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, 2022
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: 001-39263

Zentalis Pharmaceuticals, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**82-3607803**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1359 Broadway, Suite 1710 New York, New York	**10018**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code (212) 433-3791

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, $0.001 par value per share	ZNTL	The Nasdaq Global Market

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting stock held by non-affiliates of the registrant, as of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $1.30 billion based on the closing price of $28.10 as reported on The Nasdaq Global Market on such date. Solely for the purposes of this disclosure, shares of common stock held by executive officers, directors and certain stockholders of the registrant as of such date have been excluded because such holders may be deemed to be affiliates.

The number of shares of registrant's common stock outstanding as of February 27, 2023 was 59,418,460.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2022 are incorporated herein by reference in Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

BASIS OF PRESENTATION

Except where the context otherwise requires or where otherwise indicated, the terms “Zentalis,” “we,” “us,” “our,” “our company,” “Company” and “our business” refer: (1) following the consummation of our statutory conversion to a Delaware corporation on April 2, 2020, or the Corporate Conversion, in connection with our initial public offering, or IPO, to Zentalis Pharmaceuticals, Inc. and (2) prior to the completion of the Corporate Conversion, to Zentalis Pharmaceuticals, LLC.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential,” "design," "aim," or “continue” or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements about:

- our competitive position, including estimates and other information relating to our competitors and their products and product candidates, and our industry;
- our expectations, projections and estimates regarding our capital requirements, need for additional capital, financing our future cash needs, costs, expenses, revenues, capital resources, cash flows, financial performance, profitability, tax obligations, liquidity, growth, contractual obligations, the period of time our cash resources will fund our current operating plan, our internal control over financial reporting and disclosure controls and procedures;
- the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results;
- global supply chain issues and increased inflation and interest rates;
- the timing and focus of our ongoing and future preclinical studies and clinical trials, including the reporting of data from those studies and trials and the timing thereof and the timing of initiation of enrollment in our clinical trials;
- 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;
- our plans relating to dose optimization activities and the timing thereof;
- our and our collaborators' strategy, plans and expectations with respect to the development, manufacturing, supply, approval and commercialization of our product candidates and the timing thereof;
- the designs of our studies and the type of information and data expected from our studies and the expected benefits thereof;
- our ability to obtain and maintain any marketing authorizations and our ability to complete post-marketing requirements with respect thereto;
- the timing and amounts of payments from or to our collaborators and licensees, and the anticipated arrangements and benefits under our collaboration and license agreements, including with respect to milestones and royalties;
- our pipeline, including its potential, and our related research and development activities;
- our plans relating to our Cyclin E1 patient enrichment strategy and the timing of milestones related thereto;
- our plans relating to the further development of our product candidates, including program timelines, potential paths to registration, and additional indications we may pursue;
- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms and processes on a timely basis, or at all, with third-party payors for our product candidates, if approved;
- our plans, including the costs thereof, of development of any companion diagnostics;
- our plans to evaluate additional strategic opportunities to maximize the value of our pipeline;
- our plans to advance our ongoing research on protein degrader programs;
- our plans to advance IND-enabling studies for our product candidates, including our BCL-xL protein degrader product candidate;
- our plans to develop our product candidates in combination with other therapies;
- our existing collaborations 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 relating to commercializing our product candidates, if approved, including the geographic areas of focus and sales strategy;
- timing and likelihood of success of our research, development and commercialization efforts;
- timing of expected milestones and the announcement thereof;
- 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;
- the timing or likelihood of regulatory filings and approvals, including our expectation to seek an accelerated approval pathway and special designations for our product candidates for various diseases;
- our ability to obtain and maintain regulatory approval of our product candidates;
- existing regulations and regulatory developments in the United States, the European Union and other jurisdictions;
- our intellectual property position, including obtaining and maintaining patents, and the timing, outcome and impact of administrative, regulatory, legal and other proceedings relating to our patents and other proprietary and intellectual property rights, and the timing and resolution thereof;
- our facilities, lease commitments, and future availability of facilities;
- accounting standards and estimates, their impact, and their expected timing of completion;
- cybersecurity;
- expected ongoing reliance on third parties, including with respect to the development, manufacturing, supply and commercialization of our product candidates;
- insurance coverage;
- estimated periods of performance of key contracts;
- the need to hire additional personnel and our ability to attract and retain personnel, and our ability to provide competitive compensation and benefits; and
- the anticipated impact of the COVID-19 pandemic on our business.

The forward-looking statements in this Annual Report on Form 10-K are only predictions and are based largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of known and unknown risks, uncertainties, assumptions and other important factors, including those described under "Summary Risk Factors" below and in the sections in this Annual Report on Form 10-K entitled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this Annual Report on Form 10-K.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, they may turn out to be inaccurate and you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results, financial condition, performance or achievements could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

ZENTALIS™ and its associated logo are trademarks of Zentalis. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners. All website addresses given in this Annual Report on Form 10-K are for information only and are not intended to be an active link or to incorporate any website information into this document.

INDUSTRY AND OTHER DATA

This Annual Report on Form 10-K contains industry, market and competitive position data from our own internal estimates and research as well as industry and general publications and research surveys and studies conducted by third parties. Industry publications, studies and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our internal data and estimates are based upon information obtained from trade and business organizations and other contacts in the markets in which we operate and our management’s understanding of industry conditions. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research is reliable and the market definitions are appropriate, neither such research nor definitions have been verified by an independent source.

The industry in which we operate is subject to risks and uncertainties due to a variety of factors, including those described in Part I, Item 1A., “Risk Factors” in this Annual Report on Form 10-K. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part I, Item 1A., "Risk Factors" in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- 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 predict our future success and viability.
- We have incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future.
- We will require substantial additional capital to finance our operations. 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 our research and drug development programs or future commercialization efforts.
- We are substantially dependent on the success of our lead product candidates, azenosertib (ZN-c3) and/or ZN-d5, which are currently in clinical trials. If we are unable to complete development of, obtain approval for and commercialize these product candidates in a timely manner, our business will be harmed.
- The clinical trials of our product candidates may not demonstrate safety and efficacy to the satisfaction of the U.S. Food and Drug Administration, or FDA, or other comparable ex-U.S. regulatory authorities or otherwise produce positive results.
- If we are unable to successfully develop companion diagnostics for biomarkers that enable patient selection, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.
- We are developing our product candidates in combination with other therapies, which exposes us to additional risks.
- The regulatory approval processes of the FDA and other comparable ex-U.S. regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.
- We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be negatively impacted.
- Our success depends on our ability to protect our intellectual property and our proprietary platform. If we are unable to adequately protect our intellectual property and our proprietary platform, or to obtain and maintain issued patents which are sufficient to protect our product candidates, then others could compete against us more directly, which would negatively impact our business.
- Our existing collaborations are important to our business and future licenses may also be important to us and, if we are unable to maintain any of these collaborations, or if these arrangements are not successful, our business could be adversely affected.
- We rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct certain aspects of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.
- Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.
- The competition for qualified personnel is particularly intense in our industry. If we are unable to retain or hire key personnel, then we may not be able to sustain or grow our business.
- The COVID-19 pandemic has adversely impacted, and we expect will continue to adversely impact, our business, including our preclinical studies and clinical trials.

- Unfavorable global, political or economic conditions could adversely affect our business, financial condition or results of operations.

PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company focused on discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancers. We are developing a focused pipeline of potentially best-in-class oncology candidates. Our product candidates are:

- Azenosertib (ZN-c3), a potentially first-in-class Wee1 inhibitor for advanced solid tumors and hematological malignancies;
- ZN-d5, a B-cell lymphoma 2, or BCL-2, inhibitor for hematological malignancies and related disorders; and
- A heterobifunctional degrader of BCL-xL, a member of the anti-apoptotic BCL-2 proteins, for solid tumors and hematological malignancies.

We are currently evaluating azenosertib and ZN-d5 in multiple ongoing clinical trials and conducting studies to enable an Investigational New Drug, or IND, application for our BCL-xL product candidate. We also continue to use our extensive drug discovery experience and capabilities across cancer biology and medicinal chemistry, which we refer to as our Integrated Discovery Engine, to advance our ongoing research on protein degraders of undisclosed targets. We believe our product candidates are differentiated from current programs targeting similar pathways and, if approved, have the potential to significantly impact clinical outcomes of patients with cancer.

Strategy

Our goal is to become a leading oncology-focused biopharmaceutical company. Our strategy includes the following key components:

- ***Rapidly advance the clinical development of our potentially best-in-class and first-in-class Wee1 inhibitor, azenosertib, toward regulatory approval***. To date, our lead product candidate, azenosertib, has demonstrated a favorable safety profile and monotherapy anti-tumor activity across multiple tumor types in clinical trials. We have established a three-pronged clinical development plan for azenosertib: investigation as a monotherapy; in combination with chemotherapy and DNA damaging agents; and in combination with molecularly targeted agents. We are currently advancing multiple clinical trials of azenosertib in the following indications: recurrent or persistent uterine serous carcinoma, or USC; solid tumors; Cyclin E1 driven high-grade serous ovarian, fallopian tube or primary peritoneal cancer, collectively HGSOC; platinum-resistant ovarian, peritoneal or fallopian tube cancer; relapsed or refractory, or R/R, osteosarcoma; and BRAF V600E mutant metastatic colorectal cancer, or mCRC. In addition, the Dana-Farber Cancer Institute, or Dana Farber, is sponsoring a clinical trial of azenosertib in combination with chemotherapy in pancreatic cancer. We believe our clinical trials investigating azenosertib as a monotherapy in USC and Cyclin E1 driven HGSOC have the potential to generate data that would support a registration.
- ***Optimize the dose of azenosertib***. Our clinical development program for azenosertib includes activities to optimize dose and dosing schedule in order to enhance exposure, tolerability and clinical activity in both the monotherapy and combination settings. We plan to declare a monotherapy recommended Phase 2 dose, or RP2D, and provide an update on dose optimization activities, program timelines and potential paths to registration, in the first half of 2023. We believe our dose optimization work will allow us to benefit the broadest range of cancer patients and maximize value for all of our stakeholders.
- ***Execute our Cyclin E1 patient enrichment strategy for azenosertib***. Cyclin E1 acts at the G1-S checkpoint of the cell cycle and high Cyclin E1 protein expression drives premature entry into S-phase resulting in replicative stress and significantly increasing sensitivity to azenosertib. We have generated preclinical data that showed that high Cyclin E1 protein expression sensitized cancer cells to the anti-tumor effects of azenosertib. In addition, retrospective clinical data suggested that Cyclin E1 protein levels may be associated with clinical benefit from Wee1 inhibition. High Cyclin E1 protein expression and/or CCNE1 gene amplification in HGSOC is the focus of our ongoing Phase 1/2 clinical trial examining patient enrichment strategies for azenosertib. We plan to present our preclinical rationale for our Cyclin E1 patient enrichment strategy in the first half of 2023. In addition, we plan to disclose results from our Phase 1b clinical trial of azenosertib in combination with chemotherapy in platinum-resistant ovarian, peritoneal or fallopian tube cancer, including Cyclin E1 translational data, in the second half of 2023.

- ***Focus the clinical development of our potentially best-in-class BCL-2 inhibitor***. Our BCL-2 inhibitor, ZN-d5, was designed to have best-in-class potency, selectivity and pharmacokinetic, or PK, properties. We are focusing our clinical development of ZN-d5 on advancing our clinical trial investigating ZN-d5 as a monotherapy in R/R light chain amyloidosis, or AL amyloidosis, and our clinical trial investigating ZN-d5 in combination with azenosertib in R/R acute myeloid leukemia, or AML. We plan to announce interim data from our R/R AL amyloidosis trial and preliminary data from our R/R AML trial in the second half of 2023. We are also engaged in dose optimization activities for ZN-d5 and expect to declare a monotherapy RP2D for our clinical trial in R/R AL amyloidosis in the second half of 2023.
- ***Leverage our deep expertise and capabilities across cancer biology and medicinal chemistry to advance our preclinical programs***. In November 2022, we declared a development candidate for our BCL-xL protein degrader program, and we are working to advance the program through IND-enabling studies. We are also advancing our research on protein degraders of undisclosed targets utilizing our Integrated Discovery Engine.
- ***Collaborate under our existing strategic partnerships and evaluate additional strategic opportunities to maximize the value of our pipeline***. We have development collaborations with Pfizer Inc., or Pfizer, GlaxoSmithKline plc, or GSK, and Dana Farber for azenosertib. We will selectively evaluate additional strategic collaborations for our product candidates and research programs with partners whose assets and capabilities complement our own.

