock in connection with the exercise of the underwriters' option to purchase additional shares at the public offering price. Our net proceeds from the sale of shares in the IPO, including the sale of shares pursuant to the exercise of the underwriters' option to purchase additional shares, was $121.5 million, net of underwriting discounts and commissions, and other offering fees. As of December 31, 2021, we had cash, cash equivalents and short-term investments of $140.2 million. Although we believe, based on our current business plans, that our existing cash, cash equivalents and short-term investments will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in the future in order to continue the research and development of our drug candidates. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product

candidates. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years as we continue our development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products, seek to expand our product pipeline, invest in our organization, as well as incur expenses associated with operating as a public company.

We do not expect to generate any revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more product candidates, which will not be for many years, if ever. Accordingly, until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to finance our cash needs through public or private equity offerings, debt financings or other capital sources which may include strategic collaborations, licensing arrangements or other arrangements with third parties. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms or at all. If we raise funds through strategic collaborations or other similar arrangements with third parties, we may have to relinquish valuable rights to our platform technology, future revenue streams, research programs or product candidates or we may have to grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts. Our ability to raise additional funds may be adversely impacted by potential worsening of global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic or otherwise. Because of the numerous risks and uncertainties associated with our product development, we cannot predict the timing or amount of increased expenses and cannot assure you that we will ever be profitable or generate positive cash flow from operating activities. Based upon our current operating plan, we estimate that our cash, cash equivalents and short-term investments as of December 31, 2021 will be sufficient to fund our pivotal Phase 3 data timelines in LPS, Phase 2 tumor-agnostic basket trial in certain solid tumors, a Phase 2 trial in MCC, and a Phase 1 clinical trial to evaluate the safety, tolerability and efficacy of milademetan in combination with atezolizumab in patients with loss of CDKN2A and wildtype p53 advanced solid tumors, including continuing to advance our pipeline through additional preclinical studies and clinical trials.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely and expect to continue to rely for the foreseeable future, on third parties for the manufacture of our drug candidates for preclinical and clinical testing, as well as for commercial manufacture of any drugs that we may commercialize. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities. For the milademetan program, we have transferred Daiichi Sankyo Company, Limited (Daiichi Sankyo) processes to suitable contract manufacturing organizations to supply active pharmaceutical ingredients and clinical drug product for our clinical trials and in preparation for submission of marketing applications and potential future commercial supplies.

COVID-19

The ongoing COVID-19 pandemic continues to rapidly evolve, and we will continue to monitor the COVID-19 situation closely. The extent of the impact of the COVID-19 pandemic on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, clinical trial sites, contract research organizations (CROs), third-party manufacturers and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. To the extent possible, we are conducting business as usual, with necessary or advisable modifications, and most of our employees are working remotely. The increased reliance on our personnel working from home has not negatively impacted productivity, or disrupted, delayed or otherwise seriously harmed our business. The collection and integrity of subject data and clinical trial endpoints have not been negatively impacted by the COVID-19 pandemic. We will continue to monitor the evolving situation related to the COVID-19 pandemic and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, including the ability of the FDA and other regulatory authorities to perform routine functions or that we determine are in the best interests of our employees and other third parties with whom we do business. If global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. At this point, the extent to which the COVID-19 pandemic may affect

our business, operations and clinical development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain and is subject to change.

Recent Developments

In January 2022, we announced a clinical supply agreement with Roche for the supply of the anti-Programmed Death Ligand-1 (PD-L1) monoclonal antibody, atezolizumab. Clinical trials are planned to evaluate milademetan in combination with atezolizumab for the treatment of patients in genetically selected populations (MANTRA-4). Under this agreement, Rain is the sponsor of the anticipated clinical trials, and Roche will supply atezolizumab.

In November 2021, the first patient was dosed in the multicenter, single arm, open-label, Phase 2 basket trial evaluating Milademetan for the treatment of MDM2-amplified advanced solid (MANTRA-2).

In November 2021, we announced our plan to commence a Phase 2 clinical trial, named MANTRA-3, evaluating the efficacy of milademetan as a monotherapy for the treatment of patients with MCC refractory to immune checkpoint inhibition (ICI) in the second half of 2022.

We hosted an R&D day webinar on November 9, 2021, which featuring several key opinion leaders in oncology, along with members of Rain's management team, who discussed our R&D program, as well as select clinical and preclinical data.

We, in collaboration with certain research partners, presented non-clinical data on milademetan at the IASLC 2021 World Conference of Lung Cancer hosted by the International Association for the Study of Lung Cancer (Sept. 8-14, 2021) and at the AACR-NCI-EORTC (Triple Cancer Conference) 2021 on Molecular Targets and Cancer Therapeutics virtual conference (Oct. 7-10, 2021), highlighting non-clinical data in MDM2-amplified tumors, MCC, GATA3-mutant ER+ breast cancer, and mesothelioma models. On the strength of recent non-clinical data from Dana-Farber Cancer Institute presented at the Triple Cancer Conference, we are now prioritizing our financial resources towards a Phase 2 clinical trial of milademetan as monotherapy in MCC patients failing first-line checkpoint inhibitors, with a clinical trial commencement expected in the second half of 2022. The Phase 2 clinical trial of milademetan in MCC (MANTRA-3) will replace the previously planned Phase 2 clinical trial of milademetan in intimal sarcoma. We do not expect the new planned MCC trial to have significant net impact on our financial condition, cash flow or results of operations.

In July 2021, we announced that the first patient has been randomized in the multicenter, open-label, Phase 3 registrational trial (MANTRA) evaluating milademetan for the treatment of DD LPS.

In June 2021, we announced a patient referral partnership with Caris Life Sciences (Caris). Under the terms of the partnership, Caris will provide patient referral services using their molecular intelligence trials platform for our Phase 2 MDM2-amplified tumor-agnostic basket trial for milademetan (MANTRA-2).

Also in June 2021, we announced a master program and a genomic analysis platform agreement for comprehensive genomic profiling tests utilizing the genomic analysis platform of Tempus, an artificial intelligence and precision medicine company. Under the terms of the agreement, Tempus will provide both centralized tumor testing and patient matching services using their Connect & TIME Trial® Network for the Phase 2 MDM2-amplified tumor-agnostic basket trial for milademetan (MANTRA-2).

Our Development Pipeline

Our development pipeline is unified by a strategy to target oncogenic drivers through differentiated therapies for which we are able to genetically select the patients we believe will be most likely to benefit from treatment. We currently retain global development and commercialization rights to all of our product candidates. See Part 1, Item 1. "Business – Our Development Pipeline".

Collaboration and License Agreements

We are party to a number of license agreements for the in-license of our product candidates and development programs. See Note 9 to the Financial Statements.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales, licenses or collaborations and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval, we may generate revenue from future product sales. If we enter into license or collaboration agreements for any of our product candidates or intellectual property, we may generate revenue in the future from payments as a result of such license or collaboration agreements. We cannot predict if, when, or to what extent we will generate revenue from the commercialization and sale of our product candidates or from license or collaboration agreements. We may never succeed in obtaining regulatory approval for any of our product candidates.

Operating Expenses

Our operating expenses since inception have consisted solely of research and development costs, including acquisition of in-process research and development, and general and administrative costs.

Research and Development Expenses

To date, our research and development expenses have related to the discovery and clinical development of our product candidates, including acquisition of in-process research and development. Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

Research and development expenses include:

- salaries, payroll taxes, employee benefits and stock-based compensation charges for those individuals involved in research and development efforts;
- expenses incurred in connection with research, laboratory consumables and preclinical studies;
- external research and development expenses incurred under agreements with CROs and consultants to conduct and support our planned clinical trials of our product candidates;
- the cost of consultants engaged in research and development-related services and the cost to manufacture drug product for use in our preclinical studies and clinical trials;
- costs related to regulatory compliance;
- the cost of annual license fees and the cost of acquiring in-process research and development, including upfront license payments; and
- any development milestone payments that we may make under our license agreements.

We track external development costs by product candidate or development program, but we do not allocate personnel costs or other internal costs to specific development programs or product candidates as our personnel works across multiple development programs and product candidates. These costs are included in unallocated research and development expenses in the table below.

The following table summarizes our research and development expenses by product candidate or development program:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Milademetan	$ 23,261	$ 6,639
Other research and clinical candidates	1,761	7,286
Unallocated internal research and development costs	15,751	1,442
Total research and development expenses	$ 40,773	$ 15,367

We plan to substantially increase our research and development expenses for the foreseeable future as we continue to expand the development of our product candidates. The clinical development timeline, probability

of success of clinical trials and development costs can differ materially from expectations. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

Our future clinical development costs may vary significantly. See the section titled “Risk Factors—Risks Related to Product Development— Preclinical and clinical development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future 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 candidates”.

General and Administrative Expenses

General and administrative expenses consist of salaries and employee-related costs, including stock-based compensation, for personnel in executive, finance and other administrative functions, legal fees relating to intellectual property and corporate matters, professional fees for accounting and consulting services and facility-related costs. We anticipate that our general and administrative expenses will continue to increase in the future to support our continued research and development activities, pre-commercial preparation activities for our product candidates and, if any product candidate receives marketing approval, commercialization activities. We also anticipate increased expenses related to audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums and investor relations costs associated with operating as a public company.

Interest Income

Interest income consists of interest on our available-for-sale (AFS) securities.

Interest Expense

We did not have interest expense for the year ended December 31, 2021. Interest expense for year ended December 31, 2020 consisted of interest on the outstanding convertible promissory notes.

Change in Fair Value of Convertible Promissory Notes

We issued convertible promissory notes in October 2019 (the 2019 Notes) and June 2020 (the 2020 Notes) for which we had elected the fair value option. We adjusted the carrying value of our convertible promissory notes to their estimated fair value at each reporting date, with any change in fair value of the convertible promissory notes recorded as an increase or decrease to change in fair value of convertible promissory notes in our statements of operations and comprehensive loss.

The fair value of the 2019 Notes and the 2020 Notes were estimated using a scenario-based analysis that estimated the fair value of the convertible promissory notes based on the probability-weighted present value of expected future investment returns, considering possible outcomes available to the noteholders, including conversions in subsequent equity financings, settlement and dissolution.

On September 2, 2020, upon consummation of our Series B convertible preferred stock financing, the principal balance plus accrued interest earned on the 2019 Notes and the 2020 Notes automatically converted into 1,905,688 shares of Series B convertible preferred stock. Upon conversion, we no longer are required to adjust the carrying value of the convertible promissory notes at each reporting date.

Income Taxes

We are subject to corporate U.S. federal and state income taxation. As of December 31, 2021, we had federal and state net operating loss carryforwards of approximately $69.2 million and $27.8 million respectively. $0.2 million of the $69.2 million of federal net operating loss carryforwards will begin expiring in 2037 and the remaining $69.0 million can be carried forward indefinitely. The yearly utilization of such federal net operating loss carryforwards is limited to 80 percent of taxable income. On March 27, 2020, Congress enacted the Coronavirus Aid, Relief and Economic Security Act (the CARES Act), which may provide some relief from such limitations. The state tax loss carryforwards will begin expiring in 2031, if not utilized. As of December 31, 2021, we had federal

and state research and development tax credits of approximately $3.1 million and $0.9 million, respectively. If not utilized, the federal research tax credit will begin to expire in 2039. The California research tax credit can be carried forward indefinitely.

Utilization of the net operating loss carryforwards and other tax attributes may be subject to a substantial annual limitation due to the ownership change limitations provided by Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code), and similar state provisions. Specifically, under Sections 382 and 383 of the Code, 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), our ability to use such 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, upon the closing of this offering, may experience, an "ownership change." We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership.

We estimate our income tax provision, including deferred tax assets and liabilities, based on management's judgment. We record a valuation allowance to reduce our deferred tax assets to the amounts that are more likely than not to be realized. We consider future taxable income, ongoing tax planning strategies and our historical financial performance in assessing the need for a valuation allowance. If we expect to realize deferred tax assets for which we have previously recorded a valuation allowance, we will reduce the valuation allowance in the period in which such determination is first made.

We record liabilities related to uncertain tax positions in accordance with the guidance that clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements by prescribing a minimum recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return.

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, together with the changes in those items in dollars:

	Year Ended December 31,		
	2021	2020	Change
	(in thousands)		
Operating expenses:			
Research and development	$ 40,773	$ 15,367	$ 25,406
General and administrative	10,739	3,591	7,148
Total operating expenses	51,512	18,958	32,554
Loss from operations	(51,512)	(18,958)	(32,554)
Other income (expense):			
Interest income	119	32	87
Interest expense, related party	—	(135)	135
Change in fair value of convertible promissory notes, related party	—	(2,024)	2,024
Other income	1	2	(1)
Total other income (expense), net	120	(2,125)	2,245
Net loss before income tax expense	$ (51,392)	$ (21,083)	$ 30,309

Research and Development Expenses

Research and development (R&D) expenses were $40.8 million and $15.4 million for the years ended December 31, 2021 and 2020, respectively. The increase in R&D expenses was primarily related to milademetan and other research costs, including the milestone fees payable to Daiichi Sankyo of $5.5 million. Non-cash stock-based compensation expenses, included as part of personnel costs, were $2.5 million and $0.6 million for the years ended December 31, 2021 and 2020, respectively. We expect our R&D costs to continue to increase in 2022 as we continue our Phase 3 trial in LPS and our Phase 2 tumor-agnostic basket trial for milademetan.

General and Administrative Expenses

General and administrative (G&A) expenses were $10.7 million and $3.6 million for the years ended December 31, 2021 and 2020, respectively. The increase in G&A expenses was primarily due to director and officer insurance of $2.4 million, payroll-related costs of $2.3 million and various third-party G&A costs of $2.4 million. Non-cash stock-based compensation expense included in G&A expenses was $0.6 million and $0.3 million for the years ended December 31, 2021 and 2020, respectively. We have incurred and expect to continue incur additional expenses as a result of being a public company following the completion of our IPO in April 2021, including costs associated with maintaining compliance with exchange listing and SEC requirements as a public company. In addition, we expect our general and administrative expenses to continue to increase in 2022 as we continue to add personnel and build out systems and infrastructure to support our operations as a public company.

Other (Income) Expense

Other (income) expense, net with nominal amounts for the years ended December 31, 2021 and 2020 represents interest income, interest expense on the outstanding convertible promissory notes and change in the fair value of our convertible promissory notes recorded in 2020.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our research programs and product candidates. We expect that our research and development and general and administrative costs will increase in connection with conducting additional preclinical studies and clinical trials, expanding our intellectual property portfolio and providing general and administrative support for our operations. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements or other sources.

We do not currently have any approved products and have not generated any revenue from product sales since inception. To date, we have financed our operations through the issuance of convertible promissory notes and the issuance of convertible preferred stock and common stock. From our inception through December 31, 2021, we have raised aggregate gross proceeds of $9.9 million from the issuance of convertible promissory notes and $81.9 million from the issuance of convertible preferred stock. On April 27, 2021, we completed our IPO in which we issued and sold 7,352,941 shares of common stock at a public offering price of $17.00 per share. On May 11, 2021, we issued an additional 492,070 shares of common stock in connection with the exercise of the underwriters' option to purchase additional shares at the public offering price. Our net proceeds from the sale of shares in the IPO, including the sale of shares pursuant to the exercise of the underwriters' option to purchase additional shares, was $121.5 million, net of underwriting discounts and commissions, and other offering fees. As of December 31, 2021, we had cash, cash equivalents and short-term investments of $140.2 million. Although we believe, based on our current business plans, that our existing cash, cash equivalents and short-term investments will be sufficient to meet our obligations for at least the next twelve months, we anticipate that we will require additional capital in the future in order to continue the research and development of our drug candidates. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

Future Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing development activities related to milademetan and other product candidates and programs, which are still in the early stages of development. In addition, following the IPO, we expect to incur additional costs associated with operating as a public company. We expect that our expenses will increase substantially if and as we:

- continue our on-going clinical trials, initiate new clinical trials for our milademetan program and incur additional preclinical research costs for our RAD52 program;
- initiate and continue research and preclinical and clinical development of our product candidates;
- seek to identify and develop additional product candidates;

- seek marketing approvals for any of our product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing, manufacturing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- require the manufacture of larger quantities of our product candidates for clinical development and potentially commercialization;
- maintain, expand, protect and enforce our intellectual property portfolio;
- acquire or in-license other drugs and technologies;
- defend against any claims of infringement, misappropriation or other violation of third-party intellectual property;
- hire and retain additional clinical, quality control and scientific personnel;
- build out new facilities or expand existing facilities to support our ongoing development activity;
- add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our transition to a public company;
- potentially experience the effects of the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide from the ongoing COVID-19 pandemic; and
- operate as a public company.

Because of the numerous risks and uncertainties associated with the development of milademetan and other product candidates and programs and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates and programs. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of our current and future clinical trials of milademetan for our current targeted indications;
- the scope, progress, results and costs of drug discovery, preclinical research and clinical trials for RAD52 and other product candidates;
- the number of future product candidates that we pursue and their development requirements;
- the costs, timing and outcome of regulatory review of our product candidates;
- the extent to which we acquire or invest in businesses, products and technologies, including entering into or maintaining licensing or collaboration arrangements for product candidates on favorable terms, although we currently have no commitments or agreements to complete any such transactions;
- the costs of preparing, filing and prosecuting patent applications, maintaining, protecting and enforcing our intellectual property rights and defending intellectual property-related claims;
- our headcount growth and associated costs as we expand our business operations and our research and development activities;
- our ability to successfully acquire or in-license other drugs and technologies;
- the costs and timing of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval; and
- the costs of operating as a public company.

Developing drug products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or

results required to obtain marketing approval for any product candidates or generate revenue from the sale of any products for which we may obtain marketing approval. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Until such time, if ever, as we can generate product revenues to support our cost structure, we expect to finance our cash needs through public or private equity offerings, debt financings or other capital sources which may include strategic collaborations, licensing arrangements or other arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through strategic collaborations or other similar arrangements with third parties, we may have to relinquish valuable rights to our technology, future revenue streams, research programs or product candidates or may have to grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic or otherwise. Because of the numerous risks and uncertainties associated with product development, we cannot predict the timing or amount of increased expenses and cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

Cash Flows

The following table summarizes our sources and uses of cash for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (37,463)	$ (11,231)
Investing activities	(118,235)	(5,191)
Financing activities	121,615	69,491
Net (decrease) increase in cash and cash equivalents	$ (34,083)	$ 53,069

Operating Activities

We have incurred losses since inception. Net cash used in operating activities for the year ended December 31, 2021 was $37.5 million, consisting primarily of net loss of $51.4 million resulting from expenses associated with research and development activities for our lead product candidate and general and administrative expenses, partially offset by a net decrease in changes in operating assets and liabilities of $5.2 million and non-cash adjustments of $8.7 million.

Net cash used in operating activities for the year ended December 31, 2020 was $11.2 million, consisting primarily of net loss of $21.1 million offset by a net decrease from changes in operating assets and liabilities of $1.6 million and non-cash adjustments of $8.2 million.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2021 was $118.2 million, which was primarily related to purchases of available for sale securities of $163.6 million, and payment of $2.5 million to Daiichi Sankyo for in-process research and development expense, partially offset by maturities of available for sale securities of $48.0 million.

Net cash used in investing activities for the year ended December 31, 2020 was $5.2 million, which was primarily for payment to Daiichi Sankyo for in-process research and development expense.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was $121.6 million, which primarily relates to the net proceeds from IPO, after deducting underwriting discounts and commissions, and other offering fees.

Net cash provided by financing activities in the year ended December 31, 2020 was $69.5 million primarily relates to proceeds of $6.4 million from issuance of convertible promissory notes and proceeds of $63.2 million from issuance of convertible preferred stock, net of issuance costs.

Obligations and other Commitments

As discussed in Note 9 to the financial statements appearing elsewhere in this Annual Report on Form 10-K, we are party to agreements to license intellectual property. The license agreements may require us to pay future milestones if certain developmental, regulatory and commercial milestones are achieved, as well as to pay royalties on net sales of products applicable to the license agreements. We cannot estimate if milestone and/or royalty payments will occur in future periods and the agreements are cancelable by us at any time upon prior written notice to the licensor.

In the normal course of business, we enter into contracts with CROs and other vendors for preclinical studies and clinical trials, research and development supplies and other testing and manufacturing services. These contracts generally do not contain minimum purchase commitments and are cancelable by either party at any time upon prior written notice.

Our incurred and accrued research and development obligations as of December 31, 2021 and 2020 were $4.3 million and $1.5 million, respectively.

We pay the office operating lease obligation at the beginning of each month. Under our office operating leases as noted in Note 10 to the financial statements appearing elsewhere in this Annual Report on Form 10-K, our obligation as of December 31, 2021 and 2020 were $0.4 million and $0.5 million, respectively.

Critical Accounting Estimates

The discussion and analysis of our financial condition and results of operations is based upon our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States (GAAP). The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, expenses, and related disclosure of contingent assets and liabilities. On an ongoing basis, we evaluate our estimates and base our estimates on historical experience and various other assumptions that are believed to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions and could have a material impact on our reported results. While our significant accounting policies are more fully described in the notes to our financial statements included elsewhere in this Report, we believe the following accounting policies to be the most critical in understanding the judgments and estimates we use in preparing our financial statements.

Accrued Liabilities

We are required to estimate our expenses resulting from our obligations under contracts with vendors, consultants, CROs and clinical site agreements in connection with conducting preclinical activities and clinical trials. The financial terms of these contracts are subject to negotiations which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. However, some payments are made in arrears and expenditures are accrued for the time periods which services are performed on a pre-determined schedule or when contractual milestones are met. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones.

This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service

performed and the associated cost incurred when we have not yet been invoiced or otherwise notified of actual costs. During the course of a preclinical study or clinical trial, we adjust our prepaid and expense recognition if actual results differ from our estimates. To date, we have not experienced any material differences between accrued costs and actual costs incurred. The accrued research and development balances were $4.3 million and $1.5 million as of December 31, 2021 and 2020, respectively. The other accrued liabilities balances were $5.7 million and $0.9 million as of December 31, 2021 and 2020, respectively.

Stock-Based Compensation

We follow the provision of the Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) Topic 718, "Compensation – Stock Compensation" (ASC 718), which requires the measurement and recognition of compensation expense for all stock-based payment awards. We determine the fair value of restricted stock units based on the fair value of our common stock on the date of grant.

We estimate the fair value of our stock options using the Black-Scholes option pricing model, which requires us to develop subjective estimates to be used in calculating the fair value of stock options. The use of the model requires us to make estimates of subjective assumptions, such as expected stock price volatility and the estimated expected term of each award.

Stock-based compensation expense based on the fair value estimated is recognized over the requisite service period of the awards (generally the vesting period) on a straight-line basis. Prior to the IPO, the estimated fair value of the underlying common stock as determined on the date of grant by our Board of Directors. For the year ended December 31, 2021 and 2020, stock-based compensation expense was $3.1 million and $0.9 million, respectively. The following table summarizes unvested equity compensation costs not yet recognized as of the years ended December 31, 2021 and 2020.

	As of December 31,	
	2021	2020
Unvested equity compensation costs not yet recognized (in millions)	$ 9.8	$ 1.4
Weighted average period over which the unvested awards are expected to be recognized (in years)	3.1	2.3

Recent Accounting Pronouncements

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 2 to our audited financial statements for the year ended December 31, 2021, included elsewhere in this Annual Report on Form 10-K.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

We are a smaller reporting company, as defined by Rule 12b-2 under the Securities and Exchange Act of 1934 and in Item 10(f)(1) of Regulation S-K, and are not required to provide the information under this item.

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Rain Therapeutics Inc.

Opinion on the Financial Statements

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

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.

San Diego, California
March 3, 2022

Rain Therapeutics Inc.
Balance Sheets
(In thousands, except share and per share data)

	December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 24,780	$ 58,863
Short-term investments	115,438	—
Prepaid and other current assets	5,928	662
Total current assets	146,146	59,525
Property and equipment, net	165	99
Operating lease right-of-use asset	386	447
Deferred offering costs	—	385
Other assets	443	624
Total assets	$ 147,140	$ 61,080
Liabilities, convertible preferred stock, and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 6,112	$ 816
Accrued research and development	4,349	1,527
Other accrued liabilities	5,694	935
Operating lease liability, current portion	160	141
Total current liabilities	16,315	3,419
Operating lease liability, net of current portion	252	312
Other long-term liabilities	69	69
Total liabilities	16,636	3,800
Commitments and contingencies		
Series A convertible preferred stock, $0.001 par value; no shares and 3,731,208 shares authorized, issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	—	20,147
Series B convertible preferred stock, $0.001 par value; no shares and 12,542,198 shares authorized, issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	—	74,550
Total convertible preferred stock	—	94,697
Stockholders' equity (deficit):		
Common Stock, $0.001 par value; 250,000,000 and 24,000,000 shares authorized as of December 31, 2021 and December 31, 2020, respectively; 26,475,812 shares (comprised of 18,748,342 shares of common stock and 7,727,470 shares of non-voting common stock) and 3,530,975 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	27	4
Additional paid-in capital	220,530	1,149
Accumulated other comprehensive loss	(89)	—
Accumulated deficit	(89,964)	(38,570)
Total stockholders' equity (deficit)	130,504	(37,417)
Total liabilities, convertible preferred stock, and stockholders' equity (deficit)	$ 147,140	$ 61,080

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

Rain Therapeutics Inc.
Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Year Ended December 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 40,773	$ 15,367
General and administrative	10,739	3,591
Total operating expenses	51,512	18,958
Loss from operations	(51,512)	(18,958)
Other income (expense):		
Interest income	119	32
Interest expense, related party	—	(135)
Change in fair value of convertible promissory notes, related party	—	(2,024)
Other income	1	2
Total other income (expense), net	120	(2,125)
Net loss before income tax expense	(51,392)	(21,083)
Income tax expense	(2)	—
Net loss	$ (51,394)	$ (21,083)
Net loss per share, basic and diluted	$ (2.65)	$ (6.29)
Weighted-average shares used to compute net loss per share, basic and diluted	19,405,833	3,351,850
Net loss	$ (51,394)	$ (21,083)
Other comprehensive income:		
Unrealized loss on investments	(89)	—
Comprehensive loss	$ (51,483)	$ (21,083)