Our Pipeline

We are developing a focused pipeline of oncology product candidates with the potential to address significant unmet medical need for cancer patients. Two of our product candidates are currently in multiple ongoing clinical trials: azenosertib, an inhibitor of Wee1, a protein tyrosine kinase, and ZN-d5, a selective inhibitor of BCL-2. To date, azenosertib has been well tolerated and has demonstrated monotherapy anti-tumor activity across multiple tumor types in clinical trials. In addition, ZN-d5 has been well tolerated in clinical trials to date. We have also declared a development candidate for our BCL-xL degrader program, for which we are conducting IND-enabling studies.

We currently exclusively in-license worldwide development and commercialization rights to azenosertib, ZN-d5, and our BCL-xL product candidate. We out-licensed azenosertib and ZN-d5 development and commercialization rights in select Asian countries, including China, to our joint venture, Zentera Therapeutics, or Zentera. As of December 31, 2022, we held a 40.3% equity interest in Zentera. For more information about our joint venture with Zentera, see Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations—License Agreements and Strategic Collaborations" and Note 3 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

The following table summarizes our product candidate pipeline.

COMPOUND	INDICATION	DEVELOPMENT APPROACH	PRECLINICAL	EARLY CLINICAL DEVELOPMENT	LATE CLINICAL DEVELOPMENT	STATUS / EXPECTED MILESTONES
Azenosertib (ZN-c3) Wee1 Inhibitor	Uterine Serous Carcinoma	Monotherapy				FDA Fast Track Designation
	Solid Tumors	Monotherapy				Update on azenosertib dosing 1H 2023 including RP2D
	Cyclin E1 Driven Ovarian Cancer	Monotherapy				Enrolling; preclinical update to come in 1H 2023
	PARP Resistant Ovarian Cancer	Monotherapy alternating with niraparib or concurrent with niraparib				Enrolling; opened alternating cohort in 4Q 2022
	Ovarian Cancer	+ Multiple Chemotherapy Backbones				Enrolling; Phase 1 dose escalation results in 2H 2023
	Osteosarcoma	+ gemcitabine				Presented data CTOS Conf Nov 2022
	BRAF Mutant Colorectal Cancer	+ encorafenib and cetuximab				Initiated enrollment in Q1 2023
	Pancreatic Cancer	+ gemcitabine				Dana Farber Cancer Institute, funded by SU2C/Lustgarten
ZN-d5 BCL-2 Inhibitor	AL Amyloidosis	Monotherapy				Provide interim clinical data and declare RP2D for monotherapy
	NHL	Monotherapy				Continues to enroll
	AML	+ azenosertib				Provide preliminary data from clinical trial
BCL-xL Degrader	Solid Tumors and Heme Malignancies					Declared development candidate; IND enabling activities initiated

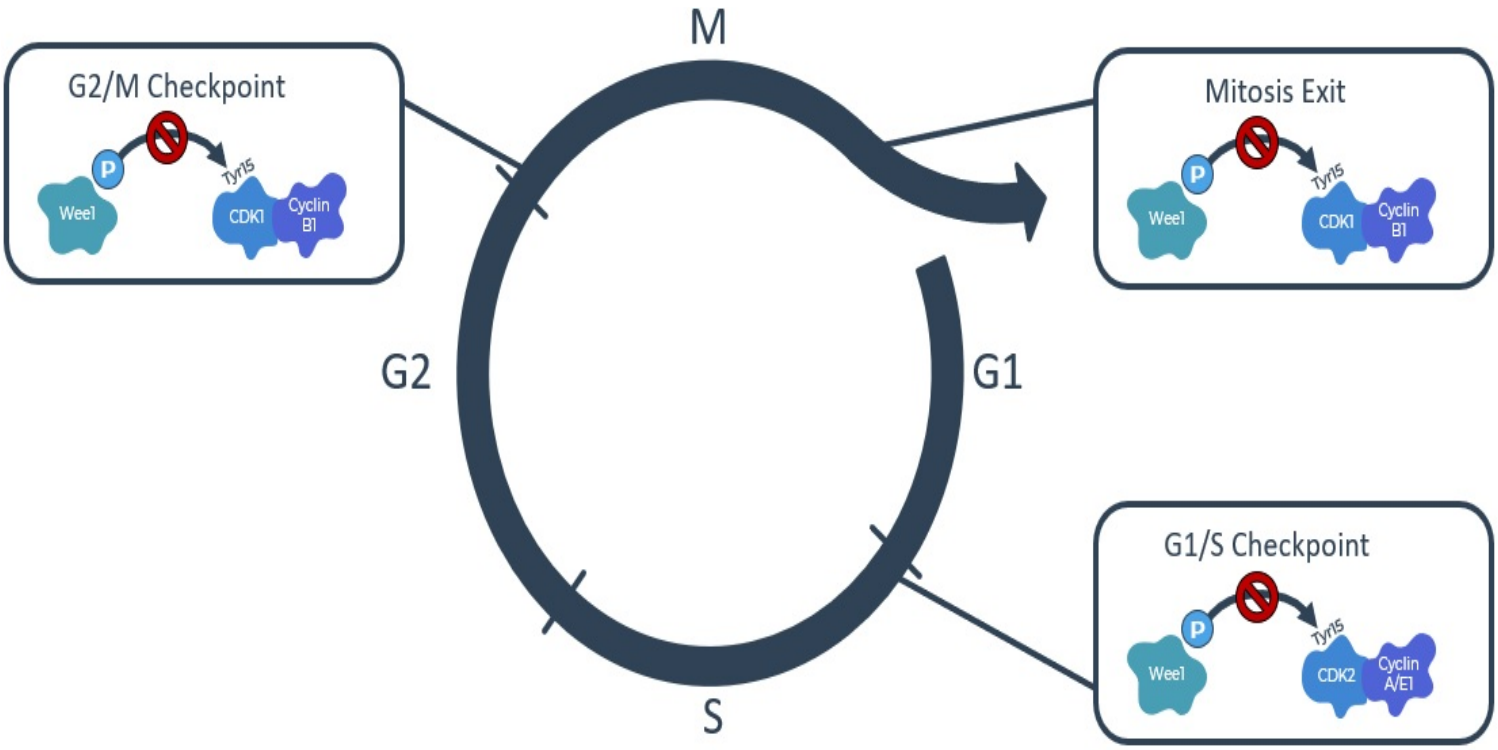
Our Development Programs

Azenosertib (Wee1 Inhibitor)

Overview

Azenosertib is a potentially best-in-class and first-in-class oral, small molecule Wee1 inhibitor. As illustrated in the figure below, the inhibition of Wee1, a DNA damage response kinase, drives cancer cells into mitosis without being able to repair damaged DNA, resulting in cell death and thereby preventing tumor growth and potentially causing tumor regression. Currently, there are no Wee1 inhibitors approved by the U.S. Food and Drug Administration, or FDA. We have designed azenosertib to have advantages over other investigational therapies targeting Wee1, including superior selectivity and PK properties. Azenosertib is currently being evaluated in the clinic for advanced solid tumors and hematological malignancies in the following three therapeutic settings of high unmet medical need:

- as a monotherapy,
- in combination with traditional chemotherapy and DNA damaging agents, and
- in combination with molecularly targeted agents.



We believe azenosertib has the potential to benefit a broad range of cancer patients due to the following:

- ***Demonstrated monotherapy anti-tumor activity across tumor types in clinical trials and preclinical studies.*** In clinical trials to date, azenosertib has demonstrated monotherapy anti-tumor activity across multiple tumor types, including USC, colorectal cancer, ovarian cancer, and non-small cell lung cancer, or NSCLC. In addition, in preclinical studies, azenosertib showed anti-tumor activity across a number of hematological and solid tumor cell lines, as well as tumor growth inhibition, DNA damage and apoptosis. Anti-tumor activity was observed in both continuous and intermittent dosing in clinical trials and preclinical studies of azenosertib.

- ***Well tolerated in clinical trials.*** In clinical trials to date, azenosertib was observed to be well tolerated across varying dosage levels, with over 200 patients having been administered azenosertib to date.

- ***Potency, selectivity and solubility.*** In our *in vitro* preclinical studies, we observed data indicating azenosertib's potential potency in inhibiting tumor growth and inducing apoptosis through DNA damage. Preclinical studies also showed that azenosertib has high selectivity for Wee1. In our preclinical studies, azenosertib produced favorable absorption, distribution, metabolism and excretion, or ADME, results.

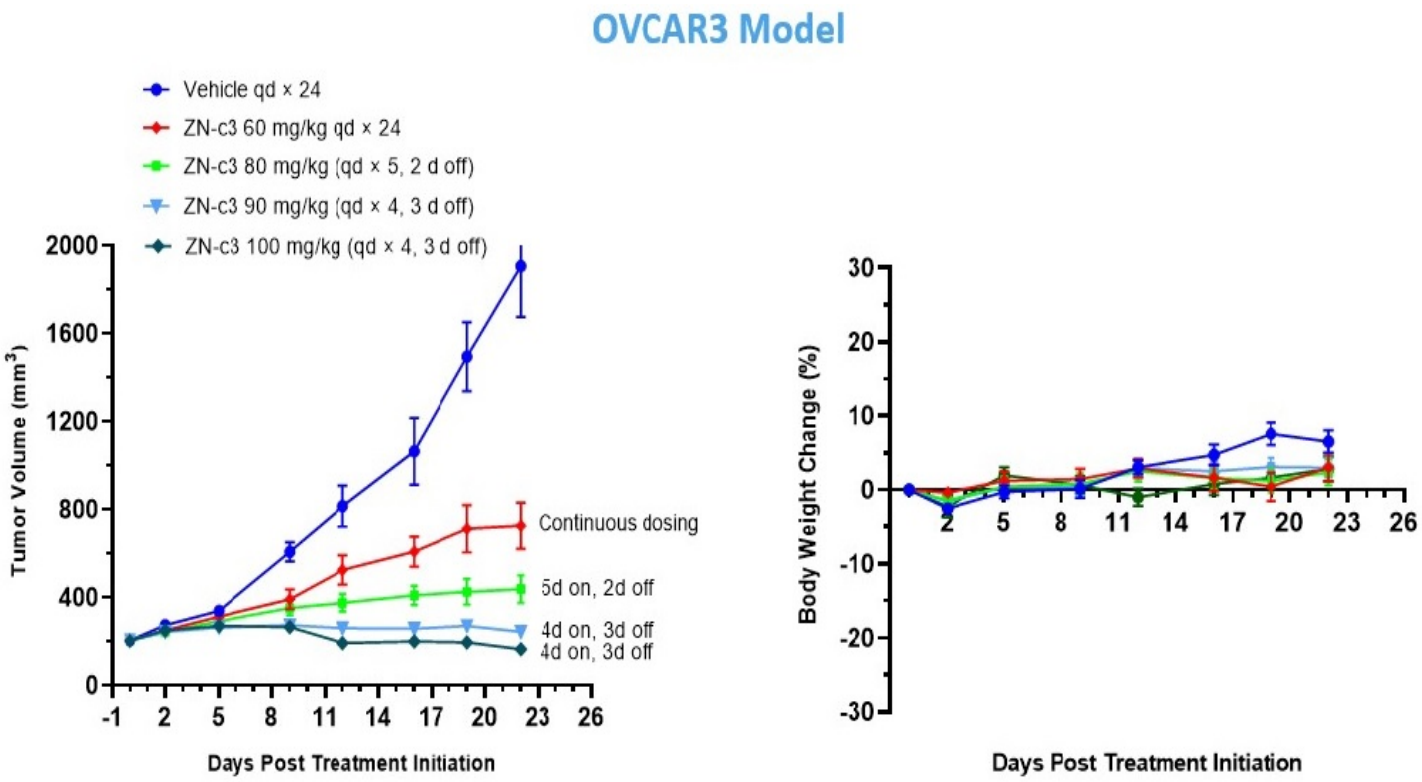
- ***PK properties.*** In our clinical studies, we observed that an increase in dose / drug exposure directly related to Wee1 target engagement. In our preclinical studies, azenosertib showed PK properties that resulted in high drug exposure in animal models. We believe this level of drug exposure may contribute to the observed sustained and lengthy tumor growth inhibition. In addition, we observed that azenosertib had favorable drug accumulation in tumors in preclinical studies.

Two key components of our azenosertib clinical development strategy are our dose optimization activities and our pursuit of Cyclin E1 as a patient enrichment strategy.