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

Rain Therapeutics Inc.
Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share amounts)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	Loss	(Deficit)
Balance as of December 31, 2019	3,731,208	$ 20,147	—	$ —	2,986,385	$ 3	$ 236	$ (17,487)	$ —	$ (17,248)
Issuance of Series B convertible preferred stock, net of issuance costs of $327	—	—	10,636,510	63,173	—	—	—	—	—	—
Conversion of convertible promissory notes into Series B convertible preferred stock	—	—	1,905,688	11,377	—	—	—	—	—	—
Vesting of restricted shares					532,455	1	—	—	—	1
Exercise of stock options	—	—	—	—	12,135	—	48	—	—	48
Stock-based compensation expense	—	—	—	—	—	—	865	—	—	865
Net loss	—	—	—	—	—	—	—	(21,083)	—	(21,083)
Balance as of December 31, 2020	3,731,208	$ 20,147	12,542,198	$ 74,550	3,530,975	$ 4	$ 1,149	$ (38,570)	$ —	$ (37,417)
Conversion of convertible preferred stock to common stock	(3,731,208)	(20,147)	(12,542,198)	(74,550)	15,069,330	15	94,682	—	—	94,697
Issuance of common stock upon IPO, net of issuance cost	—	—	—	—	7,845,011	8	121,486	—	—	121,494
Exercise of stock options	—	—	—	—	30,496	—	121	—	—	121
Stock-based compensation expense	—	—	—	—	—	—	3,092	—	—	3,092
Unrealized loss on investments	—	—	—	—	—	—	—	—	(89)	(89)
Net loss	—	—	—	—	—	—	—	(51,394)	—	(51,394)
Balance as of December 31, 2021	—	—	—	$ —	26,475,812	$ 27	$ 220,530	$ (89,964)	$ (89)	$ 130,504

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

Rain Therapeutics Inc.
Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2021	**2020**
Operating activities		
Net loss	$ (51,394)	$ (21,083)
Adjustments to reconcile net loss to cash used in operating activities:		
In-process research and development expense	5,500	5,167
Depreciation and amortization expense	71	52
Stock-based compensation expense	3,092	865
Non-cash interest expense, related party	—	135
Change in fair value of convertible promissory notes, related party	—	2,024
Amortization of premium and accretion of discounts on short-term investments, net	81	—
Fair value loss/(gain) on investments	(1)	—
Changes in operating assets and liabilities:		
Prepaid and other current assets	(5,266)	(182)
Operating lease right-of-use asset and liability, net	19	10
Other assets	181	(195)
Accounts payable	5,288	555
Accrued research and development	2,822	1,417
Other accrued liabilities	2,144	—
Other long-term liabilities	—	4
Net cash used in operating activities	(37,463)	(11,231)
Investing activities		
Purchases of short-term investments	(163,557)	—
Purchases of property and equipment	(128)	(24)
Payment of in-process research and development expense	(2,500)	(5,167)
Maturities of available for sale investments	47,950	—
Net cash used in investing activities	(118,235)	(5,191)
Financing Activities		
Proceeds from initial public offering	133,366	—
Proceeds from stock option exercises	121	48
Issuance of common stock for vesting of restricted shares	—	1
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	63,173
Proceeds from issuance of convertible promissory notes	—	6,435
Payments of issuance costs related to the initial public offering	(11,872)	(166)
Net cash provided by financing activities	121,615	69,491
Net (decrease) increase in cash and cash equivalents	(34,083)	53,069
Cash and cash equivalents at beginning of period	58,863	5,794
Cash and cash equivalents at end of period	$ 24,780	$ 58,863
Supplemental schedule of non-cash investing and financing activities:		
Conversion of convertible preferred stock to common stock	$ 94,697	$ —
Non-cash in-process research and development accrual	$ 3,000	$ —
Non-cash additions to property and equipment	$ 9	$ —
Conversion of convertible promissory notes and interest into Series B convertible preferred stock	$ —	$ 11,377
Accruals for unbilled professional fees related to the IPO	$ —	$ 219

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

Note 1 – Organization and Nature of Operations

Description of Business

Rain Therapeutics Inc. (“Rain” or the “Company”) was incorporated in the state of Delaware in April 2017. Rain is a late-stage precision oncology company developing therapies that target oncogenic drivers for which the Company is able to genetically select patients most likely to benefit. This approach includes using a tumor-agnostic strategy to select patients based on their tumors’ underlying genetics rather than histology. Rain’s lead product candidate, milademetan, is a small molecule, oral inhibitor of mouse double minute 2, which may be oncogenic in numerous cancers. In addition to milademetan, the Company is also developing a preclinical program that is focused on inducing synthetic lethality in cancer cells by inhibiting RAD52. The Company operates in one business segment and its principal operations are in the United States, with its headquarters in Newark, California.

Reverse Stock Split

On April 15, 2021 and April 16, 2021, the Company’s board of directors (the “Board of Directors”) and stockholders, respectively, approved an amended and restated certificate of incorporation of the Company to effect a 1-for-1.0799 reverse stock split of the Company’s common stock. The reverse stock split was effected on April 16, 2021. The Company’s outstanding stock options were also adjusted to reflect the 1-for-1.0799 reverse stock split of the Company’s common stock. Accordingly, all common stock and stock options and related per share amounts in these financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split. Outstanding stock options were proportionately reduced and the respective exercise prices, if applicable, were proportionately increased. The reverse stock split resulted in an adjustment to the Series A and Series B convertible preferred stock conversion prices to reflect a proportional decrease in the number of shares of common stock to be issued upon conversion.

Initial Public Offering

On April 27, 2021, the Company completed its initial public offering (“IPO”) in which the Company issued and sold 7,352,941 shares of common stock at a public offering price of $17.00 per share. On May 11, 2021, the Company issued an additional 492,070 shares of common stock in connection with the exercise of the underwriters’ option to purchase additional shares at the public offering price. The Company’s net proceeds from the sale of shares in the IPO, including the sale of shares pursuant to the exercise of the underwriters’ option to purchase additional shares, was $121.5 million, net of underwriting discounts and commissions, and other offering fees.

Immediately prior to the closing of the IPO, 8,344,905 shares of the Company’s convertible preferred stock were exchanged for 7,727,470 shares of non-voting common stock. Upon the closing of the IPO, 7,928,501 shares of the Company’s convertible preferred stock were automatically converted into 7,341,860 shares of common stock. Following the IPO, there were no shares of convertible preferred stock outstanding.

Basis of Presentation

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

Liquidity and Capital Resources

The Company has devoted substantially all of its efforts to drug discovery and development, raising capital and building operations. The Company has a limited operating history and has not generated any revenue since its inception, and the sales and income potential of the Company’s business is unproven. The Company has incurred net losses and negative cash flows from operating activities since its inception and expects to continue to incur net losses into the foreseeable future as it continues the development of its product candidates. From

inception through December 31, 2021, the Company has funded its operations through net proceeds from its IPO in April 2021, and the issuance of convertible promissory notes and convertible preferred stock.

The accompanying financial statements have been prepared assuming the Company will continue as a going concern. Management believes that the Company's current cash, cash equivalents and short-term investments will provide sufficient funds to enable the Company to meet its obligations for at least twelve months from the filing date of this report.

Note 2 – Summary of Significant Accounting Policies

Use of Estimates

The preparation of the Company's financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses and the disclosure of contingent liabilities in the Company's financial statements and accompanying notes. The most significant estimate in the Company's financial statements relates to the clinical trial expense accruals. Management evaluates its estimates on an ongoing basis. Although these estimates are based on the Company's historical experience, knowledge of current events and actions it may undertake in the future, actual results may ultimately materially differ from these estimates and assumptions.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. Cash equivalents include commercial paper, readily available money market and checking accounts.

Available-for-Sale Investments

The Company holds investment grade securities consisting of money market funds, commercial paper, corporate debt securities, U.S. government securities and U.S. agency bonds, classified as available-for-sale ("AFS") securities at the time of purchase, since it is the Company's intent that these investments be available for current operations. The Company has classified all of its AFS securities as current assets on the balance sheets even though the stated maturity date may be one year or more beyond the current balance sheet date, which reflects management's intention to use the proceeds from sales of these securities to fund its operations, as necessary.

The Company carries these securities at fair value and reports unrealized gains and losses, if any, as a separate component of accumulated other comprehensive loss. The cost of debt securities is adjusted for amortization of purchase premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income in the statements of operations and comprehensive loss. Realized gains and losses on sales of securities are determined using the specific identification method and recorded in other income (expense), net in the statement of operations and comprehensive loss.

Investments are considered to be impaired when a decline in fair value is judged to be other-than-temporary. The Company consults with its investment managers and considers available quantitative and qualitative evidence in evaluating potential impairment of its investments on a quarterly basis. If the cost of an individual investment exceeds its fair value, the Company evaluates among other factors, general market conditions, the duration and extent to which the fair value is less than cost, and the Company's intent and ability to hold the investment. Once an impairment is determined to be other-than-temporary, an impairment charge is recorded and a new cost basis in the investment is established. Declines in the value of AFS securities determined to be other than temporary are included in other income (expense), net.

Fair Value Option

As permitted under ASC 825, Financial Instruments ("ASC 825"), the Company has elected the fair value option to account for the convertible promissory notes issued in 2019 (the "2019 Notes") and 2020 (the "2020 Notes"). In accordance with ASC 825, the Company records these convertible promissory notes at fair value and records changes in fair value as a line item within other income (expense) in the accompanying statements

of operations and comprehensive loss. As a result of applying the fair value option, direct costs and fees related to the 2019 Notes and 2020 Notes were recognized in net loss as incurred and not deferred.

Fair Value of Financial Instruments

The carrying amounts of all cash equivalents, prepaid expenses and other assets, accounts payable and accrued and other current liabilities are reasonable estimates of their fair value because of the short-term nature of these items.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to significant concentration of credit risk, consist primarily of cash, cash equivalents and short-term investments. The Company maintains cash and money market deposits in a federally insured major financial institution in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institution in which those deposits are held.

Deferred Offering Costs

The Company capitalized offering costs consisting of all direct and incremental legal, professional, accounting and other third-party fees incurred in connection with the Company's IPO. Upon the completion of the IPO in April 2021, the total deferred offering costs of $2.5 million were reclassified to additional paid-in capital on the balance sheets.

Research and Development Costs

Research and development costs primarily consist of costs associated with the Company's research and development activities, including its drug discovery efforts, and the preclinical and clinical development of its product candidates. Research and development costs are expensed as incurred.

Property and Equipment

Property and equipment, net consists of computer equipment, furniture and equipment and leasehold improvements. Leasehold improvements are amortized over the remainder of the lease term. Computer equipment and furniture and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets (generally two to three years). Repairs and maintenance costs are charged to expense as incurred.

Long-Lived Assets

The Company regularly reviews the carrying value and estimated lives of all of its long-lived assets, including property and equipment, to determine whether indicators of impairment may exist which warrant adjustments to carrying values or estimated useful lives. Should an impairment exist, the impairment loss would be measured based on the excess over the carrying amount of the asset's fair value. The Company has not recognized any impairment losses from inception through December 31, 2021.

Commitments

The Company recognizes a liability with regard to loss contingencies when it believes it is probable that a liability has occurred, and the amount can be reasonably estimated. If some amount within a range of loss appears at the time to be a better estimate than any other amount within the range, the Company accrues that amount. When no amount within the range is a better estimate than any other amount, the Company accrues the minimum amount in the range. The Company has not recorded any such liabilities as of December 31, 2021.

Leases

At the inception of a contractual arrangement, the Company determines whether the contract contains a lease by assessing whether there is an identified asset and whether the contract conveys the right to control the use of the identified asset in exchange for consideration over a period of time. If both criteria are met, the Company records the associated lease liability and corresponding right-of-use asset upon commencement of the lease using the implicit rate or a discount rate based on a credit- adjusted secured borrowing rate commensurate

with the term of the lease. The Company additionally evaluates leases at their inception to determine if they are to be accounted for as an operating lease or a finance lease. Operating lease assets represent a right to use an underlying asset for the lease term and operating lease liabilities represent an obligation to make lease payments arising from the lease. Operating lease liabilities with a term greater than one year and their corresponding right-of-use assets are recognized on the balance sheet at the commencement date of the lease based on the present value of lease payments over the expected lease term. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received. As the Company's leases do not typically provide an implicit rate, the Company utilizes the appropriate incremental borrowing rate, determined as the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term and in a similar economic environment. Lease cost is recognized on a straight-line basis over the lease term and variable lease payments are recognized as operating expenses in the period in which the obligation for those payments is incurred. Variable lease payments primarily include common area maintenance, utilities, real estate taxes, insurance and other operating costs that are passed on from the lessor in proportion to the space leased by the Company. The Company has elected the practical expedient to not separate lease and non-lease components.

Preclinical Studies and Clinical Trial Accruals

The Company is required to estimate its expenses resulting from its obligations under contracts with vendors, consultants, clinical research organizations and clinical site agreements in connection with conducting preclinical activities and clinical trials. The financial terms of these contracts are subject to negotiations which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company reflects preclinical study and clinical trial expenses in its financial statements by matching those expenses with the period in which services and efforts are expended. The Company accounts for these expenses according to the progress of the preclinical study or clinical trial as measured by the timing of various aspects of the preclinical study, clinical trial or related activities. The Company determines accrual and prepaid estimates through review of the underlying contracts along with preparation of financial models taking into account correspondence with clinical and other key personnel and third- party service providers as to the progress of preclinical studies, clinical trials or other services being conducted. During the course of a preclinical study or clinical trial, the Company adjusts its expense recognition if actual results differ from its estimates. To date, the Company has not experienced any material differences between accrued costs and actual costs incurred.

In-Process Research and Development

The Company evaluates whether acquired intangible assets are a business under applicable accounting standards. Additionally, the Company evaluates whether the acquired assets have a future alternative use. Intangible assets that do not have future alternative use, such as the license the Company acquired from Daiichi, are considered acquired in-process research and development. When the acquired in-process research and development assets are not part of a business combination, the value of the consideration paid is expensed on the acquisition date. Future costs to develop these assets are recorded to research and development expenses as they are incurred.

Patent Costs

Costs related to filing and pursuing patent applications are recorded as general and administrative expense and expensed as incurred since recoverability of such expenditures is uncertain.

General and Administrative Expenses

General and administrative expenses consist of salaries, stock-based compensation, facilities and third-party expenses. General and administrative expenses are associated with the activities of the executive, finance, accounting, information technology, legal and human resource functions.

Stock-Based Compensation

Stock-based compensation expense represents the grant date fair value of equity awards recognized over the requisite service period of the awards (generally the vesting period) on a straight-line basis. The Company recognizes forfeitures as they occur. The Company estimates the fair value of stock option grants using the Black-Scholes option pricing model. Prior to the IPO, the exercise price for all stock options granted was at the estimated fair value of the underlying common stock as determined on the date of grant by the Company's Board of Directors.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions on the basis of a two-step process whereby (1) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more likely than not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement with the related tax authority. The Company recognizes interest and penalties related to unrecognized tax benefits within income tax expense. Any accrued interest and penalties are included within the related tax liability.

Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. The Company's comprehensive loss includes unrealized gains / losses from short-term investments.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding for the period, without consideration of potential dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the sum of the weighted-average number of shares of common stock plus the potential dilutive effects of potential dilutive securities outstanding during the period. Potential dilutive securities are excluded from diluted earnings or loss per share if the effect of such inclusion is antidilutive. The Company's potentially dilutive securities, which include convertible preferred stock, ESPP shares, and outstanding stock options under the Company's equity incentive plan, have been excluded from the computation of diluted net loss per share as they would be anti-dilutive to the net loss per share. For the periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to the Company's net loss position.

Recent Developments Regarding the COVID-19 Pandemic

Efforts to control the outbreak of COVID-19 have resulted in challenges to businesses and facilities in various industries around the world, including disruptions to the global economy and supply chains. To date, COVID-19 has not had a material impact on the Company's expenditures.

The Company is unable to predict the ultimate effects of COVID-19 on the U.S. or global economy or its operations. The Company continues to monitor developments affecting its workforce, suppliers, and operations. The extent of the impact of COVID-19 will depend on its duration, actions by government authorities, and impacts on the Company's customers, employees, or vendors. These developments are continuously evolving, and the Company cannot predict whether COVID-19 will have a material impact on its financial condition, results of operations or cash flows.

Recent Accounting Pronouncements

Financial Instruments. In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326)*: Measurement of Credit Losses on Financial Instruments. The objective of the standard is to provide information about expected credit losses on financial instruments at each reporting date and to change

how other-than temporary impairments on investment securities are recorded. The guidance is effective for the Company beginning on January 1, 2023, with early adoption permitted. The Company does not anticipate that the adoption of ASU 2016-13 will have a significant impact on its financial statements or the related disclosures.

Income Taxes. In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which simplifies the accounting for income taxes. ASU 2019-12 is effective for the Company for the fiscal year beginning after December 15, 2021 and early adoption is permitted. The Company does not anticipate that the adoption of ASU 2019-12 will have a significant impact on its financial statements or the related disclosures.

Debt and Equity Instruments. In August 2020, the FASB issued ASU 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)*, which addresses the complexity associated with applying generally accepted accounting principles for certain financial instruments with characteristics of liabilities and equity. The guidance is effective for the Company beginning on January 1, 2024, with early adoption permitted. The Company elected to adopt this standard on January 1, 2020 under the modified retrospective transition method with no material impact on its financial statements or the related disclosures.

There were no other significant updates to the recently issued accounting standards other than as disclosed herein for the year ended December 31, 2021. Although there are several other new accounting pronouncements issued or proposed by the FASB, based on the Company's preliminary assessment, the Company does not believe any of those accounting pronouncements have had or will have a material impact on its financial position or operating results.

Note 3 – Fair Value Measurements

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or non-recurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities.

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

Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

The carrying amounts of cash, prepaid expenses and other current assets, deferred offering costs, other assets, accounts payable, accrued research and development, other current liabilities and other long-term liabilities are reasonable estimates of their fair value due to the short-term nature of these accounts.

The Company's money market funds under cash and cash equivalents are classified using Level 1 inputs within the fair value hierarchy because they are valued using quoted market prices, broker or dealer quotations, or alternative pricing sources with reasonable levels of price transparency. There were no transfers between levels of the fair value hierarchy during the years ended December 31, 2021 and 2020, respectively.

The following table summarizes financial assets that the Company measured at fair value on a recurring basis, classified in accordance with the fair value hierarchy (in thousands):

	Fair Value Measurements at Reporting Date Using:			
	Level 1	Level 2	Level 3	Total
As of December 31, 2021				
Money market funds	$ 10,585	$ —	$ —	$ 10,585
Commercial paper	—	84,616	—	84,616
U.S. government securities	27,824		—	27,824
U.S. agency bonds	—	8,531	—	8,531
Corporate debt securities	—	8,265	—	8,265
Total cash equivalents and short-term investments	$ 38,409	$ 101,412	$ —	$ 139,821
Reported as:				
Cash and cash equivalents (includes cash of $397)				$ 24,780
Short-term investments				115,438
Total cash, cash equivalents and short-term investments				$ 140,218

	Fair Value Measurements at Reporting Date Using:			
	Level 1	Level 2	Level 3	Total
As of December 31, 2020				
Cash equivalents	$ 19,257	$ —	$ —	$ 19,257

There were no liabilities measured at fair value on a recurring basis as of December 31, 2021 and 2020.

The following table provides a reconciliation of all liabilities measured at fair value using Level 3 significant unobservable inputs (in thousands) during the year ended December 31, 2020.

	Convertible Promissory Notes
Fair value as of December 31, 2019	$ 2,751
Issuance of convertible promissory notes	6,435
Conversion to convertible preferred stock (excluding interest expense)	(11,210)
Change in fair value of convertible promissory notes (Note 7)	2,024
Fair value as of December 31, 2020	$ —

Convertible Promissory Notes

As further described in Note 7, the Company issued convertible promissory notes in October 2019 (the “2019 Notes”) and in June 2020 (the “2020 Notes”) to investors. The Company elected the ASC 825, Financial Instruments, fair value option for the convertible promissory notes. The fair value of the convertible promissory notes was determined using a scenario-based analysis that estimated the fair value of the convertible promissory notes based on the probability-weighted present value of expected future investment returns, considering possible outcomes available to the noteholders, including conversions in subsequent equity financings. The 2019 Notes and 2020 Notes were valued upon issuance, remeasured to fair value each reporting period and remeasured immediately prior to conversion into Series B convertible preferred stock based on changes in the expected time to closing ranging from 0 to 0.67 years and the relevant discount rate of 25% during the period. In September 2020, the 2019 Notes and 2020 Notes were converted to 1,905,688 shares of Series B convertible preferred stock.

In September 2020, all outstanding convertible promissory notes with a total fair value of $11.2 million and accrued interest of $167,000 were converted to 1,905,688 shares of Series B convertible preferred stock. Upon conversion, the Company no longer is required to adjust the carrying value of the convertible promissory notes at each reporting date.

Note 4 – Investments

Financial assets measured at fair value on a recurring basis consist of the Company's cash equivalents and AFS securities. The Company obtains pricing information from its investment manager and generally determines the fair value of investment securities using standard observable inputs, including reported trades, broker/dealer quotes, and bids and/or offers.

Investments are classified as Level 1 within the fair value hierarchy if their quoted prices are available in active markets for identical securities. Investments in money market funds and U.S. government securities were classified as Level 1 instruments.

Investments in commercial paper, corporate debt securities and U.S. agency bonds are valued using Level 2 inputs. The Company classifies investments within Level 2 if the investments are valued using model driven valuations using observable inputs such as quoted market prices, benchmark yields, reported trades, broker/dealer quotes or alternative pricing sources with reasonable levels of price transparency. Investments are held by custodians who obtain investment prices from a third-party pricing provider that incorporates standard inputs in various asset price models.

The following table summarizes, by major types of cash equivalents, and investments that are measured at fair value on a recurring basis (in thousands):

	December 31, 2021			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
Money market funds	$ 10,585	—	—	$ 10,585
Commercial paper	84,642	2	(28)	84,616
U.S. government securities	27,870	—	(46)	27,824
U.S. agency bonds	8,546	—	(15)	8,531
Corporate debt securities	8,267	—	(2)	8,265
Cash equivalents and investments	$ 139,910	$ 2	$ (91)	$ 139,821

The contractual maturities of the Company's AFS securities were as follows (in thousands):

	December 31, 2021
Due within one year	$ 105,173
Due within one to two years	10,265
Available-for-Sale Investments	$ 115,438

The available-for-sale investments are classified as current assets, even though the stated maturity date may be one year or more beyond the current balance sheet date, which reflects management's intention to use the proceeds from sales of these securities to fund the Company's operations, as necessary. As of December 31, 2020, the Company did not own any investments. There were no realized gains or losses due to investment sales for the year ended December 31, 2021. As of December 31, 2021, $129.2 million of the Company's marketable securities were in gross unrealized loss positions, of which none had been in such position for greater than 12 months and $23.8 million will mature within three months of December 31, 2021.

At each reporting date, the Company performs an evaluation of its marketable securities to determine if any unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include (i) the financial strength of the issuing institution, (ii) the length of time and extent for which fair value has been less than the cost basis and (iii) the Company's intent and ability to hold its investments in unrealized loss positions until their amortized cost basis has been recovered. Based on the Company's evaluation, it determined that its unrealized losses were not other-than-temporary at December 31, 2021. The Company does not intend to sell the investments before maturity and it is unlikely that the Company will be required to sell the investments before recovery of their amortized cost bases.

Note 5 - Balance Sheet Details

Prepaid and Other Current Assets

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

	Year Ended December 31,	
	2021	2020
Prepaid insurance	$ 827	$ —
Prepaid research	4,329	371
Prepaid other	96	159
FICA tax credit receivable	452	110
Deposits	19	22
Other current assets	205	—
Prepaid and Other Current Assets	$ 5,928	$ 662

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

	Year Ended December 31,	
	2021	2020
Computer equipment	$ 50	$ 45
Furniture and equipment	204	72
Leasehold improvements	67	67
	$ 321	$ 184
Less: accumulated depreciation and amortization expense	$ (156)	(85)
Property and Equipment, net	$ 165	$ 99

Depreciation expense for years ended December 31, 2021 and 2020 were $0.1 million, respectively.

Other Non-Current Assets

Other non-current assets consist of the following (in thousands):

	Year Ended December 31,	
	2021	2020
FICA tax credit receivable	$ 298	$ 549
Deposits	75	75
Other	70	—
Other non-current assets	$ 443	$ 624

Note 6 – Related Party Transactions

As further described in Note 7, the Company issued the 2019 Notes in October 2019 to certain holders of convertible preferred stock, for an aggregate purchase price of $2.5 million and the 2020 Notes in June 2020 to certain holders of convertible preferred stock, for an aggregate purchase price of $6.4 million. In September 2020, all outstanding convertible promissory notes with a total fair value of $11.2 million and accrued interest of $167,000 were converted to 1,905,688 shares of Series B convertible preferred stock. The change in fair value of the convertible promissory notes for the year ended December 31, 2020 was $2.0 million.

Note 7 – Convertible Promissory Notes

In October 2019, the Company entered into a convertible note purchase agreement with certain holders of preferred stock and issued the 2019 Notes for an aggregate purchase price of $2.5 million. The 2019 Notes bore an interest rate of the lesser of (a) 5% per annum and (b) the maximum rate permissible by law. The 2019 Notes were due and payable on demand from the holders on or after 18 months after the date of issuance ("2019 Notes Maturity Date"), unless repaid in full or automatically converted per the Automatic Conversion feature. Under the Automatic Conversion feature, the 2019 Notes were to automatically convert to convertible preferred stock, upon the closing of the Company's next issuance of preferred stock for capital-raising purposes resulting in net proceeds to the Company of at least $10.0 million (excluding any amounts received in connection with the conversion of the 2019 Notes) ("Future Qualifying Financing"). The 2019 Notes would convert into that whole number of shares of the securities equal to the number obtained by dividing the principal plus accrued interest of the 2019 Notes by 80% of the price per share paid by cash investors in the Future Qualifying Financing. The convertible notes included other optional redemption features as follows (i) optionally converted upon a non-qualified equity financing with a conversion price of 80% of the price paid per share in such financing, (ii) any time after the 2019 Notes Maturity Date, demand immediate repayment of an amount equal to the then-outstanding loan balance, or convert the outstanding loan balance into shares of common stock of the Company in an amount equal to the ratio of the then-outstanding loan balance over the ratio of $38.4 million divided by the number of shares of capital stock of the Company outstanding, (iii) automatically upon the occurrence of change in control or an IPO with a conversion of the loan balance into shares of common stock in an amount equal to the ratio of the then-outstanding loan balance over the ratio of $76.8 million divided by the fully diluted capitalization prior to the change in control or IPO, or demand immediate repayment of two times the outstanding loan balance, and (iv) upon certain events of default, immediately due and payable in full.