Dose Optimization

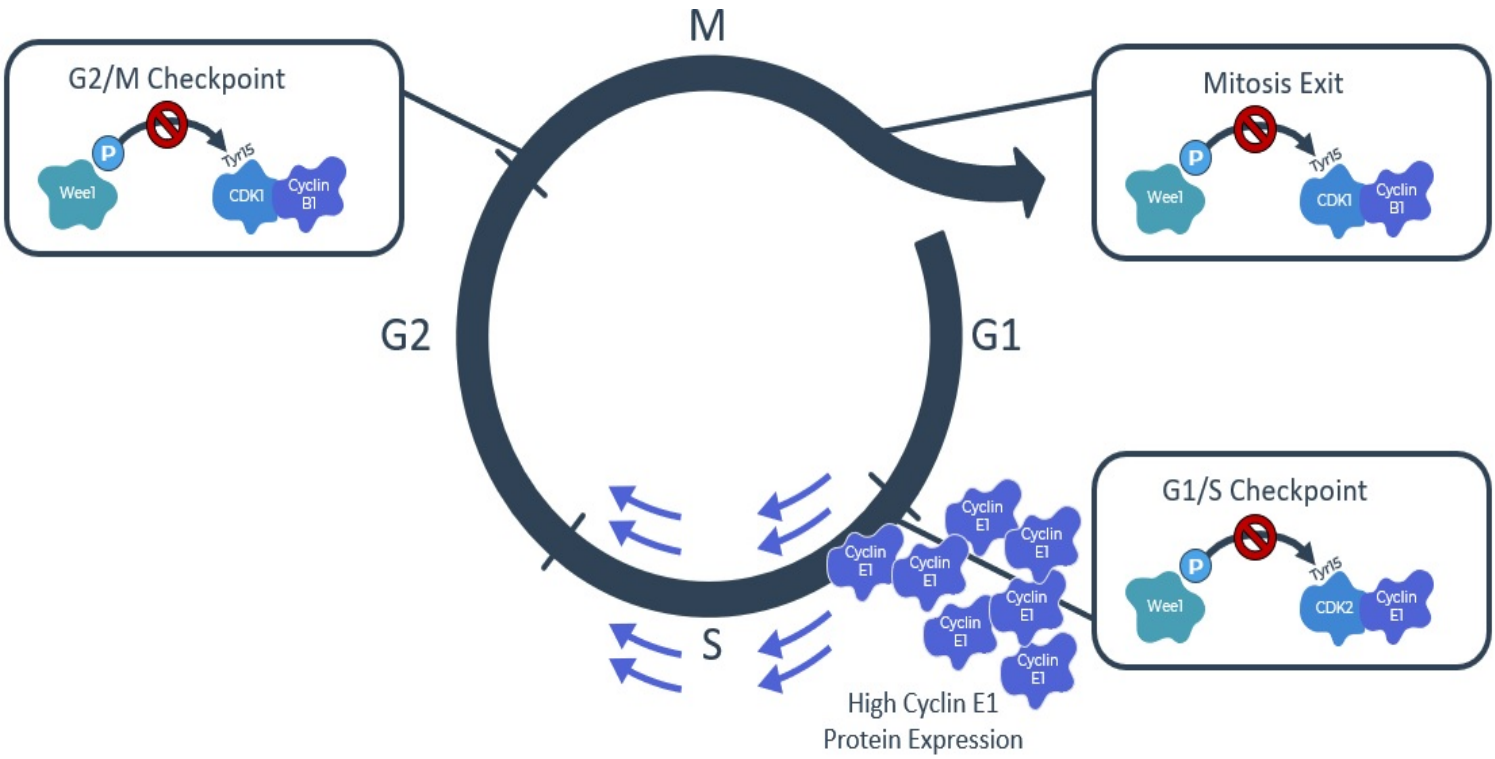
To date, azenosertib has demonstrated a favorable safety profile and monotherapy anti-tumor activity when administered on a continuous daily dosing schedule. Preclinical data show that higher doses delivered on an intermittent schedule have the potential to lead to higher PK exposures and a more favorable therapeutic index. For example, we assessed the efficacy and tolerability of azenosertib in *in vitro* preclinical studies across a variety of solid tumor cell lines, The figure

below shows intermittent dosing results from an ovarian cancer model, OVCAR3. We observed that azenosertib's tolerability was maintained while its potency in inhibiting tumor growth and inducing DNA damage and apoptosis increased with intermittent dosing.



Cyclin E1 Biomarker Strategy

As shown in the diagram below, high Cyclin E1 protein expression acts at the G1-S checkpoint by driving premature entry into S-phase resulting in replicative stress and significantly increasing sensitivity to azenosertib.



Historical, published clinical data showed that CCNE1 gene amplification was associated with poor prognosis and chemotherapy response across tumor types including in triple negative breast cancer and carboplatin-treated ovarian cancer models. We have also generated preclinical data that showed that high Cyclin E1 protein expression sensitized cancer cells to the anti-tumor effects of azenosertib as well as preliminary retrospective clinical data that suggested that high Cyclin E1 protein levels may be associated with clinical benefit from azenosertib. High Cyclin E1 protein expression and/or CCNE1 gene amplification in HGSOC is the focus of our ongoing Phase 2 clinical trial examining enrichment strategies for azenosertib described below. We believe this trial has the potential to allow us to demonstrate efficacy in an enriched patient population that has shown evidence of clinical sensitivity to Wee1 inhibition.

Development Program

Monotherapy - Phase 2 Clinical Trial in Recurrent or Persistent Uterine Serous Carcinoma (USC) (ZN-c3-004)

Azenosertib is currently being evaluated as a monotherapy in a Phase 2 clinical trial in adult women with USC. As of a September 14, 2022 data cutoff, a total of 43 patients were enrolled and dosed. Azenosertib was well tolerated. The most common treatment related adverse events, or AEs, were nausea (60.5% all grades/9.3% grade 3 or higher), fatigue (46.5% all grades/9.3% grade 3 or higher), diarrhea (37.2% all grades/7.0% grade 3 or higher) and vomiting (32.6% all grades/7.0% grade 3 or higher). We anticipate declaring an azenosertib monotherapy RP2D in the first half of 2023, and we plan to update the timeline of this USC study thereafter. The FDA granted Fast Track designation in November 2021 to azenosertib in patients with advanced or metastatic USC who have received at least one prior platinum-based chemotherapy regimen for management of advanced or metastatic disease. We believe that the study design in this patient population has the potential to support registration in the United States.

USC is an aggressive form of endometrial cancer that accounts for approximately 10-15% of all endometrial cancers. In a recent study, the median 5-year survival for Stage III or IV USC was approximately 26.2%. USC is responsible for approximately 40-50% of endometrial cancer deaths. The current standards of care for USC are platinum based chemotherapy (first line) and pembrolizumab plus lenvatinib (second line). We believe there is a high unmet need for a therapeutic option in later line USC patients after prior platinum-based chemotherapy and pembrolizumab plus lenvatinib treatment. USC is characterized by TP53 mutations, often concomitantly with oncogenic mutations or amplifications that can increase replication stress. USC may therefore be uniquely sensitive to further interference of cell cycle regulation by Wee1 inhibition.

Monotherapy - Phase 1 Dose Optimization Clinical Trial in Solid Tumors (ZN-c3-001)

We are currently evaluating azenosertib as a monotherapy in a Phase 1 dose optimization clinical trial for the treatment of solid tumors. We announced preliminary efficacy data from this trial with a data cutoff of May 15, 2021 from 34 patients, where we showed five confirmed partial responses, or cPRs, to azenosertib in monotherapy across several tumor types, including ovarian cancer (-69% cPR), colorectal cancer (-51% cPR), NSCLC (-49% cPR), and USC (-49% cPR) and (-43% cPR). We announced preliminary safety data from this trial at the 2022 American Association of Cancer Research, or AACR, Annual Meeting in April 2022. As of a January 21, 2022 data cutoff, there were 32 patients evaluated for safety and azenosertib was well tolerated. The most common treatment related AEs were nausea (71.9% all grades/3.1% grade 3 or higher), fatigue (53.1% all grades/18.8% grade 3 or higher), diarrhea (46.9% all grades/6.3% grade 3 or higher) and vomiting (46.9% all grades/0% grade 3 or higher).

We also announced preliminary efficacy data from the Phase 1 monotherapy expansion cohort in USC from this trial at the 2022 AACR Annual Meeting. As of a January 21, 2022 data cutoff, there were 11 evaluable patients in the USC cohort, with 27.3% demonstrating an objective response rate, or ORR, and 90.9% demonstrating a disease control rate, or DCR.

Monotherapy - Phase 2 Clinical Trial in Cyclin E1 Driven High-Grade Serous Ovarian Cancer, Fallopian Tube, or Primary Peritoneal Cancer (HGSOC) (ZN-c3-005)

We are evaluating azenosertib as a monotherapy in a Phase 2 clinical trial in patients with Cyclin E1 driven HGSOC. Our Cyclin E1 enrichment strategy is supported by preclinical data that showed that high Cyclin E1 protein expression sensitized cancer cells to the anti-tumor effects of azenosertib as well as preliminary retrospective clinical data that Cyclin E1 protein levels may be associated with clinical benefit from Wee1 inhibition.

HGSOC is a form of ovarian cancer that accounts for approximately 75% of all ovarian cancers. The “high-grade” in "high-grade serous ovarian carcinomas" refers to ovarian carcinomas that are classified as grade 3. “Serous” means that the tumor arose from the serous membrane, in the epithelial layer in the abdominopelvic cavity. Patients with HGSOC often respond well to treatment, and can experience remission; however, it is common for HGSOC patients to recur over a period of time, with the majority of recurrences occurring within three years. Outcomes for patients with platinum-resistant HGSOC are poor, with median overall survival reported at less than 12 months.

Combination - Phase 1/2 Clinical Trial of Azenosertib and PARPi in Platinum-Resistant Ovarian Cancer (ZN-c3-006)

We are evaluating azenosertib in combination with GSK's PARP inhibitor, niraparib (ZEJULA®), in a Phase 1/2 clinical trial in platinum-resistant ovarian cancer patients who have failed PARP inhibitor, or PARPi, maintenance treatment as part of a clinical collaboration with GSK. This study is currently enrolling two cohorts — one with concurrent dosing of the two drugs, and one with azenosertib and niraparib administered on a dose escalating, alternating schedule of one week of azenosertib followed by one week of niraparib. This clinical study is supported by preclinical data that showed that combining azenosertib and niraparib resulted in synergistic cell killing in ovarian *in vivo* models.

Ovarian cancer is a common gynecologic malignancy and common cause of gynecologic cancer death. Worldwide, over 295,000 women were diagnosed with ovarian cancer in 2018 and nearly 185,000 died from this disease. Despite initial therapy with cytoreductive surgery and platinum-based chemotherapy, the disease will relapse in most patients. Of those diagnosed with stage III or IV ovarian cancer, more than 70% will have a recurrence of their disease within the first five years.

There is an increasing population of patients who develop acquired PARPi resistance. Multiple potential mechanisms of acquired resistance to platinum-based chemotherapies and PARPi have been described in literature, although few have been identified in clinical samples. A key mechanism of clinical resistance is the acquisition of reversion mutations, which are somatic base substitutions or insertions/deletions, or indels, that are typically close to the primary protein-truncating mutation and restore the open reading frame, or ORF, of the gene and functional protein, switching the neoplastic cell from homologous recombination repair, or HRR, deficient to proficient. Tumor cells with one or more mutations in the homologous recombination pathway are vulnerable to the inhibition of the DNA damage repair mechanism mediated by PARP. However, despite good initial response rates of PARPi therapy with significant increases of both progression free survival, or PFS, and overall survival, or OS, most cancers eventually develop resistance. The combination of DNA damage response inhibitors, such as Wee1 and PARP inhibitors may be a promising approach for patients with advanced ovarian cancer with disease progression following PARP inhibitor maintenance therapy.

Combination - Phase 1b Clinical Trial of Azenosertib and Chemotherapy in Platinum-Resistant Ovarian, Peritoneal or Fallopian Tube Cancer (ZN-c3-002)

Azenosertib is currently being evaluated in combination with each of paclitaxel, carboplatin, pegylated liposomal doxorubicin (PLD) and gemcitabine in four separate cohorts in a Phase 1b clinical trial in patients with platinum-resistant ovarian, peritoneal or fallopian tube cancer. We provided a preliminary efficacy and safety update at the 2022 AACR Annual Meeting in April 2022, highlighting that azenosertib in combination with chemotherapy demonstrated strong anti-tumor activity

in a heavily pretreated population and was well tolerated. As of the January 28, 2022 data cutoff, there were 43 evaluable patients for efficacy, with an ORR of 30.2% across all evaluable chemotherapy cohorts (paclitaxel, carboplatin and PLD). In the paclitaxel cohort, there were 8 evaluable patients and an ORR of 62.5%; in the carboplatin cohort, there were 11 evaluable patients and an ORR of 45.5%; and in the PLD cohort, there were 24 evaluable patients and an ORR of 12.5%. As of the January 28, 2022 data cutoff, there were 56 evaluable patients for safety. The most common treatment related AEs were nausea (48.2% all grades/5.4% grade 3 or higher), neutropenia (41.1% all grades/32.1% grade 3 or higher), thrombocytopenia (37.5% all grades/17.9% grade 3 or higher), vomiting (30.4% all grades/7.1% grade 3 or higher) and anemia (26.8 all grades/7.1% grade 3 or higher).

Epithelial ovarian cancer is the most lethal of all female genital tract cancers. Platinum chemotherapy is the cornerstone of treatment for epithelial ovarian cancer, typically combined with paclitaxel. Platinum resistance, defined as relapse within six months following completion of platinum chemotherapy, occurs in 20–30% of cases. The sensitivity of ovarian cancers to platinum chemotherapy is in part due to a high prevalence of aberrations in the DNA repair pathway of homologous recombination.

Combination - Phase 1/2 Clinical Trial of Azenosertib and Chemotherapy in Relapsed or Refractory Osteosarcoma (ZN-c3-003)

Azenosertib is currently being evaluated in combination with gemcitabine, in a Phase 1/2 clinical trial in adult and pediatric patients with R/R osteosarcoma. We reported initial results from this trial at the 2022 Connective Tissue Oncology Society, or CTOS, Annual Meeting in November 2022. As of a October 24, 2022 data cutoff, there were 12 patients evaluable for efficacy, with approximately 33% of patients demonstrating event-free survival, or EFS, at 18 weeks (compared to approximately 12% at 18 weeks for this indication historically). As of the October 24, 2022 data cutoff, there were 17 patients evaluable for safety. Azenosertib demonstrated a manageable safety profile with 82.4% experiencing treatment related AEs of which 52.9% were grade 3 or higher. The most common treatment related AEs were platelet count decreased/thrombocytopenia (47.1% all grades/35.3% grade 3 or higher), fatigue (29.4% all grades/5.9% grade 3 or higher), nausea (29.4% all grades/0% grade 3 or higher) and rash (29.4% all grades/5.9% grade 3 or higher). We received orphan drug designation and rare pediatric disease designation from the FDA for azenosertib in osteosarcoma.

Osteosarcoma is the primary malignant bone tumor that most commonly affects children, adolescents, and young adults. The current management strategy for newly diagnosed osteosarcoma includes neoadjuvant chemotherapy followed by surgical removal of the primary tumor along with all clinically evident metastatic disease, plus the addition of adjuvant chemotherapy after surgery. Five-year survival rates in the US between 2010-2016 were 77% (localized), 65% (regional), 26% (distant) and 60% (overall). The standard of care for localized disease is neoadjuvant cytotoxic chemotherapy followed by primary resection and adjuvant cytotoxic chemotherapy; recurrent or metastatic osteosarcomas are usually resistant to standard of care, and treatment options for refractory osteosarcomas are extremely limited. The Wee1 kinase is often upregulated in osteosarcoma, preserving the G2-M checkpoint and allowing tumor growth and metastases, making Wee1 inhibition a potential therapeutic avenue in the treatment of osteosarcoma.

Combination - Phase 1/2 Clinical Trial of Azenosertib with Encorafenib and Cetuximab (BEACON Regimen) in BRAF V600E Mutant Metastatic Colorectal Cancer (mCRC) (ZN-c3-016)

We are collaborating with Pfizer to evaluate azenosertib in combination with encorafenib and cetuximab, an FDA-approved standard of care known as the BEACON regimen, in patients with BRAF V600E mutant mCRC in a Phase 1/2 clinical trial. In preclinical studies, Wee1 inhibition has shown synergy with many targeted agents in mutationally driven cancers, and the addition of azenosertib to the BEACON regimen enhanced anti-tumor activity in a cell-line-derived xenograft model. We initiated enrollment in this clinical trial in the first quarter of 2023.

Mutations in BRAF are recurrently detected in human cancer, including melanoma, colorectal, thyroid, NSCLC, and hairy cell leukemia. BRAF encodes a serine/threonine protein kinase that is part of the RAS/RAF/MEK/ERK pathway. The majority of mutations in BRAF result in V600E substitution, and these patients generally have a poor prognosis. A recent study of the BEACON regimen evaluated the safety and efficacy of the encorafenib + cetuximab doublet. The findings showed that the confirmed ORR was 19.5% (95% confidence interval, or CI, 14.5% to 25.4%) and 1.8% (95% CI, 0.5% to 4.6%) for control. Median PFS was 4.3 months (95% CI, 4.1 to 5.4). Despite the approval of encorafenib and cetuximab in previously treated BRAF V600E mutant mCRC, treatment options for patients with second and third line disease remains a high unmet medical need.

Combination - Phase 1/2 Clinical Trial of Azenosertib and Chemotherapy in Pancreatic Cancer

We have also agreed to support the Dana Farber-sponsored Phase 1/2 clinical trial evaluating azenosertib and chemotherapy, gemcitabine, in platinum-resistant pancreatic cancer patients.

Pancreatic ductal adenocarcinoma, or PDA, is a highly lethal malignancy with a recently reported 5-year survival rate of 7%. Major reasons for this poor prognosis include the following: (i) late diagnosis with about two-thirds of patients presenting locally advanced or metastatic disease, for which curative surgery is not available; (ii) aggressive clinical behavior with rapid progression through local and distant metastases; and (iii) intrinsic resistance to conventional chemotherapy and radiotherapy.

ZN-d5 (BCL-2 Inhibitor)

Overview

ZN-d5 is a potentially best-in-class selective, oral small molecule inhibitor of BCL-2. BCL-2 is a protein that plays a critical role in the regulation of cell death, known as apoptosis. The overexpression of BCL-2 is frequently detected in numerous cancer types, which prevents apoptosis of cancer cells. Utilizing our medicinal chemistry expertise, we have designed ZN-d5 to have best-in-class potency, selectivity and PK properties. ZN-d5 is currently being evaluated in the clinic in patients with hematological malignancies in both the monotherapy and combination settings.

We believe ZN-d5 has the potential to benefit cancer patients due to the following:

- ***Demonstrated activity in clinical data and preclinical models***. Preliminary efficacy data from our clinical trials has demonstrated that ZN-d5 is clinically active. In addition, our preclinical models demonstrated that ZN-d5 was observed to be potent in cell lines and xenograft models across a variety of hematological malignancies.

- ***Well tolerated in clinical trials and preclinical studies***. In clinical trials to date, ZN-d5 has been well tolerated. In addition, in our animal toxicity studies, the safety profile of ZN-d5 showed that it was well tolerated across various dosage levels.

- ***Selectivity***. In our preclinical *in vitro* studies, ZN-d5 showed more than 10 times greater selectivity for BCL-2 than BCL-xL. The inhibition of BCL-xL is a known cause of thrombocytopenia, a commonly reported toxicity in patients treated with venetoclax (VENCLEXTA®). We believe ZN-d5's greater selectivity for BCL-2 over BCL-xL, observed in preclinical studies, may support the use of ZN-d5 in combination with other drugs whose safety profiles, when used as monotherapies or in combination with other anti-neoplastic molecules, are associated with a high rate of thrombocytopenia.

Role of BCL-2 in Hematological Cancers

The BCL-2 family of protein is most notable for its critical role in the regulation of apoptosis at the mitochondrion. Based upon their functions, BCL-2 family proteins are classified into pro-apoptotic and anti-apoptotic members. The anti-apoptotic BCL-2 proteins include BCL-2, B-cell lymphoma extra-large, or BCL-xL, BCL2L2L, or BCL-w, myeloid cell leukemia-1, or MCL-1, and BCL-2 related protein Al.

The overexpression of BCL-2 and/or BCL-xL proteins is frequently detected in many different types of cancers, including chronic lymphatic leukemia, or CLL, , small lymphocytic lymphoma, or SLL, AML, non-Hodgkin lymphoma, or NHL (including follicular lymphoma, or FL, mantle-cell lymphoma, or MCL, diffuse large B-cell lymphoma, or DLBCL), Waldenström’s macroglobulinemia, multiple myeloma, or MM, and small cell lung cancer, or SCLC. These overexpressed proteins prevent apoptosis of cancer cells. We believe the use of small molecule inhibitors to block the protein-protein interactions of BCL-2 and/or BCL-xL with their pro-apoptotic partners has the potential to restore the normal apoptosis process in cancer cells. This therapeutic strategy has been validated in clinical trials and through the FDA's approval of venetoclax (VENCLEXTA®).

There have been many attempts to develop a new class of anticancer therapies that target BCL-2 and/or BCL-xL proteins. The intracellular localization of the BCL-2 family proteins on the mitochondrial membrane prevents the use of antibodies and other large molecules to target these anti-apoptotic BCL-2 family proteins. The large surface area involved in BCL-2 protein-protein interactions, or PPIs, also makes BCL-2 family proteins difficult targets for small molecule drugs. Currently, venetoclax (VENCLEXTA®) is the only FDA-approved BCL-2 inhibitor and, to our knowledge, there are only a small number of additional agents in active clinical development.

Development Program

ZN-d5 is being evaluated in the following monotherapy and combination clinical trials:

Monotherapy - Phase 1/2 Clinical Trial in Relapsed or Refractory Light Chain Amyloidosis (R/R AL Amyloidosis) (ZN-d5-003)

ZN-d5 is being evaluated as a monotherapy in a Phase 1/2 clinical trial in R/R AL amyloidosis. BCL-2 inhibition has demonstrated clinical activity in R/R AL amyloidosis; however, there are currently no FDA-approved BCL-2 inhibitors for the treatment of R/R AL amyloidosis. This Phase 1/2 study in patients with R/R AL amyloidosis consists of a dose escalation phase to establish the monotherapy RP2D in this setting, and an expansion phase to further assess the safety and efficacy of ZN-d5 in this population. The study is expected to enroll up to approximately 140 patients.

R/R AL amyloidosis is a plasma cell disorder in which a non-malignant clonal population of plasma cells secrete high levels of a misfolding immunoglobulin light chain can become deposited in tissues, causing widespread organ damage. Though not a malignancy, R/R AL amyloidosis is a difficult and progressive disease that is commonly treated with agents active against multiple myeloma, a malignancy of plasma cells, which can include stem cell transplant and, more commonly, combinations of chemotherapy, proteosome inhibitors, immunomodulating agents, dexamethasone, and monoclonal antibodies that target plasma cells. R/ R AL amyloidosis is a rare disease that is often progressive despite multiple lines of therapy, and we believe represents an unmet medical need. R/R AL amyloidosis has an estimated worldwide prevalence of 75,000 patients and there are approximately 4,000 new cases in the United States each year. Since BCL-2 inhibition has been associated with clinical activity in multiple myeloma, agents inhibiting BCL-2 could be effective therapies for R/R AL amyloidosis.

Monotherapy - Phase 1 Clinical Trial in Non-Hodgkin Lymphoma (NHL) (ZN-d5-001)

We are evaluating ZN-d5 as a monotherapy in a Phase 1 dose escalation clinical trial in patients with NHL. As of the database cutoff date of November 3, 2021, 23 patients with NHL were evaluable for safety. At our R&D Day in December 2021, we reported preliminary interim data from the NHL patients in this study. As of the November 3, 2021 database cutoff date, ZN-d5 was well tolerated, with 73.9% of the NHL patients having experienced AEs (30.4% grade 3 or higher), not all of which were related ZN-d5. Anemia (21.7% all grades/8.7% grade 3 or higher), diarrhea (13.0% all grades/4.3% grade 3 or higher), and nausea and vomiting (8.7% each all grades/0% grade 3 or higher) comprise the most commonly experienced AEs. Investigator-reported responses using the Lugano 2014 classification among 11 patients with diffuse large B-cell lymphoma included a complete response, an unconfirmed PR, and two subjects with stable disease, as of the database cutoff date of November 3, 2021.

NHL is a group of malignant neoplasms originating in lymphoid tissue, mainly lymph nodes. The vast majority of NHL are of B-cell origin, of which the most common subtypes are diffuse large B-cell lymphoma (about 30%) and follicular lymphoma (about 20%) account for approximately 50% and 30% respectively. Survival rates vary depending on the cancer's stage, subtype and response to initial therapy. Elevated BCL-2 protein expression in hematological cancers has been directly correlated with poor responses to conventional therapies and radiation. ZN-d5 is mechanistically similar to approved drug venetoclax (VENCLEXTA®), though it is more highly selective for BCL-2 over B-cell lymphoma-extra-large than venetoclax, which may reduce thrombocytopenia and provide higher therapeutic benefit for this patient population, particularly when combined with other anti-cancer agents where modification of therapeutic doses due to the development of cytopenias could impact efficacy.