In June 2020, the Company entered into a convertible note purchase agreement with certain holders of preferred stock and issued the 2020 Notes for an aggregate purchase price of $6.4 million. The 2020 Notes bore an interest rate of the lesser of (a) 5% per annum and (b) the maximum rate permissible by law. The 2020 Notes were due and payable on demand from the holders on or after 18 months after the date of issuance ("2020 Notes Maturity Date"), unless repaid in full or automatically converted per the Automatic Conversion feature. Under the Automatic Conversion feature, the 2020 Notes were to automatically convert to convertible preferred stock, upon the closing of the Company's next issuance of preferred stock for capital-raising purposes resulting in net proceeds to the Company of at least $10.0 million (excluding any amounts received in connection with the conversion of the 2020 Notes) ("Qualifying Financing"). The 2020 Notes would convert into that whole number of shares of the securities equal to the number obtained by dividing the principal plus accrued interest of the 2020 Notes by 80% of the price per share paid by cash investors in the Qualifying Financing. The convertible notes included other optional redemption features as follows (i) optionally converted upon a non-qualified equity financing with a conversion price of 80% of the price paid per share in such financing, (ii) any time after the 2020 Notes Maturity Date, demand immediate repayment of an amount equal to the then-outstanding loan balance, or convert the outstanding loan balance into shares of common stock of the Company in an amount equal to the ratio of the then-outstanding loan balance over the ratio of $38.4 million divided by the number of shares of capital stock of the Company outstanding, (iii) automatically upon the occurrence of change in control or an IPO with a conversion of the loan balance into shares of common stock in an amount equal to the ratio of the then-outstanding loan balance over the ratio of $76.8 million divided by the fully diluted capitalization prior to the change in control or IPO, or demand immediate repayment of two times the outstanding loan balance, (iv) automatically upon the consummation of a transaction in which the Company merges with a public company and (v) upon certain events of default, immediately due and payable in full.

For the year ended December 31, 2020, the Company recognized interest expense of $135,000 in connection with the 2019 Notes and 2020 Notes. In September 2020, all outstanding convertible promissory notes with a total fair value of $11.2 million and accrued interest of $167,000 were converted to 1,905,688 shares of Series B convertible preferred stock.

Note 8 – Convertible Preferred Stock and Stockholders' Equity (Deficit)

In 2020, the Company amended its Certificate of Incorporation to authorize the issuance of 24,000,000 shares of common stock, par value $0.001 per share, and 16,273,406 shares of preferred stock, par value $0.001 per share, of which 3,731,208 shares were designated Series A convertible preferred stock and 12,542,198 shares were designated Series B convertible preferred stock.

In connection with the reverse stock split on April 16, 2021, the Company filed a certificate of amendment to its certificate of incorporation, which authorized 260,000,000 shares of capital stock, consisting of 250,000,000 shares of common stock, par value $0.001 per share, and 10,000,000 shares of undesignated preferred stock, par value $0.001 per share that may be issued from time to time by the Company's Board of Directors in one or more series. Of the 250,000,000 shares of common stock, 200,000,000 shares were designated as "Common Stock" and 50,000,000 shares were designated as "Non-Voting Common Stock".

Rights, preferences, powers, privileges and restrictions, qualifications and limitations for holders of the Company's Common Stock and Non-Voting Common Stock are:

a) Voting Common Stock Voting Rights. Each holder of Voting Common Stock, as such, shall be entitled to one vote for each share of Voting Common Stock held of record by such holder on all matters on which stockholders generally are entitled to vote; provided, however, that, except as otherwise required by law, holders of Voting Common Stock, as such, shall not be entitled to vote on any amendment to the Certificate of Incorporation, including any certificate of designations relating to any series of Preferred Stock (each hereinafter referred to as a "Preferred Stock Designation"), that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation (including any Preferred Stock Designation).

b) Non-Voting Common Stock Voting Rights. Non-Voting Common Stock (i) shall be non-voting except as may be required by law and (ii) shall not entitle the holder thereof to vote on the election of directors at any time.

c) Non-Voting Common Stock Conversion. Each holder of shares of Non-Voting Common Stock shall have the right to convert each share of Non-Voting Common Stock held by such holder into one share (subject to appropriate adjustment in the event of any stock dividend, stock split, reverse stock split, combination or other similar recapitalization with respect to the Voting Common Stock) of Voting Common Stock at such holder's election by providing written notice to the Corporation; provided, however, that such shares of Non-Voting Common Stock may only be converted into shares of Voting Common Stock during such time or times as immediately prior to or as a result of such conversion would not result in the holder(s) thereof beneficially owning (for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended and the rules and regulations promulgated thereunder (collectively, the "Exchange Act")), when aggregated with affiliates with whom such holder is required to aggregate beneficial ownership for purposes of Section 13(d) of the Exchange Act, in excess of the Beneficial Ownership Limitation. The "Beneficial Ownership Limitation" means initially 9.99% of the Voting Common Stock. Any holder of Non-Voting Common Stock may increase the Beneficial Ownership Limitation with respect to such holder, not to exceed 19.99% of the Voting Common Stock, upon 61 days' prior written notice to the Corporation and may decrease the Beneficial Ownership Limitation at any time upon providing written notice of such election to the Corporation; provided, however, that no holder may make such an election to change the percentage with respect to such holder unless all holders managed by the same investment advisor as such electing holder make the same election. Before any holder of Non-Voting Common Stock shall be entitled to convert any shares of Non-Voting Common Stock into shares of Voting Common Stock, such holder shall (A) surrender the certificate or certificates therefor (if any), duly endorsed, at the principal corporate office of the Corporation or of any transfer agent for the Non-Voting Common Stock, and (B) provide written notice to the Corporation, during regular business hours at its principal corporate office, of such conversion election (in form satisfactory to the Corporation) and shall state therein the name or names (i) in which the certificate or certificates representing the shares of Voting Common Stock into which the shares of Non-Voting Common Stock are so converted are to be issued (if such shares of Voting Common Stock are certificated) or (ii) in which such shares of Voting Common Stock are to be registered in book-entry form (if such shares of Voting Common Stock are uncertificated). If the shares of Voting Common Stock into which the shares of Non-Voting Common Stock are to be converted are to be issued in a name or names other than the name of the holder of the shares of Non-Voting Common Stock being converted, such notice shall be accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the holder. The Corporation shall, as soon as practicable thereafter, issue and deliver at such office to such holder, or to the nominee or nominees of such holder, a certificate or certificates representing the number of shares of Voting Common Stock to which such holder shall be entitled upon such

conversion (if such shares of Voting Common Stock are certificated) or shall register such shares of Voting Common Stock in book-entry form (if such shares of Voting Common Stock are uncertificated). Such conversion shall be deemed to be effective immediately prior to the close of business on the date of such surrender of the shares of Non-Voting Common Stock to be converted following or contemporaneously with the provision of written notice of such conversion election as required by this section, the shares of Voting Common Stock issuable upon such conversion shall be deemed to be outstanding as of such time, and the person or persons entitled to receive the shares of Voting Common Stock issuable upon such conversion shall be deemed to be the record holder or holders of such shares of Voting Common Stock as of such time. Notwithstanding anything herein to the contrary, shares of Non-Voting Common Stock represented by a lost, stolen or destroyed stock certificate may be converted if the holder thereof notifies the Corporation or its transfer agent that such certificate has been lost, stolen or destroyed and makes an affidavit of that fact acceptable to the Corporation and executes an agreement acceptable to the Corporation to indemnify the Corporation from any loss incurred by it in connection with such certificate. The effectiveness of any conversion of any shares of Non-Voting Common Stock into shares of Voting Common Stock is subject to the expiration or early termination of any applicable premerger notification and waiting period requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the rules and regulations promulgated thereunder.

d) Dividends. Subject to the rights of the holders of any outstanding series of Preferred Stock, the holders of shares of Common Stock shall be entitled to receive any dividends to the extent permitted by law when, as and if declared by the board of directors of the Corporation (the “Board”).

e) Liquidation. Upon the dissolution, liquidation or winding up of the Corporation, subject to the rights of the holders of any outstanding series of Preferred Stock, the holders of shares of Common Stock shall be entitled to receive the assets of the Corporation available for distribution to its stockholders ratably in proportion to the number of shares held by them. The Non-Voting Common Stock shall rank on parity with the Voting Common Stock as to distributions of assets upon dissolution, liquidation or winding up of the Corporation, whether voluntary or involuntary.

Convertible Preferred Stock

Series A Convertible Preferred Stock. In April 2018, the Company entered into a Series A convertible preferred stock purchase agreement, pursuant to which the Company issued 2,098,269 shares of Series A convertible preferred stock for an aggregate purchase price of $11.0 million, net of issuance costs. In December 2018, the Company issued an additional 1,390,788 shares of Series A convertible preferred stock for an aggregate purchase price of $7.3 million, net of issuance costs.

Series B Convertible Preferred Stock. In September 2020, the Company entered into a Series B convertible preferred stock purchase agreement, pursuant to which the Company issued 10,636,510 shares of Series B convertible preferred stock for an aggregate purchase price of $63.2 million, net of issuance costs.

Rights, preferences, powers, privileges and restrictions, qualifications and limitations for holders of the Company’s Series A convertible preferred stock and Series B convertible preferred stock are:

- Dividends: Each holder of the Company’s Series A and Series B convertible preferred stock is entitled to receive non-cumulative dividends, when and if declared by the Company’s Board of Directors. No dividends have been declared to date.
- Liquidation Preferences: In the event of any liquidation, dissolution or winding up of the Company, the holders of the Series A and Series B convertible preferred stock shall be entitled to receive, prior and in preference to any distribution of any of the assets of the Company to the holders of common stock, an amount per share equal to the original issue price plus declared but unpaid dividends.
- Conversion: Each share of Series A and Series B convertible preferred stock is convertible at the option of the holder, at any time, into the number of shares of common stock determined by dividing the applicable purchase price by the applicable conversion price at the time of conversion. Each share of Series A and Series B convertible preferred stock will be automatically converted into common stock immediately upon (i) the closing of a firm commitment underwritten IPO resulting in at least $50.0 million of gross proceeds to the Company or (ii) the receipt by the Company of a written request for automatic conversion from the holders of a majority of the outstanding shares of Series A and Series B convertible preferred stock.

- Voting: The holders of the Series A and Series B convertible preferred stock are entitled to one vote for each share of common stock into which such shares of Series A and Series B convertible preferred stock could then be converted; and with respect to such vote, such holders shall have full voting rights and powers equal to the voting rights and powers of the holders of the common stock.
- Redemption: The Series A and Series B convertible preferred stock are not explicitly redeemable at the option of the holder at a specified date in the future or at the option of the Company.

Prior to the IPO, the Company's Series A and Series B convertible preferred stock were classified as temporary equity on the accompanying balance sheet instead of in stockholders' equity (deficit) as events triggering redemption that were not solely within the Company's control because the preferred stockholders had the ability to effect a liquidation event. The Company determined not to adjust the carrying values of the Series A and Series B convertible preferred stock to the liquidation preferences of such shares because of the uncertainty of whether or when such liquidation events would occur.

On April 27, 2021, immediately prior to the closing of the IPO, 8,344,905 shares of the Company's convertible preferred stock were exchanged for 7,727,470 shares of Non-Voting common stock and 7,928,501 shares of the Company's convertible preferred stock converted into 7,341,860 shares of common stock. There were no outstanding shares of the Company's convertible preferred stock as of December 31, 2021.

Equity Incentive Plan

In August 2020, the Company's Board of Directors amended the Amended and Restated 2018 Stock Option—Stock Issuance Plan (the "2018 Plan") to increase the maximum number of shares of common stock that may be issued over the term of the plan. The 2018 Plan provides for the grant of stock options, non-statutory stock options, incentive stock options and stock issuances to employees, nonemployees and consultants of the Company.

In April 2021, the Company's 2021 Equity Incentive Plan (the "2021 Plan") was approved by the Company's Board of Directors and became effective on April 15, 2021. Upon the effectiveness of the 2021 Plan, no further grants may be made under the Company's 2018 Plan.

The 2021 Plan allows the Company to grant equity-based awards to its officers, employees, directors and other key persons (including consultants). The Company initially reserved up to 3,246,120 shares of common stock for issuance under the 2021 Plan, plus (i) 1,722 shares that remained available for the issuance of awards under the 2018 Plan at the time the 2021 Plan became effective, and (ii) any shares subject to outstanding options or other share awards that were granted under the 2018 Plan that terminate or expire prior to exercise or settlement; are forfeited because of the failure to vest; or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price. The 2021 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2022 and each January 1 thereafter through January 31, 2032, by 4.0% of the outstanding number of shares of common stock on the immediately preceding December 31, or such lesser number of shares as determined by the Company's Board of Directors.

A summary of the Company's stock option activities during the year ended December 31, 2021 are as follows (in thousands, except share and per share amounts and years):

	Total Options	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contract Term	Aggregate Intrinsic Value
Outstanding as of December 31, 2020	882,942	$ 3.72	9.0	$ 1,263
Granted	932,296	$ 12.80		
Exercised	(30,496)	$ 3.96		$ 171
Forfeited or cancelled	(50,046)	$ 7.00		
Outstanding as of December 31, 2021	1,734,696	$ 8.50	8.8	$ 7,594
Vested and expected to vest as of December 31, 2021	1,734,696	$ 8.50	8.8	$ 7,594
Vested and exercisable as of December 31, 2021	621,869	$ 4.15	8.2	$ 5,429

The weighted-average grant date fair values of option grants during the years ended December 31, 2021 and 2020 were $12.14 and $2.74 per share, respectively. The weighted-average grant date fair values of options forfeited during the years ended December 31, 2021 and 2020 were $6.08 and $2.82 per share, respectively.