Combination - Phase 1/2 Clinical Trial of ZN-d5 and Azenosertib in Relapsed or Refractory Acute Myeloid Leukemia (R/R AML) (ZN-d5-004C)

ZN-d5 is being evaluated in combination with azenosertib in a Phase 1/2 dose escalation clinical trial in patients with R/R AML. The Phase 1 portion of this trial will escalate the doses of both drugs to identify the RP2D for the combination, which will be assessed in Phase 2 expansion cohort(s). This study is expected to enroll up to approximately 100 patients. This clinical trial is supported by preclinical models that showed that the combination of ZN-d5 with azenosertib yielded a significant enhancement of activity in several indications, including R/R AML, as compared to activity shown with either of these product candidates as a single agent. Preclinical models also showed that the combination of ZN-d5 with azenosertib was well tolerated in mice. We believe we are the only company to have both a Wee1 inhibitor and a BCL-2 inhibitor in clinical development.

R/ R AML is defined by the malignant clonal expansion of a progenitor cells coupled with a differentiation arrest. Of all subtypes of leukemia, R/R AML accounts for the highest percentage (62%) of leukemic deaths. Patients unable to tolerate induction chemotherapy owing to age or comorbid conditions are traditionally treated with hypomethylating agents, or HMA, or low-dose cytarabine, or LDAC. More recently, venetoclax (VENCLEXTA®), a small molecule BH3 mimetic BCL-2 inhibitor, has become a standard treatment, in combination with HMA or LDAC, for this population. However, a substantial portion of patients do not respond to, or relapse after, treatment with venetoclax-based combinations. ZN-d5 is mechanistically similar to venetoclax, though it is designed to be more highly selective for BCL-2 over BCL-xL than venetoclax which may reduce thrombocytopenia. Given the established utility of BH3 mimetics and the potential role of Wee1 inhibition in treating R/ R AML, combining the BCL-2 inhibitor ZN-d5 with the Wee1 inhibitor ZN-c3 may provide a meaningful benefit for patients and provide advantages over existing regimens.

BCL-xL Heterobifunctional Degrader

Overview

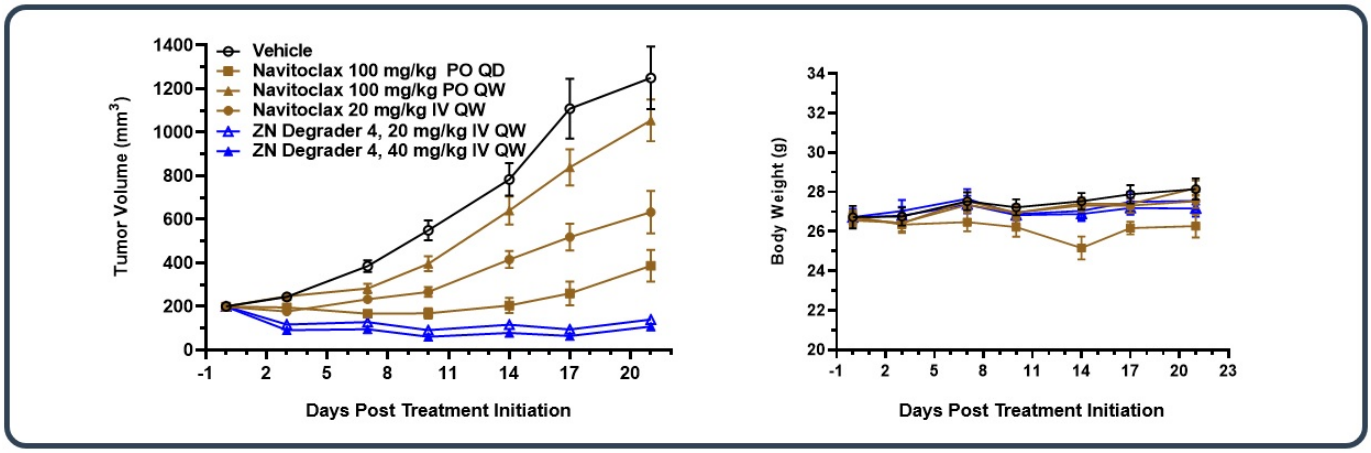
In November 2022, we announced that we identified a BCL-xL protein degrader candidate and initiated IND-enabling studies. We are developing a BCL-xL heterobifunctional degrader based on non-functional or dysfunctional E3 ubiquitin ligase complex in platelets, allowing for the potential mitigation of dose-limiting thrombocytopenia historically associated with BCL-xL inhibitors.

BCL-xL is a member of the anti-apoptotic BCL-2 protein family and participates in the regulation of the intrinsic apoptosis pathway. BCL-xL is often upregulated in hematological and solid malignancies. It is involved in tumor survival and resistance to chemotherapy and venetoclax (VENCLEXTA®). Navitoclax, a dual BCL-2/BCL-xL inhibitor, has shown clinical activity in hematopoietic malignancies but was found to be dose-limited because of thrombocytopenia driven by BCL-xL inhibition.

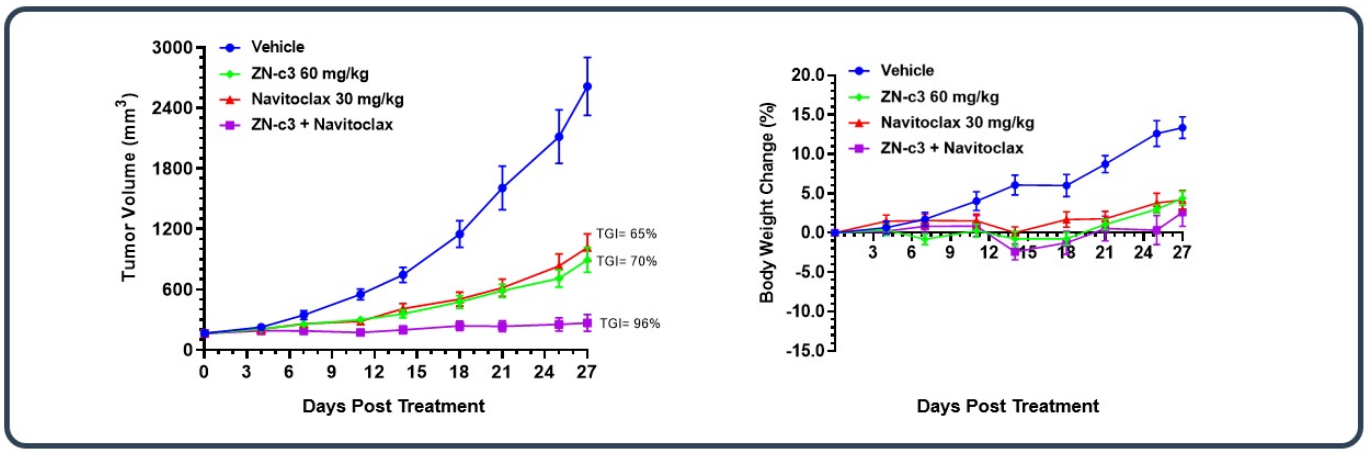
We believe our BCL-xL candidate has the potential to meet an unmet medical need based on its potency observed to date. As demonstrated in preclinical models, the degradation of BCL-xL in tumor cells with our BCL-xL protein degrader candidate was associated with a decrease in cell viability.

Preclinical Results

As shown in the diagrams below, in the MOLT4 tumor model (T-ALL), our BCL-xL protein degrader candidate demonstrated strong activity and was well tolerated at the evaluated doses. This model also showed that our BCL-xL protein degrader candidate was more efficacious than navitoclax.



We also believe that the development of our BCL-xL protein degrader candidates offers an opportunity for development in combination with other cancer agents, such as azenosertib. As shown below, azenosertib combined with a low dose of navitoclax resulted in synergistic anti-tumor activity in the T-ALL model MOLT-4:



Integrated Discovery Engine

We are also currently advancing our research on protein degraders and other undisclosed targets utilizing our Integrated Discovery Engine. Our Integrated Discovery Engine has enabled us to take each of our clinical-stage product candidates from initial discovery to IND submission in less than three years, with a total of four FDA-cleared INDs in a span of five years. We begin our process of drug discovery by identifying fundamental biological pathways of cancers based upon a number of factors, including validation of the pathway through prior clinical outcomes and ability to impact large patient populations. We then analyze existing marketed products and compounds in development that target these cancer pathways and assess their limitations, efficacy, safety, tolerability, PK, patient convenience and potential to be used in combination with other therapies. Next, we use our medicinal chemistry expertise and extensive understanding of structure based drug design and target-structure activity relationships to design product candidates with properties that we believe can address observed limitations and suboptimal drug characteristics of marketed products or other compounds in development, including potency, solubility, route of administration and PK properties.

We believe overcoming these limitations may also allow us to develop these product candidates for use in combination with other therapies, including with our internally-developed product candidates, if approved. Finally, we strive to generate preclinical data to support that such candidates could have a differentiated product profile in our expected lead indications before advancing a compound into clinical development.

Manufacturing

We currently do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely for the foreseeable future, on third-party contract manufacturing organizations, or CMOs, to produce our product candidates for preclinical and clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval. We require that our CMOs produce bulk drug substance and finished drug product in accordance with current Good Manufacturing Practices, or cGMPs, and all other applicable laws and regulations. We maintain agreements with our CMOs that include confidentiality and intellectual property provisions to protect our proprietary rights related to our product candidates.

We have engaged CMOs to manufacture, package, label and distribute azenosertib and ZN-d5 for preclinical and clinical use. We obtain our clinical trial supplies from these CMOs on a purchase order basis and do not have long-term supply arrangements in place. Although we do not currently have contractual arrangements in place for redundant supply for each component of the supply chain for either of these product candidates, we currently mitigate potential supply risks for azenosertib and ZN-d5 through inventory management. More broadly, for each of our product candidates, we intend to identify and qualify additional manufacturers to provide the raw materials, active pharmaceutical ingredient and drug product prior to seeking regulatory approval.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid technological advancement, significant competition and an emphasis on intellectual property. While we believe that our product candidates, development capabilities, experience and scientific knowledge provide us with competitive advantages, we face potential competition from many

different sources, including major and specialty pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with current therapies and new therapies that may become available in the future.

Many of the companies against which we may compete have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. 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 patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize medicines that are safer, more effective, have fewer or less severe side effects, are more convenient or less expensive than any medicines we may develop. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in competitors establishing a strong market position before we are able to enter the market. We believe that the key competitive factors affecting the success of any of our product candidates, if approved, will include efficacy, combinability, safety profile, convenience, cost, level of promotional activity devoted to them and intellectual property protection.

Azenosertib

Aprea Therapeutics, Inc., or Aprea, has disclosed that it is clinically evaluating a selective Wee1 inhibitor, ATRN-W1051. ATRN-W1051 was originally developed by Atrin Pharmaceuticals, Inc., which was acquired by Aprea in May 2022. Aprea has disclosed that ATRN-W1051 is currently in preclinical development and that it plans to study ATRN-W1051 as both a monotherapy and in combination with standard of care for the treatment of multiple cancers. Debiopharm has disclosed that it is clinically evaluating a selective Wee1 inhibitor, Debio 0123, as both a monotherapy and in combination with carboplatin, for the treatment of advanced solid tumors. Impact Therapeutics has disclosed that it is investigating IMP7068, a Wee1 inhibitor, currently in a Phase 1 trial for advanced solid tumors. Shouyao Holdings has disclosed that it is investigating SY-4835, a Wee1 inhibitor, in a Phase 1 trial for patients with advanced solid tumors. Schrödinger, Inc., or Schrödinger, has disclosed that it is evaluating multiple selective Wee1 inhibitors as potential monotherapy or combination therapy approaches for the treatment of gynecological cancers and other solid tumors. Schrödinger has disclosed that its Wee1 program is currently in preclinical development and that it plans to select a Wee1 inhibitor development candidate and initiate IND-enabling studies in 2023, with the expectation of submitting an IND in the first half of 2024.

ZN-d5

AbbVie Inc. has developed and received regulatory approval for venetoclax (VENCLEXTA®), a BCL-2 inhibitor used to treat hematological malignancies. Ascentage Pharma is clinically evaluating a selective BCL-2 inhibitor, lisaftoclax (APG-2575) as both a monotherapy and in combination with other agents for the treatment of multiple hematologic malignancies and solid tumors. BeiGene, Ltd. is clinically evaluating BGB-11417, a selective BCL-2 inhibitor in hematologic malignancies as a monotherapy or in combination with other agents.