Employee Stock Purchase Plan

The 2021 Employee Share Purchase Plan (the "ESPP") was approved by the Board of Directors and became effective on April 15, 2021. The ESPP initially reserved and authorized the issuance of up to 259,689 shares of common stock to participating employees. Under the ESPP, eligible employees can contribute up to 15% of their eligible compensation, as defined in the ESPP, towards the purchase of the Company's common stock at a price of 85% of the lower of the fair market value of the Company's common stock on the first trading day of the offering period or on the last trading day of the offering period. The ESPP provides for twenty-four-month offering periods with four six-month purchase periods in each offering period. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2022 and each January 1 thereafter through January 31, 2032, by 1.0% of the total number of shares of common stock outstanding on December 31 of the preceding calendar year. As of December 31, 2021, no shares had been issued under the ESPP, and 259,689 shares authorized under the ESPP were available for issuance. In January 2022, the Company issued 26,804 shares under the ESPP.

Liability for Restricted Stock

In 2017, the Company entered into restricted stock purchase agreements with various employees for 3,518,842 shares of common stock, which are subject to time-based vesting. The Company had the option to repurchase any unvested shares at the original purchase price upon any voluntary or involuntary separation of an employee from the Company. The shares purchased pursuant to the restricted stock purchase agreements were not deemed, for accounting purposes, to be outstanding until those shares vest. The cash received in exchange for unvested shares of the restricted stock granted were recorded as a liability on the accompanying balance sheet and were transferred into common stock and additional paid-in capital as the restricted stock vested.

The Company issued 532,455 shares in 2020 in connection with the vesting of the restricted stock. As of December 31, 2020, no shares remained subject to repurchase by the Company.

Stock-Based Compensation Expense

The Company recognized stock-based compensation expense as follows (in thousands):

	Year Ended December 31,	
	2021	**2020**
Research and development	$ 2,486	$ 581
General and administrative	606	284
Stock-based compensation expense	$ 3,092	$ 865

The weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of the stock option grants were as follows:

	Year Ended December 31,	
	2021	**2020**
Risk-free interest rate	0.8% - 1.3%	0.2% - 0.9%
Expected volatility	113.2% - 118.7%	96.9% - 116.2%
Expected term (in years)	5.0 – 6.1	1.5 – 6.1
Expected dividend yield	0%	0%

As of December 31, 2021, the unrecognized compensation cost related to outstanding options was $9.8 million and is expected to be recognized as expense over approximately 3.1 years.

The weighted average assumptions used in Black-Scholes option pricing model to estimate the fair value of purchase rights granted under the ESPP were as follows:

	Year Ended December 31, 2021
Risk-free interest rate	0.1%
Expected volatility	127.8%
Expected term (in years)	1.4
Expected dividend yield	0%

As of December 31, 2021, there was $0.5 million of unrecognized compensation cost related to the ESPP and is expected to be recognized over approximately 1.5 years.

The determination of the fair value of share-based payment awards utilizing the Black-Scholes option-pricing model is affected by the Company's stock price and the following assumptions:

Risk-free interest rate. The risk-free interest rate assumption is based on the U.S. Treasury instruments, the terms of which were consistent with the expected term of the Company's stock-based awards.

Expected volatility. Due to the Company's limited operating history and lack of company-specific historical or implied volatility, the expected volatility assumption was determined by examining the historical volatilities of a group of industry peers whose share prices are publicly available.

Expected term. The expected term represents the weighted-average period the stock-based awards are expected to be outstanding. The Company uses the simplified method for estimating the expected term. The simplified method calculates the expected term as the average of the time-to-vesting and the contractual life of the stock-based awards.

Expected dividend yield. The expected dividend assumption is based on the Company's history and expectation of dividend payouts. The Company has not paid and does not intend to pay dividends.

Forfeitures. The Company reduces stock-based compensation expense for actual forfeitures during the period.

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance consist of the following:

	As of December 31,	
	2021	2020
Stock options	1,734,696	882,942
Reserved for future equity award grants	2,933,930	582,203
Reserved for future ESPP issuances	259,689	—
Convertible preferred stock	—	15,069,330
Common stock reserved for future issuance	4,928,315	16,534,475

Note 9 – License and Clinical Supply Agreements

The Company has entered into license agreements, accounted for as asset acquisitions, under which the Company is required to use commercially reasonable efforts to meet certain specified development and regulatory milestones related to the licensed technologies within specified time periods. In consideration of the rights granted to the Company under the agreements, the Company is required to make cash milestone payments to the licensors upon the completion of certain development, regulatory and commercial milestones. For the arrangements that the Company accounted for as asset acquisitions, contingent consideration liabilities are recorded as an additional cost of the acquired assets when the contingency is resolved, and the consideration is paid or becomes payable. Additionally, the Company has agreed to pay royalties on net sales of products applicable to the license agreements. The Company may terminate the agreements upon written notice to the licensors.

Daiichi Sankyo License Agreement

On September 2, 2020, the Company licensed the rights to milademetan (DS-3032b) for all human prophylactic or therapeutic uses in all countries and territories of the world from Daiichi Sankyo Company, Limited, ("Daiichi Sankyo"), a Japanese corporation (the "Daiichi Sankyo License Agreement"). Daiichi Sankyo conducted clinical studies of milademetan prior to the Company's licensing the rights to this product. The Company refers to this product candidate as milademetan.

In accordance with the terms of the Daiichi Sankyo License Agreement, the Company paid Daiichi Sankyo an initial upfront payment of $5.0 million during the year ended December 31, 2020.

Under the Daiichi Sankyo License Agreement, the Company obtained worldwide, sublicensable exclusive rights to seven families of patents with respect to milademetan. The Company is solely responsible under the Daiichi Sankyo License Agreement for the research, development and registration of milademetan. Pursuant to the Daiichi Sankyo License Agreement, Daiichi Sankyo had the right to continue to conduct three clinical trials and prepare final reports with respect to these clinical trials, and such right expires upon all subjects completing the study treatment. The Company has agreed to reimburse Daiichi Sankyo certain third-party expenses incurred while conducting such trials. The Company made clinical trials payments of $0.2 million under the Daiichi Sankyo License Agreement for the year ended December 31, 2021. The Company made no clinical trials payments to Daiichi Sankyo for the year ended December 31, 2020. As of December 31, 2021, the accrued Daiichi Sankyo reimbursable clinical trials costs were $2.0 million, which was recorded in accrued research and development in the balance sheet.

The Company is required to make aggregate future milestone payments of up to $222.5 million, contingent on the attainment of certain development, regulatory and sales milestones. On July 20, 2021, the Company announced that the first patient has been randomized in the multicenter, open-label, Phase 3 registrational trial (MANTRA) evaluating milademetan for the treatment of de-differentiated liposarcoma. Accordingly, pursuant to the Daiichi Sankyo License Agreement, the Company recorded $5.5 million in milestone fees as research and development expense in the statement of operations. Of the $5.5 million milestone fees, $2.5 million was paid in the third quarter of 2021 and $3.0 million was accrued as part of accrued research and development in the balance sheet as of December 31, 2021.

Additionally, the Company is required to pay Daiichi Sankyo a high single digit royalty based on the annual net sales of the Products, subject to reduction at an agreed rate upon the expiration of the licensed patent in the particular country where the Products are sold. To date, no royalty payments have been made to Daiichi Sankyo under the Daiichi Sankyo License Agreement. The royalty obligation terminates on a country-by-country and Product-by-Product basis on the later of: (i) loss of all market exclusivity for such Product in such country, (ii) the last-to-expire patent that covers the Licensed Compound or the Product in such country and (iii) twelve years from launch of the first Product sold by the Company in such country.

Unless sooner terminated or extended, the Daiichi Sankyo License Agreement will remain in full force and effect until the Company, its affiliates and its sublicensees cease all development and commercial activity related to milademetan. Either party may terminate the Daiichi Sankyo License Agreement for cause in the event of an uncured material breach (subject to a 90-day cure period). However, the Company may only terminate the Daiichi Sankyo License Agreement with respect to the countries affected by such uncured material breach. Daiichi Sankyo may also terminate the Daiichi Sankyo License Agreement in the event of Rain's bankruptcy or insolvency. Additionally, Daiichi Sankyo may terminate the Daiichi Sankyo License Agreement immediately upon written notice if the Company, its affiliates or its sublicensors initiate or join any challenge to the validity or enforceability of a licensed patent, subject to certain exclusions. Furthermore, the Company may terminate the Daiichi Sankyo License Agreement in its entirety or on a country-by-country basis for bona fide material concerns regarding the (i) lack of safety for human use arising from toxicity of the Licensed Compound or Product(s), (ii) lack of efficacy of the Licensed Compound or Product(s) or (iii) adverse economic impact to the Company in connection with its continued development of the Products, in each case, upon six months' prior written notice to Daiichi Sankyo. In addition, if the Company is acquired by a third party that is developing and commercializing a competing compound and the acquiring party decides not to discontinue the development or commercialization of such competing compound, such third party must terminate the Daiichi Sankyo License Agreement within 30 days of such acquisition if it does not discontinue such development or commercialization. Upon termination of the Daiichi Sankyo License Agreement by Daiichi Sankyo for the Company's uncured material breach or by the Company for its bona fide material concerns regarding the safety, efficacy or adverse economic impacts relating to the Licensed Compound or Products, or its development thereof, the Company is required to, among other actions, if requested by Daiichi Sankyo (i) transfer to Daiichi Sankyo ongoing clinical trials, data, reports, records

and materials, (ii) grant to Daiichi Sankyo an exclusive, irrevocable, sublicensable, fully paid-up license under any patents and know-how that are controlled and actually used by the Company at the time of termination in connection with the Products to allow Daiichi Sankyo exploit the Licensed Compound or Products in countries that are affected by the termination, (iii) grant to Daiichi Sankyo an exclusive, irrevocable, sublicensable, fully paid up license to use trademarks that are specific to the Products and (iv) assign any applicable sublicenses.

Drexel License Agreement and Sponsored Research Agreement

On July 30, 2020 (the "Effective Date"), the Company entered into an intellectual property license agreement (the "Drexel License Agreement") with Drexel University ("Drexel"). Pursuant to the Drexel License Agreement, Drexel granted to the Company (i) a worldwide, exclusive license to make and commercialize products under a single issued patent and two patent applications related to RAD52 inhibitors for the treatment of cancer (the "Patent Rights") and (ii) a worldwide, nonexclusive license to make, use and commercialize certain technical information and know-how related to the Patent Rights. The license grant includes the right to sublicense after the first anniversary of the Effective Date, subject to express conditions set forth in the Drexel License Agreement.

The Company is obligated to use commercially reasonable efforts to (i) develop, commercialize, market and sell licensed products in a manner consistent with a development plan and (ii) achieve certain milestone events, including, among other things, receiving investigational new drug application ("IND") approval for a licensed product by the fourth anniversary of the Effective Date. Under the Drexel License Agreement, for a period of five years from the Effective Date, the Company is granted a first option to license Drexel's rights in certain improvements, developments or inventions developed by Drexel (or jointly by the parties) during the five-year period that are directly related to the licensed products or to RAD52 or compounds that have been generated to specifically target RAD52.

In addition to a one-time, non-refundable initiation fee of $20,000 paid in four equal installments of $5,000 each within ten days after the Effective Date and six, twelve and eighteen months after the Effective Date, the Drexel License Agreement requires the Company to make further payments to Drexel of up to an aggregate of $6.25 million, for the achievement of specified development milestones for certain licensed products. The Company is also required to reimburse Drexel (i) after the filing of the first IND for the first licensed product, for all costs related to the filing, prosecution and maintenance of the Patent Rights accumulated prior to the Effective Date, and (ii) for all reasonable costs related to the filing, prosecution and maintenance of the Patent Rights after the Effective Date. In addition, the Company is also required to pay Drexel, on a quarterly basis, a low single digit royalty on net sales by the Company, its affiliates and sublicensees of certain licensed products, subject to specified reductions and a minimum quarterly royalty payment of up to $6,250.

Lastly, the Company is also obligated to pay Drexel (i) an annual license maintenance fee of $15,000 commencing upon filing of the first IND for a licensed product until the first sale of the first licensed product, (ii) a sublicense fee of low double digits percentage on all consideration received by the Company from its sublicensees, subject to certain reductions and (iii) a one-time transaction fee equal to the actual amount of Drexel's licensing and legal expenses in connection with the Drexel License Agreement and the Sponsored Research Agreement the parties simultaneously entered into with the Drexel License Agreement (the Sponsored Research Agreement).

The Company made payments of $34,387 and $11,720 under the Drexel License Agreement for the years ended December 31, 2021 and 2020, respectively.

Unless sooner terminated or extended, the term of the Drexel License Agreement with respect to any licensed product and country continues until the later of (i) the expiration or abandonment of the last-to-expire valid claim of the Patent Rights that covers the sale of such licensed product in such country, (ii) the expiration of any granted statutory period of marketing and/or data exclusivity for such licensed product that confers upon the Company exclusive commercialization, (iii) the month of the first sale of a generic equivalent of such licensed product in such country and (iv) ten years after the first sale of the first licensed product.

The Company may terminate the Drexel License Agreement at any time by providing 60 days' prior written notice to Drexel, in which case the Company will be required to cease exploitation of all licensed products, terminate all permitted sublicenses and pay all amounts owed to Drexel under the Drexel License Agreement and the Sponsored Research Agreement through the effective date of termination. Drexel may terminate the Drexel License Agreement for the Company's uncured material breach (with 30-135 day cure periods), for the

Company's bankruptcy or insolvency, for the Company's uncured material default under the Sponsored Research Agreement, or if the Company challenges the validity or enforceability of the licensed patent rights.

Roche Clinical Supply Agreement

In December 2021, the Company entered into a clinical supply agreement with Roche for the supply of the anti-Programmed Death Ligand-1 (PD-L1) monoclonal antibody, atezolizumab. Clinical trials are planned to evaluate milademetan, in combination with atezolizumab for the treatment of patients in genetically selected populations. Under this agreement, Rain is the sponsor of the anticipated clinical trials, and Roche will supply atezolizumab. The Company does not have any financial commitments to Roche under this agreement.

Note 10 – Commitments and Contingencies

Leases

In September 2018, the Company entered into a noncancelable operating lease agreement for office space for its corporate headquarters in Newark, California with an initial term of 5.25 years. The lease commenced in January 2019 and ends March 2024. Under the terms of the lease, the Company pays annual base rent, subject to an annual fixed percentage increase of 3% on March 1st of each year. The Company is obligated to pay for its share of direct expenses including operating expense and taxes, which are considered variable lease costs and are expensed as incurred.

In March 2020, Governor Newsom issued State of California Executive Order No. N-33-20 instructing all individuals in California to stay at home due to the COVID-19 pandemic. In connection with such order, the Company entered into an amendment to the noncancelable operating lease agreement in June 2020. The amendment provided the Company rent relief for three months in 2020. In consideration of the rent relief, the Company agreed to adjust the base rent annual fixed percentage increase of 3% on February 1st of each year and extend the lease until September 2024. The amendment was determined to be a lease modification that qualified as a change of accounting on the existing lease and not a separate contract. Remeasurement of the right-of-use asset and operating lease liabilities at the date of modification did not result in a material increase of the right-of-use asset and operating lease liabilities.

The future minimum lease payments required under the operating lease are summarized as follows (in thousands):

	As of December 31, 2021
2022	167
2023	171
2024	129
Total minimum lease payments	$ 467
Less: amount representing interest	(55)
Present value of operating lease liabilities	$ 412
Operating lease liabilities, current	160
Operating lease liabilities, non-current	252
Total operating lease liabilities	$ 412
Weighted-average remaining lease term (in years)	2.7
Weighted-average incremental borrowing rate	10.0%

The table below summarizes the Company's lease costs and cash payments in connection with operating lease obligations (in thousands):

	Year Ended December 31,	
	2021	2020
Total operating lease expense	$ 160	$ 130
Operating cash flows used for operating lease	$ 162	$ 130

Contingencies

In the event the Company becomes subject to claims or suits arising in the ordinary course of business, the Company would accrue a liability for such matters when it is probable that future expenditures will be made, and such expenditures can be reasonably estimated.

Note 11 – Employee Benefits

The Company has a defined contribution 401(k) plan available to eligible employees. Under the terms of the plan, employees may make voluntary contributions as a percent of compensation, limited to the maximum amount allowable under federal tax regulations. The Company, at its discretion, may make certain contributions to the 401(k) plan. The Company made matching contributions of $233,831 and $79,000 for the years ended December 31, 2021 and 2020, respectively.

Note 12 – Income Taxes

The Company recorded de minimis state income tax expense for the years ended December 31, 2021 and 2020 primarily as a result of the Company maintaining a full valuation allowance against its loss from operations for tax purposes. The net losses for the years ended December 31, 2021 and 2020 were generated solely in the United States.

The provision for income taxes is comprised of the following (in thousands):

	Year Ended December 31,	
	2021	2020
Current:		
State	$ 2	$ —
Provision for income taxes	$ 2	$ —

The provision for income taxes differs from the amount computed by applying the federal statutory income tax rate to income before taxes as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Federal tax benefit at statutory rate	$ (10,792)	$ (4,426)
State taxes	604	(1,640)
Change in fair value of convertible promissory notes	—	425
Non-deductible expenses	490	(11)
Convertible note interest	—	28
R&D credits	(2,177)	(187)
Change in valuation allowance	11,870	5,797
Other	7	14
Provision for income taxes	$ 2	$ —

Deferred income taxes reflect the tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The components of deferred income tax assets and liabilities are as follows (in thousands):

	As of December 31,	
	2021	2020
Deferred tax assets:		
Accrued expenses and other	$ 407	$ 188
Fixed assets	10	11
Intangibles	2,378	1,698
Net operating losses	16,993	8,254
R&D and Orphan Drug credits	2,615	438
Stock-based compensation	287	236
Lease liability	87	135
Other	2	—
Total deferred tax assets	$ 22,779	$ 10,960
Valuation allowance	(22,698)	(10,827)
Total net deferred tax assets	$ 81	$ 133
Deferred tax liabilities:		
Right-of-use asset	$ (81)	(133)
Total deferred tax liabilities	$ (81)	$ (133)
Net deferred tax assets	$ —	$ —

Realization of deferred tax assets is dependent upon the Company's ability to generate sufficient taxable income within the carryforward period. In assessing the realizability of some portion or all of the deferred tax assets, the Company evaluated both positive and negative evidence to determine if some or all of its deferred tax assets should be recognized. Based on the available objective evidence, the Company has concluded it is not more likely than not that its deferred tax assets will be realized.

Therefore, a valuation allowance in the amount of $22.7 million has been recorded for 2021 against the Company's deferred tax assets.

The net valuation allowance increased by $11.9 million and $5.8 million during the years ended December 31, 2021 and 2020, respectively.

The following table sets forth the Company's federal and state net operating loss carryforwards as of December 31, 2021 (in thousands):

	Amount	Expiration Years
Net operating losses, Federal—pre TCJA	$ 159	2037
Net operating losses, Federal—post TCJA	$ 69,085	N/A
Net operating losses, state	$ 27,801	2031-2041
R&D and Orphan Drug credits, Federal	$ 3,110	2039-2041
R&D credits, California	$ 948	N/A

Utilization of the Company's net operating loss and R&D credits may be subject to substantial limitations due to the ownership changes limitations provided by the Internal Revenue Code and similar state provisions. Such annual limitations could result in the expiration of the net operating loss before their utilization. Sections 382 and 383 of the Internal Revenue Code ("IRC Sections 382 and 383") impose limitations on a corporation's ability to utilize its net operating losses and credit carryforwards if it experiences an "ownership change" as defined by IRC Sections 382 and 383. The Company has performed an analysis under Section 382 of the Internal Revenue Code which subjects the amount of pre-change net operating losses and certain other tax attributes that can be utilized to an annual limitation. Based on the analysis, ownership changes have occurred in 2018 and 2021.

The Company is required to recognize in the financial statements the impact of a tax position, if that position is more likely than not of being sustained on audit, based on the technical merits of the position.

The following table reflects changes in the gross unrecognized tax benefits (in thousands):

	Year Ended December 31,	
	2021	2020
Balance at beginning of year	$ 402	$ 215
Additions based on tax positions related to current year	1,040	187
Balance at end of year	$ 1,442	$ 402

The Company recognizes interest and penalties as a component of income tax expense. There were no interest or penalties recognized in the statements of operations and comprehensive loss. The total unrecognized tax benefits of $1.4 million and $0.4 million were recorded as of December 31, 2021 and 2020, respectively, which, if recognized currently, should not impact the effective tax rate due to the Company maintaining a full valuation allowance. The Company expects the unrecognized tax benefits will not change significantly within the next 12 months.

The Company is subject to examination by the United States federal and state tax authorities for the tax years 2017 and later.

Note 13 – Net Loss Per Share

The following tables summarize the computation of the basic and diluted net loss per share (in thousands, except share and per share data):

	Year Ended December 31,	
	2021	2020
Numerator:		
Net loss	$ (51,394)	$ (21,083)
Denominator:		
Weighted-average shares of common stock outstanding, basic and diluted	19,405,833	3,519,728
Less: weighted-average unvested common stock	—	(167,878)
Weighted-average shares used to compute net loss per share, basic and diluted	19,405,833	3,351,850
Net loss per share, basic and diluted	$ (2.65)	$ (6.29)

The following table sets forth the outstanding potentially dilutive securities that have been excluded in the calculation of diluted net loss per share because their inclusion would be anti-dilutive:

	As of December 31,	
	2021	2020
Stock options	1,734,696	882,942
Series A convertible preferred stock	—	3,731,208
Series B convertible preferred stock	—	12,542,198
ESPP shares	85,031	—
Total	1,819,727	17,156,348

Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

Item 9A. CONTROLS AND PROCEDURES.

Management's Evaluation of Disclosure Controls and Procedures

As of December 31, 2021, our management, with the participation and supervision of our principal executive officer and our principal financial officer, evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost benefit relationship of possible controls and procedures. Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective as of December 31, 2021 to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and our principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Controls over Financial Reporting

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting due to a transition period established by rule of the SEC for newly public companies.

Attestation Report of the Registered Public Accounting Firm

As an emerging growth company, we are not required to provide an attestation report on our internal control over financial reporting issued by the Company's independent registered public accounting firm.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2021, that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. OTHER INFORMATION.

None.

Item 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

Not applicable.

PART III

Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

The information required by this Item will be set forth in the Company's definitive proxy statement to be filed with the SEC in connection with the Company's 2022 Annual Meeting of Stockholders (the "2022 Proxy Statement") within 120 days of the end of the Company's fiscal year ended December 31, 2021 and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive, principal financial and principal accounting officers, or persons performing similar functions. Our Code of Business Conduct and Ethics is posted on our website located at www.rainthera.com, under "Governance Documents." We intend to disclose on our website any amendments to, or waivers from, the code of business conduct and ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K within four business days following the date of the amendment or waiver.

Item 11. EXECUTIVE COMPENSATION.

The information required by this Item will be set forth in the Company's 2022 Proxy Statement 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 will be set forth in the Company's 2022 Proxy Statement and is incorporated herein by reference.

Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.

The information required by this Item will be set forth in the Company's 2022 Proxy Statement and is incorporated herein by reference.

Item 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES.

The information required by this Item will be set forth in the Company's 2022 Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

The following documents are filed as part of this report on Form 10-K:

(a) Financial Statements:

Reference is made to the Index to the registrant's Financial Statements under Item 8 in Part II of this Form 10-K.

(b) Financial Statement Schedules:

Financial statement schedules have been omitted because the required information is not present or not present in the amounts sufficient to require submission of the schedule or because the information is already included in the financial statements or notes thereto.

(c) Exhibits:

The documents listed in the following Exhibit Index are incorporated by reference or are filed with this Annual Report on Form 10-K.

Exhibit Index

Exhibit Number	Description of Exhibit
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference from Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on April 27, 2021 (Commission File No. 001-40356)).
3.2	Bylaws of the Registrant (incorporated by reference from Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed on April 27, 2021 (Commission File No. 001-40356)).
4.1	Form of Common Stock Certificate of the Registrant (incorporated by reference from Exhibit 4.1 of the Registrant's Amendment No. 1 to Registration Statement on Form S-1 filed on April 9, 2021 (Commission File No. 333-254998)).
4.2	Amended and Restated Investors' Rights Agreement, dated September 2, 2020, by and among the Registrant and certain of its stockholders (incorporated by reference from Exhibit 4.2 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
4.3*	Description of Securities.
10.1	Form of Indemnification Agreement for directors and executive officers (incorporated by reference from Exhibit 10.1 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.2+	Amended and Restated 2018 Stock Option/Stock Issuance Plan and form of award agreement thereunder (incorporated by reference from Exhibit 10.2 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.3+	2021 Equity Incentive Plan (incorporated by reference from Exhibit 10.3 of the Registrant's Amendment No. 2 to Registration Statement on Form S-1 filed on April 19, 2021 (Commission File No. 333-254998)).
10.4+	2021 Employee Stock Purchase Plan (incorporated by reference from Exhibit 10.4 of the Registrant's Amendment No. 2 to Registration Statement on Form S-1 filed on April 19, 2021 (Commission File No. 333-254998)).
10.5+	Director Offer Letter, dated March 19, 2018, by and between the Registrant and Tran Nguyen (incorporated by reference from Exhibit 10.5 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.6+	Director Offer Letter, dated March 19, 2018, by and between the Registrant and Peter Radovich (incorporated by reference from Exhibit 10.6 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.7+	Employment Agreement, dated September 10, 2020, by and between the Registrant and Avanish Vellanki (incorporated by reference from Exhibit 10.7 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.8+	Employment Agreement, dated September 10, 2020, by and between the Registrant and Robert Doebele (incorporated by reference from Exhibit 10.8 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.9+	Offer Letter, dated October 1, 2020, by and between the Registrant and Nelson Cabatuan (incorporated by reference from Exhibit 10.9 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).

10.10#	License Agreement, dated September 2, 2020, between the Registrant and Daiichi Sankyo Company, Limited (incorporated by reference from Exhibit 10.10 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.11#	Intellectual Property License Agreement, dated July 30, 2020, by and between the Registrant and Drexel University (incorporated by reference from Exhibit 10.11 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.12	Office Lease Agreement, dated September 25, 2018, between the Registrant and BSP Senita 8000 Jarvis, LLC, as amended (incorporated by reference from Exhibit 10.12 of the Registrant's Registration Statement on Form S-1 filed on April 2, 2021 (Commission File No. 333-254998)).
10.13	Exchange Agreement, dated April 17, 2021, by and among the Registrant and the stockholders listed therein (incorporated by reference from Exhibit 10.13 of the Registrant's Amendment No. 2 to Registration Statement on Form S-1 filed on April 19, 2021 (Commission File No. 333-254998)).
10.14	Rain Therapeutics Inc. Executive Severance Plan (incorporated by reference from Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed on August 17, 2021 (Commission File No. 001-40356)).
23.1*	Consent of Independent Registered Public Accounting Firm.
31.1*	Certification of the principal executive officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934.
31.2*	Certification of the principal financial officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934.
32.1 (1)	Certification of the principal executive officer and principal financial officer pursuant to 18 U.S.C. Section 1350 and Rule 13a-14(b) under the Securities Exchange Act of 1934
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document.
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

* Filed herewith.
\+ Indicates management contract or compensatory plan.
\# Portions of the exhibit have been omitted for confidentiality purposes.