Intellectual Property

We strive to protect the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on know-how relating to our proprietary technology and product candidates and continuing innovation to develop, strengthen and maintain our proprietary position. In addition, we plan to rely on data exclusivity, market exclusivity and patent term extensions or adjustments when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to defend and enforce our proprietary rights, including any patents that we may own in the future; and to operate without infringing the valid and enforceable patents and other proprietary rights of third parties. Intellectual property rights may not address all potential threats to our competitive advantage.

With respect to our product candidates and processes we intend to develop and commercialize in the normal course of business, we intend, or understand that our licensors intend, to pursue patent protection covering, when possible, compositions, methods of use, dosing and formulations. We or our licensors also may pursue patent protection with respect to manufacturing and drug development processes and technologies. Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies. We

or our licensors may not be able to obtain patent protections for our compositions, methods of use, dosing and formulations, manufacturing and drug development processes and technologies throughout the world. Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the United States can provide exclusionary rights for 20 years from the earliest non-provisional or PCT filing date. In addition, in certain instances, the term of an issued U.S. patent that is directed to or claims an FDA-approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called "patent term extension." The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the United States varies in accordance with the laws of the jurisdiction, but typically is also 20 years from the earliest non-provisional or PCT filing date plus any extensions of term that may be available under national law. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent. Patent term may be inadequate to protect our competitive position on our products for an adequate amount of time.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of biopharmaceuticals has emerged in the United States. The relevant patent laws and their interpretation outside of the United States are also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our technology or product candidates and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. We cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology, and our issued patents may be challenged, invalidated, deemed unenforceable or circumvented, which could limit our ability to stop competitors from marketing-related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent directed to such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

In-licensed Patents and Patent Applications

Our wholly owned subsidiary, Zeno Management, Inc., or ZMI, has exclusively in-licensed or is the owner/assignee of issued patents and patent applications directed to our technology across our pipeline in the United States and many other major jurisdictions worldwide, including Europe, Japan and China. Certain issued patents and patent applications directed to azenosertib, ZN-d5 and our BCL-xL product candidate have been exclusively in-licensed from Recurium IP Holdings, LLC, or Recurium IP. For additional information on our license agreement with Recurium IP, see Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations—License Agreements and Strategic Collaborations" and Note 14 to our audited consolidated financial statements included elsewhere in this Annual Report.

The expected expiration dates for issued patents, or patents that may issue from any patent applications, directed to our Wee1 inhibitor program, including azenosertib, are between 2038 and 2043 plus any extensions or adjustments of term available under national law. The expected expiration dates for the patents, or patents that may issue from any patent applications, directed to our BCL-2 inhibitor program, including ZN-d5, are between 2039 and 2043 plus any extensions or adjustments of term available under national law. The expected expiration date for the patent, or patents that may issue from any patent applications, directed to our BCL-xL protein degrader program is 2043 plus any extensions or adjustments of term available under national law. However, there can be no assurance that any of the pending patent applications will issue. Furthermore, there can be no assurance that we will benefit from any patent term extension or favorable adjustments to the term

of any of the issued patents or patents that may issue from any pending patent applications in the future. The applicable authorities, including the FDA in the United States and the U.S. Patent and Trademark Office, or USPTO, may not agree with our assessment of whether such patent term extensions or adjustments should be granted, and, if granted, they may grant more limited extensions or adjustments than we request.

Trademarks

Our trademark portfolio contains the following trademarks applications or registrations. U.S. trademark applications are pending for each of the marks ZENTALIS and the stylized "Z" mark. Applications to register each of the marks ZENTALIS and the stylized "Z" have been filed internationally.

Furthermore, we rely upon know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality and invention assignment agreements with our commercial partners, collaborators, employees, and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with an employee or a third party. These agreements may be breached, and we may not have adequate remedies for any such breach. To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

License Agreements and Strategic Collaborations

Recurium IP Holdings, LLC License Agreement

In December 2014, our wholly owned subsidiary, Zeno Pharmaceuticals, Inc., entered into a license agreement, or the Recurium Agreement, with Recurium IP, which was subsequently amended, under which Zeno Pharmaceuticals, Inc. was granted an exclusive worldwide license to certain intellectual property rights owned or controlled by Recurium IP to develop and commercialize pharmaceutical products for the treatment or prevention of disease, other than for providing pain relief. Following certain corporate restructuring disclosed elsewhere in this Annual Report on 10-K, our wholly owned subsidiary, ZMI, became the Zentalis contracting party to the Recurium Agreement. The intellectual property rights licensed by ZMI under the Recurium Agreement include certain intellectual property covering azenosertib, ZN-d5 and our BCL-xL product candidate. See Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations—License Agreements and Strategic Collaborations" and Note 14 to our audited consolidated financial statements included elsewhere in this Annual Report for additional information.

Pfizer Development Agreement

In April 2022, we entered into a development agreement with Pfizer to collaborate to advance the clinical development of azenosertib. We did not grant Pfizer any economic ownership or control of azenosertib or the rest of our pipeline. In October 2022, we announced our first clinical development collaboration with Pfizer to initiate a Phase 1/2 dose escalation study of azenosertib, in combination with encorafenib and cetuximab (an FDA-approved standard of care known as the BEACON regimen) in patients with BRAF V600E mutant mCRC.

GlaxoSmithKline Clinical Trial Collaboration and Supply Agreement

In April 2021, we entered into a clinical trial collaboration and supply agreement with GSK pursuant to which we are evaluating the combination of azenosertib and niraparib, GSK's poly (ADP-ribose) polymerase (PARP) inhibitor, in patients with platinum-resistant ovarian cancer. See Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations—License Agreements and Strategic Collaborations" for additional information.

Zentera Therapeutics

In May 2020, each of our wholly owned subsidiaries Zeno Alpha, Inc., K-Group Alpha, Inc. and K-Group Beta, Inc. entered into a collaboration and license agreement with our joint venture, Zentera, pursuant to which we collaborate with Zentera on the development and commercialization of ZN-c5, ZN-d5 and azenosertib, respectively, in each case for the treatment or prevention of disease, other than for pain, in the People's Republic of China, Macau, Hong Kong and Taiwan. As disclosed in August 2022, we are discontinuing clinical development of ZN-c5. See Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations—License Agreements and Strategic Collaborations" and Note 14 to our audited consolidated financial statements included elsewhere in this Annual Report for additional information.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the New Drug Application, or NDA, or Biologics License Application, or BLA, process before it may be legally marketed in the United States.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA's Good Laboratory Practice, or GLP, requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice, or GCP, requirements to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA/BLA after completion of all pivotal trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA/BLA to permit commercial marketing of the product for particular indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, a sponsor must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The IND includes results of animal and *in vitro* studies assessing the toxicology, PK, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under 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 separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected AEs, 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.

Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

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 postmarketing requirements, including Phase 4 clinical trials, as a condition of approval of an NDA/BLA.

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.

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 1, at the end of Phase 2, and before an NDA/BLA 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. Alternatively, sponsors planning for a Phase 2 registration study will utilize the meetings at the end of the Phase 1 trial to discuss Phase 1 clinical results and present plans for the Phase 2 registration study that they believe will support approval of the new drug.

U.S. Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA/BLA requesting approval to market the product. The submission of an

NDA/BLA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs/BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA conducts a preliminary review of all NDAs/BLAs within the first 60 days after submission, before accepting the application for filing, to determine whether it is sufficiently complete to permit a substantive review because incompleteness can lead to refusal to file. The FDA may request additional information rather than accept an NDA/BLA for filing. In this event, the NDA/BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA/BLA 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, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA/BLA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two (2) months to make a "filing" decision after it the application is submitted.

The FDA may refer an application for a novel drug to an advisory committee if they feel there is an issue regarding the benefit/risk of the drug. 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/BLA, the FDA will typically 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 and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA/BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs.

After the FDA evaluates an NDA/BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications and outlines post-marketing requirements with milestone dates. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA/BLA identified by the FDA and may require additional clinical data, such as an additional clinical trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA/BLA or, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA/BLA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for a particular indication(s) and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The FDA may also approve the NDA/BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Once a drug is approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also mandate post-marketing requirements, including one or more Phase 4 post-market studies and surveillance, to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs/BLAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the

pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates.

Fast Track Designation

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, product candidates are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. 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. With regard to a fast track product, the FDA may consider for review sections of the NDA/BLA 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/BLA, the FDA agrees to accept sections of the NDA/BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA/BLA.

Breakthrough Therapy Designation

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

Any product candidate submitted to the FDA for approval, including a product candidate with a fast track designation or breakthrough therapy designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval.

Priority Review

An NDA/BLA is eligible for priority review if the product candidate has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six (6) months of the FDA's acceptance for filing date as compared to ten months for review of new molecular entity NDAs/BLAs under its current PDUFA review goals.

Accelerated Approval

In addition, a product candidate may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA generally requires that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled confirmatory clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required confirmatory studies in a timely manner, or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

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

Orphan Drug Designation

Under the U.S. Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic product 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 the product available in the United States for this type of disease or condition will be recovered from sales of the product in the United States. An applicant must request orphan drug designation before submitting an NDA/BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Orphan drug designation entitles a party to financial incentives such as opportunities for limited grant funding towards clinical trial costs, research tax advantages, and user fee waivers. If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity. This means the FDA may not approve any other applications, including full NDAs/BLAs, to market the same drug, as defined by the FDA, for the same disease or condition for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of either a different product for the same disease or condition or the same product for a different disease or condition. Orphan exclusivity also could block the approval of a product for seven years if a competitor obtains approval of the same drug or if such drug is determined to be contained within the competitor's product for the same disease or condition. If a drug designated as an orphan product receives marketing approval for a disease or condition broader than what is designated, it may not be entitled to orphan exclusivity. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Rare Pediatric Disease Priority Review Voucher Program

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer, including by sale, the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

For purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare diseases or conditions within the meaning of the Orphan Drug Act. Congress has only authorized the Rare Pediatric Disease Priority Review Voucher program until September 30, 2024. Consequently, sponsors of marketing applications approved after that date will not receive the voucher unless Congress reauthorizes the Rare Pediatric Disease Priority Review Voucher program before that time. However, even if the program is not reauthorized, if a drug candidate receives Rare Pediatric Disease Designation before October 1, 2024, the sponsor of the marketing application for such drug will be eligible to receive a voucher if the application for the designated drug is approved by the FDA before October 1, 2026.

Post-approval Requirements

Any products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug 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 cGMP, which impose certain 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 and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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

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

The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

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 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, or ANDA, or an NDA submitted under Section 505(b)(2), or 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.

The 2010 Patient Protection and Affordable Care Act, or PPACA, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars.

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

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was first licensed. This 12-year exclusivity period is referred to as the reference product exclusivity period and bars approval of a biosimilar but notably does not prevent approval of a competing product pursuant to a full BLA (i.e., containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of the product). The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. The law also includes an extensive process for the innovator biologic and biosimilar manufacturer to litigate patent infringement, validity, and enforceability prior to the approval of the biosimilar.

Foreign Government Regulation

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials, marketing authorization, post-marketing requirements and any commercial sales and distribution of our product candidates.

Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or prior to marketing of the product candidates in those countries. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. The approval process varies from country to country, can involve additional testing beyond that required by FDA, and may be longer or shorter than that required for FDA approval. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements, may be subject to, among other things, fines or operating restrictions.

Other Healthcare Laws

Pharmaceutical and medical device manufacturers are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal anti-kickback, fraud and abuse, false claims, consumer fraud, pricing reporting, and transparency laws and regulations as well as similar state and foreign laws in the jurisdictions outside the U.S. Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, additional reporting obligations and oversight if we become subject

to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufactures to provide scientific and clinical support for the use of a product to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

Third-party payors are increasingly reducing reimbursements for pharmaceutical products and services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are more and more challenging the prices charged, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States. By way of example, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers, which will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, absent additional congressional action. In addition, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, or AMP, beginning January 1, 2024.

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. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services, or HHS, to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. In addition, 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.