(1) The certifications on Exhibit 32 hereto are deemed not "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that Section. Such certifications will not be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

Item 16. FORM 10-K SUMMARY.

None.

SIGNATURES

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

Company Name

Date: March 3, 2022

By: /s/ Avanish Vellanki
Avanish Vellanki
Chairman and Chief Executive Officer
(principal executive officer)

Date: March 3, 2022

By: /s/ Nelson Cabatuan
Nelson Cabatuan
Senior Vice President of Finance and Administration
(principal financial and accounting officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Avanish Vellanki, Nelson Cabatuan and Jamie S. Blose, and each of them, the true and lawful attorneys-in-fact and agents of the undersigned, with full power of substitution and resubstitution, for and in the name, place and stead of the undersigned, to sign in any and all capacities (including, without limitation, the capacities listed below), this Annual Report on Form 10-K, any and all amendments thereto, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, and hereby grants to such attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and anything necessary to be done to enable the registrant to comply with the provisions of the Securities Exchange Act and all the requirements of the Securities and Exchange Commission, as fully to all intents and purposes as the undersigned might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitute, or substitutes, may lawfully do or cause to be done by virtue hereof.

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/ Avanish Vellanki **Avanish Vellanki**	Chief Executive Officer and Chairman (*principal executive officer*)	March 3, 2022
/s/ Nelson Cabatuan **Nelson Cabatuan**	Senior Vice President of Finance and Administration (*principal financial and accounting officer*)	March 3, 2022
/s/ Franklin Berger **Franklin Berger**	Director	March 3, 2022
/s/ Aaron Davis **Aaron Davis**	Director	March 3, 2022
/s/ Gorjan Hrustanovic **Gorjan Hrustanovic, Ph.D.**	Director	March 3, 2022

/s/ Tran Nguyen **Tran Nguyen**	Director	March 3, 2022
/s/ Peter Radovich **Peter Radovich**	Director	March 3, 2022
/s/ Stefani Wolff **Stefani Wolff**	Director	March 3, 2022

Exhibit 4.3

DESCRIPTION OF REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

General

The following is a summary of the material terms of our capital stock, as well as other material terms of our amended and restated certificate of incorporation and amended and restated bylaws and certain provisions of Delaware law. This summary does not purport to be complete and is qualified in its entirety by the provisions of our certificate of incorporation and bylaws, copies of which are filed as exhibits to our Annual Report on Form 10-K, to which this exhibit is also appended.

Our authorized capital stock consists of 200,000,000 shares of common stock, $0.001 par value per share, 50,000,000 shares of non-voting common stock, $0.001 par value per share, and 10,000,000 shares of "blank check" preferred stock, $0.001 par value per share.

Common Stock and Non-Voting Common Stock

Our amended and restated certificate of incorporation authorizes the issuance of up to 200,000,000 shares of our common stock and 50,000,000 shares of our non-voting common stock. All outstanding shares of our common stock and non-voting common stock are validly issued, fully paid and nonassessable.

Holders of our common stock and our non-voting common stock have identical rights, provided that, (i) except as otherwise expressly provided in our amended and restated certificate of incorporation or as required by applicable law, on any matter that is submitted to a vote by our stockholders, holders of our common stock are entitled to one vote per share of common stock, and holders of our non-voting common stock are not entitled to any votes per share of non-voting common stock, including for the election of directors, and (ii) holders of our common stock have no conversion rights, while holders of our non-voting common stock shall have the right to convert each share of our non-voting common stock into one share of common stock at such holder's election, provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 9.99% of our common stock immediately prior to and following such conversion (the "Beneficial Ownership Limitation"), unless otherwise as expressly provided for in our amended and restated certificate of incorporation. However, the Beneficial Ownership Limitation may be increased or decreased to any other percentage (not to exceed 19.99%) designated by such holder of non-voting common stock upon 61 days' notice to us.

Voting Rights

Our common stock is entitled to one vote per share on any matter that is submitted to a vote of our stockholders, and our non-voting common stock is not entitled to any votes per share. Except as otherwise expressly provided in our amended and restated certificate of incorporation or required by applicable law, all shares of common stock and non-voting common stock will have the same rights and privileges and rank equally, share ratably, and be identical in all respects for all matters, including those described below.

Dividends

Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock and non-voting common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

Liquidation Rights

On our liquidation, dissolution, or winding-up, the holders of common stock and non-voting common stock will be entitled to share equally, identically, and ratably in all assets remaining after the payment of any liabilities, liquidation preferences and accrued or declared but unpaid dividends, if any, with respect to any outstanding

preferred stock, unless a different treatment is approved by the affirmative vote of the holders of a majority of the outstanding shares of such affected class, voting separately as a class.

Preferred Stock

Under the terms of our amended and restated certificate of incorporation, our board of directors (the "Board") has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the dividend, voting and other rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our Board may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock and non-voting common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of our common stock and non-voting common stock and the voting and other rights of the holders of our common stock and non-voting common stock. We have no current plans to issue any shares of preferred stock.

Registration Rights

We are party to the amended and restated investors' rights agreement, effective as of September 2, 2020 (the "IRA") which provides that certain of our stockholders have certain registration rights described below. The registration of shares of our common stock pursuant to the exercise of registration rights described below would enable holders to sell these shares without restriction under the Securities Act of 1933, as amended (the "Securities Act") when the registration statement is declared effective. We will pay all expenses related to any demand, piggyback, or Form S-3 registration described below, with the exception of underwriting discounts and commissions.

The registration rights described below will expire upon the earliest to occur of: (i) April 27, 2024; (ii) the closing of a deemed liquidation event (as defined in our amended and restated certificate of incorporation) or (iii) with respect to any particular holder, at such time that such holder can sell its shares, under Rule 144 or another similar exemption under the Securities Act, during any three-month period without registration.

Demand Registration Rights

The holders of registrable securities are entitled to certain demand registration rights. At any time after October 19, 2021, holders who are major investors and hold a majority of the registrable securities then outstanding may request that we register at least 40% of the registrable securities then outstanding.

Piggyback Registration Rights

Subject to certain specified exceptions, if we propose to register any of our securities under the Securities Act either for our own account or for the account of other stockholders, the holders of shares having registration rights are entitled to written notice and certain "piggyback" registration rights allowing them to include their shares in our registration statement. These registration rights are subject to specified conditions and limitations, including the right of the underwriters, in their sole discretion, to limit the number of shares included in any such offering under certain circumstances, but not below 30% of the total amount of securities included in such offering.

Form S-3 Registration Rights

At any time after we are qualified to file a registration statement on Form S-3, and subject to limitations and conditions, holders who are major investors and hold at least 30% of the registrable securities then outstanding may make a written request that we prepare and file a registration statement on Form S-3 under the Securities Act covering their shares, so long as the aggregate price to the public, net of the underwriters' discounts and commissions, is at least $5,000,000. We will prepare and file the Form S-3 registration statement as requested, unless, in the good faith judgment of our Board, such registration would be materially detrimental to the company and its stockholders and filing should be deferred. We may defer only once in any 12-month period, and such deferral shall not exceed 90 days after receipt of the request. In addition, we are not obligated to prepare or file any of these registration statements (i) within 30 days before or 90 days after the effective date of a registration

statement pursuant to demand or piggyback registration rights or (ii) if two of these registrations have been completed within any 12-month period.

Anti-Takeover Effects of Our Amended and Restated Certificate of Incorporation, Amended and Restated Bylaws and Delaware Law

Our amended and restated certificate of incorporation and our amended and restated bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our Board rather than pursue non-negotiated takeover attempts.

- **Issuance of undesignated preferred stock**: Under our amended and restated certificate of incorporation, our Board has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our Board. The existence of authorized but unissued shares of preferred stock enables our Board to make it more difficult to attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.
- **Classified board**: Our amended and restated certificate of incorporation establishes a classified Board consisting of three classes of directors, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders to succeed the directors of the same class whose terms are then expiring, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of our Board.

- **Election and removal of directors and board vacancies**: Our amended and restated certificate of incorporation provides that directors will be elected by a plurality vote. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that our Board has the right to increase or decrease the size of the Board and to fill vacancies on the Board. Directors may be removed only for cause by the affirmative vote of the holders of at least 66 2/3% of the votes that all our stockholders would be entitled to cast in an annual election of directors. Only our Board is authorized to fill vacant directorships. In addition, the number of directors constituting our Board may be set only by resolution adopted by a majority vote of the directors then in office. These provisions prevent stockholders from increasing the size of our Board and gaining control of our Board by filling the resulting vacancies with its own nominees.
- **Requirements for advance notification of stockholder nominations and proposals**: Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors that specify certain requirements as to the timing, form and content of a stockholder's notice. Business that may be conducted at an annual meeting of stockholders will be limited to those matters properly brought before the meeting. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at annual meetings of stockholders.
- **No written consent of stockholders**: Our amended and restated certificate of incorporation provides that all stockholder actions be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our amended and restated bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

- **No stockholder ability to call special meetings:** Our amended and restated certificate of incorporation and amended and restated bylaws provide that only our Board may be able to call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders.

- **Amendments to certificate of incorporation and bylaws**: Any amendment to our amended and restated certificate of incorporation must be approved by a majority of our Board as well as, if required by law or our amended and restated certificate of incorporation, a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of provisions to Board classification, stockholder action, certificate amendments and liability of directors must be approved by not less than 66 2/3% of the outstanding shares entitled to vote on the amendment, voting together as a single class. Any amendment to our amended and restated bylaws must be approved by either a majority of our Board or not less than 66 2/3% of the outstanding shares entitled to vote on the amendment, voting together as a single class.

These provisions are designed to enhance the likelihood of continued stability in the composition of our Board and its policies, to discourage certain types of transactions that may involve an actual or threatened acquisition of our company and to reduce our vulnerability to an unsolicited acquisition proposal. We also designed these provisions to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Delaware General Corporation Law Section 203

As a Delaware corporation, we are also subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in a business combination specified in the statute with an interested stockholder (as defined in the statute) for a period of three years after the date of the transaction in which the person first becomes an interested stockholder, unless the business combination is approved in advance by a majority of the independent directors or by the holders of at least two-thirds of the outstanding disinterested shares. The application of Section 203 of the Delaware General Corporation Law could also have the effect of delaying or preventing a change of control of us.

Exclusive Forum Selection Clause

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the sole and exclusive forum to the fullest extent permitted by law for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a breach of fiduciary duty owed by any director, officer or other employee to us or our stockholders; (3) any action asserting a claim against us or any director or officer or other employee arising pursuant to the Delaware General Corporation Law; (4) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or bylaws; or (5) any other action asserting a claim that is governed by the internal affairs doctrine, shall be the Court of Chancery of the State of Delaware (or another state court or the federal court located within the State of Delaware if the Court of Chancery does not have or declines to accept jurisdiction), in all cases subject to the court's having jurisdiction over indispensable parties named as defendants. Our amended and restated certificate of incorporation provides that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act but the forum selection provisions will not apply to claims brought to enforce a duty or liability created by the Exchange Act. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against us or our directors or officers. It is possible that a court could find that such provisions are inapplicable for a particular claim or action or that such provisions are unenforceable. In addition, under the Securities Act, federal courts have concurrent jurisdiction over all suits brought to enforce any duty or liability created by the Securities Act, and investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

Transfer Agent and Registrar

American Stock Transfer & Trust Company, LLC serves as the transfer agent and registrar for our common stock.

Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol “RAIN.” Our non-voting common stock is not listed on any securities exchange.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-255548) pertaining to the Rain Therapeutics Inc. 2021 Equity Incentive Plan, the Rain Therapeutics Inc. 2021 Employee Stock Purchase Plan, and the Rain Therapeutics Inc. Amended and Restated 2018 Stock Option/Stock Issuance Plan of Rain Therapeutics Inc. of our report dated March 3, 2022, with respect to the financial statements of Rain Therapeutics Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2021.

/s/ Ernst & Young LLP

San Diego, California
March 3, 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, Avanish Vellanki, certify that:

1. I have reviewed this Annual Report on Form 10-K of Rain Therapeutics Inc.;

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

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

4. The registrant's other certifying officer 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 is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) 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

   (c) 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 3, 2022

By: /s/ Avanish Vellanki
Avanish Vellanki
Chairman 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, Nelson Cabatuan, certify that:

1. I have reviewed this Annual Report on Form 10-K of Rain Therapeutics Inc.;

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

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

4. The registrant's other certifying officer 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 is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) 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

   (c) 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 3, 2022

By: /s/ Nelson Cabatuan
Nelson Cabatuan
Senior Vice President of Finance and Administration
(principal financial and accounting officer)

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Rain Therapeutics Inc. (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

1. The Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

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

Date: March 3, 2022

By: /s/ Avanish Vellanki

Avanish Vellanki

Chairman and Chief Executive Officer
(principal executive officer)

Date: March 3, 2022

By: /s/ Nelson Cabatuan

Nelson Cabatuan

Senior Vice President of Finance and Administration
(principal financial and accounting officer)

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Note: A signed original of this written statement required by § 906 has been provided to Rain Therapeutics Inc. and will be retained by Rain Therapeutics Inc. and furnished to the Securities and Exchange Commission or its staff upon request.