FDA Approval and Regulation of Companion Diagnostics

If safe and effective use of a therapeutic 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 therapeutic product or new therapeutic product 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 therapeutic treatments for cancer 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, each medical device commercially distributed in the United States generally requires either FDA clearance of a 510(k) premarket notification, or approval of a premarket approval, or a PMA application. Under the FDCA, medical devices are classified into one of three classes—Class I, Class II or Class III—depending on the degree of risk associated with each medical device and the extent of manufacturer and regulatory control needed to ensure its safety and effectiveness. While most Class I devices—devices that generally pose a low risk to users—are exempt from the 510(k) premarket notification requirement, manufacturers of most Class II devices are required to submit to the FDA a premarket notification under Section 510(k) of the FDCA requesting permission to commercially distribute the device. The FDA's permission to commercially distribute a device subject to a 510(k) premarket notification is generally known as 510(k) clearance. Devices deemed by the FDA to pose the greatest risks, or devices that have a new intended use, or use advanced technology that is not substantially equivalent to that of a legally marketed device, are automatically placed in Class III,

requiring approval of a PMA unless down-classified in accordance with the "*de novo*" process, which is a route to market for novel medical devices that are low to moderate risk and are not substantially equivalent to a predicate device.

To obtain 510(k) clearance, a manufacturer must submit to the FDA a premarket notification demonstrating that the proposed device is "substantially equivalent" to a predicate device already on the market. A predicate device is a legally marketed device that is not subject to premarket approval, i.e., a device that was legally marketed prior to May 28, 1976 (pre-amendments device) and for which a PMA is not required, a device that has been reclassified from Class III to Class II or I, or a device that was found substantially equivalent through the 510(k) process. If the FDA agrees that the device is substantially equivalent to a predicate device currently on the market, it will grant 510(k) clearance to commercially market the device. If the FDA determines that the device is "not substantially equivalent" to a previously cleared device, the device is automatically designated as a Class III device. The device sponsor must then fulfill more rigorous PMA requirements or request down-classification of the device through the "*de novo*" process.

The PMA process is more demanding than the 510(k) premarket notification process, and 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, or 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.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. For example, the California Consumer Privacy Act, or CCPA, became effective on January 1, 2020. The CCPA gives California consumers (defined to include all California residents) certain rights, including the right to ask companies to disclose the types of personal information collected, specific pieces of information collected by a company, the categories of sources from which such information was collected, the business purpose for collecting or selling the consumer's personal information, and the categories of third parties with whom a company shares personal information. The CCPA also imposes obligations on companies to provide notice to California consumers regarding a company's data processing activities. Additionally, the CCPA gives California consumers the

right to ask companies to delete a consumer's personal information and places limitations on a company's ability to sell personal information, including providing consumers a right to opt out of sales of their personal information. Further, the California Privacy Rights Act, or CPRA, which generally went into effect on January 1, 2023, and significantly expands the CCPA to incorporate additional provisions, including a requirement that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also expands personal information rights of California residents, including creating a right to opt out of sharing of personal information with third parties for advertising, expanding the lookback period for the right to know about personal information held by businesses, and expanding the right to erasure for information held by third parties.

In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. For example, the European Union General Data Protection Regulation, or GDPR, imposes strict requirements for processing the personal data of individuals within the European Economic Area, or EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance. Further, from January 1, 2021, companies have had to comply with the GDPR and also the United Kingdom GDPR, or UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Environmental, Social and Governance (ESG)

Social

Zentalis aims to drive positive social impact, including by improving the lives of cancer patients through our therapeutics and our focus on Diversity, Equity and Inclusion, or DE&I. Below are a few initiatives that demonstrate our focus on social impact:

- **Safety**. We prioritize the safety and well-being of our patients and our employees. Our employees receive annual trainings on general safety, on-site lab safety procedures, quality assurance and standard operating procedures to help ensure that we are managing risks and operating safely. The COVID-19 pandemic continues to present a public health challenge around the world. We have continued to evaluate our practices to address our employees' health and well-being.

- **DE&I**. We are committed to being an equal opportunity employer and enhancing DE&I across our business. We are proud of the gender diversity we have cultivated throughout the company and our management team. Based on data collected when hired, over 50% of our employees self-identified as women, over 50% of our VPs and above self-identified as women, over 50% of our Executive Leadership Team self-identified as women. Based on recently collected data, of the six members of our Board of Directors, three self-identified as women or from a diverse racial or ethnic group. We intend to continue to develop our DE&I practices and improve performance across our workforce. Our Code of Business Conduct and Ethics prohibits discrimination of any protected group and our employees participate in regular anti-harassment training.

- **Compensation and Benefits**. We are dedicated to building a talented team and strive to offer competitive compensation, including salaries, bonuses and equity awards, and benefits to attract and retain top talent in order to support our business objectives, assist in the achievement of our strategic goals and create value for our stockholders. We formally review employee performance annually and provide merit increases, bonus payments and annual equity awards, subject to achievement of certain goals. In addition to offering benefits such as medical, dental, vision, 401(k) with company matching, flexible spending for healthcare and dependent care, life insurance and both short and long-term disability, we offer work / life balance benefits and employee development opportunities. These include flexible time off , voluntary life-illness-accident insurance, wellness challenges and healthy food options onsite. We also have a variety of company-wide events designed to support camaraderie and encourage teamwork and collaboration. In 2021, we completed the first offering period under the Zentalis Pharmaceuticals, Inc. 2020 Employee Stock Purchase Plan for all full-time employees who elected to participate – a benefit we are proud to offer and that we believe helps to foster our corporate culture and encourage collaboration towards our shared business success.

Human Capital Management

As of December 31, 2022, Zentalis had 156 full-time employees, all of whom are based in the United States. We believe our workforce is highly skilled, with 37% of our employees holding an MD, PhD, or PharmD degree. Of these full-time employees, 114 employees are engaged in research and development activities. None of these employees is represented by labor unions or covered by any collective bargaining agreements.

Zentalis relies on skilled, innovative, and passionate employees to conduct our research, development and business activities. The biopharmaceutical industry is very competitive and recruiting and retaining employees is critical to the continued success of our business. As detailed above, to attract, maintain and motivate our team of ambitious professionals, it is our goal to offer competitive compensation and benefits, a collaborative work environment, ongoing skills development initiatives, attractive career advancement opportunities, and a culture that values DE&I. At Zentalis, we strive for everyone's voice to be heard, for the work to be meaningful, and for employees to think outside of the box.

Environmental

Zentalis aims to minimize the environmental impacts of our business, with the goal of being "green chemists," by applying our science in the labs carefully to efficiently use and conserve precious resources. We encourage all employees to reduce waste and emissions through recycling and other energy conservation measures. Here are a few of the initiatives that demonstrate our focus on environmental impact:

- We prioritize disposing of all hazardous materials and waste in a responsible manner; following strict protocols for the storage, treatment and disposal of hazardous, flammable, chemical or biological waste.
- Our employees are required to promptly report any known or suspected violations of environmental laws or any events that may result in a discharge or emission of hazardous materials.
- We have recycling protocols in all facilities for both regular recyclables and lab waste.

In addition, 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 waste.

Governance

Zentalis prioritizes governance systems and policies that promote fair, transparent and efficient business practices. Here are a few initiatives that demonstrate our focus on good governance:

- Our Board of Directors and Executive Leadership Team oversee all ESG issues.
- We have employee trainings, procedures and policies in place to train our employees on data privacy and cybersecurity. Trainings take place at regular intervals and cover threats and phishing risk. We also have a defined information security incident response plan that is designed to assist Zentalis in detecting and managing cybersecurity incidents.
- We have adopted a Code of Business Conduct and Ethics, and we conduct regular trainings on a variety of related topics, including insider trading compliance and anti-harassment.

Corporate Information

We were initially formed as Zeno Pharmaceuticals, Inc., a Delaware corporation, in December 2014. In conjunction with a corporate restructuring, Zeno Pharma, LLC, a Delaware limited liability company, was formed, and in December 2017 acquired Zeno Pharmaceuticals, Inc., pursuant to a merger agreement. As a result of this merger, Zeno Pharmaceuticals, Inc. became a wholly-owned subsidiary of Zeno Pharma, LLC. In December 2019, Zeno Pharma, LLC changed its name to Zentalis Pharmaceuticals, LLC. In April 2020, in connection with our IPO, Zentalis Pharmaceuticals, LLC was converted to a Delaware corporation pursuant to a statutory conversion and changed its name to Zentalis Pharmaceuticals, Inc.

Available Information

Our Internet address is www.zentalis.com. At our investor relations website, https://ir.zentalis.com/, we make available free of charge a variety of information for investors, including our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements for our annual meetings of stockholders, and any amendments to those reports, as soon as reasonably practicable after we electronically file that material with or furnish it to the SEC. The information found on our website is not part of this Annual Report on Form 10-K or any other report we file with, or furnish to, the SEC. The SEC also maintains a website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is https://www.sec.gov.

Item 1A. Risk Factors

You should carefully consider the risks and uncertainties described below and the other information in this Annual Report on Form 10-K, including our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K and in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. Such risks and uncertainties may be amplified by the COVID-19 pandemic and its potential impact on our business and the global economy. Our business, financial condition, results of operations or prospects could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common stock could decline and you could lose all or part of your investment. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. See "Cautionary Note Regarding Forward-Looking Statements." Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain important factors, including those set forth below.

Risks Related to Our Financial Position 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 predict our future success and viability.

We are a clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We have no products approved for commercial sale and have not generated any revenue from product sales. To date, we have devoted substantially all of our resources and efforts to organizing and staffing our company, business planning, executing partnerships, raising capital, discovering, identifying and developing potential product candidates, securing related intellectual property rights and conducting preclinical studies and clinical trials of our product candidates, including the ongoing clinical trials of azenosertib and ZN-d5. We have not yet demonstrated our ability to obtain marketing approvals, manufacture a product at commercial scale or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. As a result, it may be more difficult for you to accurately predict our future success or viability than it could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by clinical stage biopharmaceutical companies in rapidly evolving fields. We also may need to transition from a company with a research and development focus to a company capable of supporting commercial activities. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

We have incurred significant net losses since inception, and we expect to continue to incur significant net losses for the foreseeable future.

We have incurred net losses in each reporting period since our inception, we have not generated any revenue from product sales to date, and we have financed our operations principally through private financings, our IPO, and follow-on public offerings of our common stock. We have incurred net losses of $237.1 million and $166.1 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $596.4 million. Our losses have resulted principally from expenses incurred in research and development of our product candidates and from management and administrative costs and other expenses that we have incurred while building our business infrastructure. We expect that it will be several years, if ever, before we have a commercialized product and generate revenue from product sales. Even if we succeed in receiving marketing approval for and commercializing one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses as we discover, develop and market additional potential products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we continue our research and development efforts and seek to obtain regulatory approval and commercialization of our product candidates. The net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital and our ability to achieve and maintain profitability.

Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve a number of objectives.

Our business depends entirely on the successful discovery, development and commercialization of our product candidates. We currently generate no revenues from sales of any products. We have no products approved for commercial sale and do not anticipate generating any revenue from product sales for the next several years, if ever. Our ability to generate revenue and achieve profitability depends significantly on our ability, or any future collaborator's ability, to achieve a number of objectives, including:

- successful and timely completion of preclinical and clinical development of our product candidates, including azenosertib and ZN-d5 and any other future product candidates, as well as the associated costs, including any unforeseen costs we have incurred and may continue to incur as a result of preclinical study or clinical trial delays due to public health emergencies, including the COVID-19 pandemic, global economic issues, including rising inflation and interest rates, or the ongoing military conflict in Ukraine, among other causes;
- the availability or successful development of companion diagnostics for biomarkers associated with our product candidates or any other future product candidates;
- establishing and maintaining relationships with contract research organizations, or CROs, and clinical sites for the clinical development, both in the United States and internationally, of our product candidates, including azenosertib and ZN-d5, and any other future product candidates;
- timely receipt of marketing approvals from applicable regulatory authorities for any product candidates for which we successfully complete clinical development;
- maintaining marketing approvals, including making any required post-marketing approval commitments to applicable regulatory authorities;
- developing an efficient and scalable manufacturing process for our product candidates, including obtaining finished products that are appropriately packaged for sale;
- establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for product candidates that we develop, if approved;
- successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether in-house or with one or more collaborators;
- a continued acceptable safety profile following any marketing approval of our product candidates;
- commercial acceptance of our product candidates by patients, the medical community and third-party payors;
- identifying, assessing and developing new product candidates;
- obtaining, maintaining and expanding our intellectual property rights, including patents, trade secrets and know how, and regulatory exclusivity, both in the United States and internationally;
- protecting our rights in our intellectual property portfolio;
- defending against third-party interference or infringement claims, if any;
- negotiating favorable terms in any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- obtaining adequate pricing, coverage and reimbursement by hospitals, government and third-party payors for product candidates that we develop;
- addressing any competing therapies and technological and market developments; and
- attracting, hiring and retaining qualified personnel, especially in the current labor market.

We may never be successful in achieving our objectives and, even if we do, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations.

We will require substantial additional capital to finance our operations. 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 our research and drug development programs or future commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we initiate and conduct clinical trials of, and seek marketing approval for, azenosertib, ZN-d5 and our other 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 commercializing any approved product candidate. Our expenses could increase beyond our

expectations if we are required by the FDA, the European Medicines Agency, or the EMA, or other regulatory agencies to perform clinical trials or preclinical studies in addition to those that we currently anticipate. We may also incur costs related to collaborating with certain diagnostic companies for the development, manufacturing and supply of companion diagnostic tests for biomarkers associated with our product candidates and any future product candidates. Other unanticipated costs may also arise. In addition, if we obtain marketing approval for any of our product candidates, including azenosertib and ZN-d5, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution. Because the design and outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidate we develop. We have also incurred, and expect to continue to incur additional costs associated with operating as a public company, particularly now that we are no longer an emerging growth company. Accordingly, we will need to obtain substantial additional funding in order to maintain our continuing operations.

As of December 31, 2022, we had cash and cash equivalents and marketable securities of $437.4 million. Based on current business plans, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2022 will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2025, but will not be sufficient to fund all of the activities that are necessary to complete the development of our product candidates. 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. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources, which may dilute our stockholders or restrict our operating activities. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Market volatility resulting from public health emergencies such as the COVID-19 pandemic, global supply chain disruptions, international political instability, rising inflation and interest rates or other factors could also adversely impact our ability to access capital as and when needed. 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.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

We are substantially dependent on the success of our lead product candidates, azenosertib and/or ZN-d5, which are currently in clinical trials. If we are unable to complete development of, obtain approval for and commercialize these product candidates in a timely manner, our business will be harmed.

Our future success is dependent on our ability to timely complete clinical trials, obtain marketing approval for and successfully commercialize our lead product candidates. We are investing significant efforts and financial resources in the research and development of our product candidates, which will require additional clinical development, evaluation of clinical, preclinical and manufacturing activities, marketing approval from government regulators, substantial investment and significant marketing efforts before we can generate any revenues from product sales. We are not permitted to market or promote any other product candidate before we receive marketing approval from the FDA and comparable ex-U.S. regulatory authorities, and we may never receive such marketing approvals.

The success of our lead product candidates will depend on several factors, including the following:

- the successful and timely completion of our ongoing and planned clinical trials;
- maintaining and establishing relationships with CROs and clinical sites for the clinical development of our product candidates both in the United States and internationally;
- the frequency and severity of AEs observed in clinical trials;
- efficacy, safety and tolerability profiles that are satisfactory to the FDA or any comparable ex-U.S. regulatory authority for marketing approval;
- the timely receipt of marketing approvals from applicable regulatory authorities;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- the availability or successful development of companion diagnostics for biomarkers associated with our product candidates or any other future product candidates;

- the maintenance of existing or the establishment of new supply arrangements with third-party drug substance and drug product suppliers and manufacturers for clinical development of our product candidates;
- the maintenance of existing, or the establishment of new, scaled production arrangements with third-party manufacturers to obtain finished products that are appropriate for commercial sale of our product candidates if approved, including for supplies of drugs that we are testing in combination with our product candidates;
- obtaining and maintaining our intellectual property rights, including patents, trade secrets and know how, and regulatory exclusivity, both in the United States and internationally;
- the protection of our rights in our intellectual property portfolio;
- the successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

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. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive marketing approvals for our product candidates, we may not be able to continue our operations.

We have and in the future may enter into collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any of these collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates.

We have and in the future may seek third-party collaborators for the research, development and commercialization of one or more of our product candidates. For example, we are collaborating with Pfizer on development of azenosertib, GSK on development of azenosertib, Dana Farber on development of azenosertib, and Zentera on development of certain of our product candidates, including azenosertib and ZN-d5, in certain Asian jurisdictions including China. Our likely collaborators in any future collaboration arrangements we may enter into include large and mid-size pharmaceutical companies and biotechnology companies. If we were to enter into any collaboration arrangements with third parties, those agreements may limit our control over the amount and timing of resources that our collaborators dedicate to the development and commercialization of any product candidates we may seek to develop with them. We cannot predict the success of any collaboration in which we have entered or may enter. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our research programs, our product candidates and any future research programs or product candidates we may develop pose the following risks to us:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations.
- Collaborators may not pursue development and commercialization of any product candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or market considerations, including as a result of a sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition or business combination that diverts resources or creates competing priorities. If this were to happen, we may need additional capital to pursue further development or commercialization of the applicable product candidates.
- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, use our product candidates in clinical trials in an unsafe manner, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing.
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.

- Subject to certain diligence obligations, collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products.
- Collaborators may not properly obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use proprietary information in a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation.
- Collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in cases where that applies, we would not have the exclusive right to commercialize the collaboration intellectual property.
- Disputes may arise between our collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.
- We may lose certain rights under circumstances identified in our collaborations, including if we undergo a change of control.
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.
- Collaborators may be unable to maintain compliance with applicable laws, regulations and guidance, including good practice quality guidelines and regulations, including GLP, GCP and cGMP, or to secure approval for clinical development plans from the FDA or comparable ex-U.S. regulatory authorities.
- We may require certain regulatory, clinical, manufacturing, financial and other information from our collaborators, which, if not provided in a timely manner or at all, could affect our ability to meet our business objectives and/or comply with applicable laws, regulations and guidance.

If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed and we may need additional resources to develop our product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, marketing approval and commercialization described in this annual report apply to the activities of our collaborators.

We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of any product candidates we may develop. These and other similar relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of several factors. If we license rights to any product candidates we or our collaborators may develop, we may not be able to realize the benefit of those transactions if we are unable to successfully integrate them with our existing operations and company culture.

Our long-term prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.

Our future operating results are dependent on our ability to successfully discover, develop, obtain regulatory approval for and commercialize product candidates beyond those we currently have in clinical development. A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from preclinical testing or early clinical trials of a product candidate may not be predictive of the results that will be obtained in later stage clinical trials of the product candidate.

The success of other product candidates we may develop will depend on many factors, including the following:

- generating sufficient data to support the initiation or continuation of clinical trials;
- obtaining regulatory permission to initiate clinical trials;
- contracting with the necessary parties to conduct clinical trials;
- successful enrollment of patients in, and the completion of, clinical trials on a timely basis;
- the timely manufacture of sufficient quantities of the product candidate for use in clinical trials; and
- AEs in the clinical trials.

Even if we successfully advance any other product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this "Risk Factors" section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from our other product candidates.

The regulatory approval processes of the FDA and other comparable ex-U.S. regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

We are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Ex-U.S. regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and other comparable ex-U.S. regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. 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. Even if we eventually complete clinical testing and receive approval of any regulatory filing for our product candidates, the FDA and other comparable ex-U.S. regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested. We have not submitted for, or obtained, regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or other comparable ex-U.S. regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA or other comparable ex-U.S. regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA or other comparable ex-U.S. regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA or other comparable ex-U.S. regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or other comparable ex-U.S. regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- if the FDA or comparable regulatory authority requires approval or clearance of a companion diagnostic for a particular product candidate, and the FDA or comparable regulatory authority does not provide such approval or clearance, then the product candidate may not be approved for marketing; and/or

- the approval policies or regulations of the FDA or other comparable ex-U.S. regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In addition, the policies and practices of the FDA and other regulatory authorities' with respect to clinical trials may change and additional government regulations may be enacted. For example, in recent years the FDA has issued draft guidance and launched programs aiming to reform and modernize the dose optimization procedures used by clinical trial sponsors during the development of oncology drugs. Although these efforts have not yet resulted in any formal changes to the FDA's regulations or policies, changes in the FDA's thinking with respect to dose selection and optimization could require us to change the design of our planned or ongoing clinical trials or otherwise conduct additional preclinical, clinical or manufacturing studies beyond those we currently anticipate, which could increase our costs and/or delay the development of our product candidates. The FDA has also issued a draft guidance regarding diversity in clinical trials. The purpose of this guidance is to provide recommendations to sponsors developing medical products on the approach for developing a Race and Ethnicity Diversity Plan to enroll representative numbers of participants from underrepresented racial and ethnic populations in the United States. If implemented, the FDA will evaluate the Race and Ethnicity Diversity Plan as an important part of the sponsor's development program. This could require us to change the way we enroll our planned clinical trials, which could increase our costs and/or delay the development of our product candidates.

In addition, the regulatory landscape related to clinical trials in the European Union, or EU, recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials, including those that are ongoing, will become subject to the provisions of the CTR. Compliance with the CTR requirements by us, our collaborators and third-party service providers, such as CROs, may impact our development plans.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we obtain approval of our product candidates, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, a REMS, or similar risk management measures. Regulatory authorities may not approve the price we intend to charge for products we may develop, 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. Any of the foregoing scenarios could seriously harm our business.

The clinical trials of our product candidates may not demonstrate safety and efficacy to the satisfaction of the FDA or other comparable ex-U.S. regulatory authorities or otherwise produce positive results.

Before obtaining marketing approval from the FDA or other comparable ex-U.S. regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete and its ultimate outcome is uncertain. A failure of one or more clinical trials can occur at any stage of the process. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials, including that potential biomarkers, even if validated preclinically, may not be functionally validated in clinical trials. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs. We cannot guarantee that the FDA or comparable ex-U.S. regulatory authorities will interpret trial results as we do, and more trials could be required before we are able to submit applications seeking approval

of our product candidates, which may require us to expend significant resources that may not be available to us. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

In addition, we may rely in part on preclinical, clinical and quality data generated by CROs, our collaborators and other third parties for regulatory submissions for our product candidates. While we have or will have agreements governing our relationships with these third parties, we have limited influence over their actual performance. If these third parties do not make data available to us, or, if applicable, make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed, and we may need to conduct additional studies or collect additional data independently. In either case, our development costs would increase.

We do not know whether our future clinical trials will begin on time or enroll patients on time, or whether our ongoing and/or future clinical trials will be completed on schedule or at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- the FDA or comparable ex-U.S. regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory authorizations to commence a trial or reaching a consensus with regulatory authorities on trial design;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval from one or more IRBs or ethics committees;
- IRBs or ethics committees refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes to clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- manufacturing sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trial at the rate we expect, or failing to return for post-treatment follow-up;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of serious AEs in trials of the same class of agents conducted by other companies;
- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable ex-U.S.regulatory authorities to temporarily or permanently shut down due to violations of cGMP regulations or similar ex-U.S. requirements or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCP, or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; and/or
- if we are collaborating with a third party on a clinical trial, our collaborator may not devote sufficient resources to or prioritize our clinical trial.

In addition, disruptions caused by the COVID-19 pandemic have caused and may continue to cause 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 trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable ex-U.S. regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable ex-U.S. regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs or ethics committees for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Further, conducting clinical trials in ex-U.S. countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in ex-U.S. countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with ex-U.S. regulatory schemes, as well as political and economic risks relevant to such ex-U.S. countries.

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

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues.

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

If we are unable to successfully develop companion diagnostics for biomarkers that enable patient selection, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

A key component of our strategy includes the use of companion diagnostics to guide patient selection of our product candidates. In some cases, a diagnostic tool may be commercially available, for example, on a tumor-profiling panel. If not already commercially available, we may be required to seek collaborations with diagnostic companies for the development of diagnostics for biomarkers associated with our product candidates. We may have difficulty in establishing or maintaining such development relationships, and we will face competition from other companies in establishing these collaborations.

There are also several risks associated with biomarker identification and validation. We, in collaboration with any diagnostic partners, may not be able to identify predictive biomarkers for one or more of our programs. We may not be able to validate potential biomarkers (e.g., certain genomic mutations) or their functional relevance preclinically in relevant *in vitro* or *in vivo* models. Data analytics and information from databases that we rely on for identifying or validating some of our biomarker-target relationships may not accurately reflect potential patient populations or may be based on incorrect methodology. Potential biomarkers, even if validated preclinically, may not be functionally effective or validated in human clinical trials.

If we, in collaboration with these parties, are unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so, the development of our product candidates may be adversely affected. The development of companion diagnostic products requires a significant investment of working capital and may not result in any future income. This could require us to raise additional funds, which could dilute our current investors or impact our ability to continue our operations in the future.

There are also risks associated with diagnostics that are commercially available, including that we may not have access to reliable supply for such diagnostics, and that we may not be able to obtain reimbursement for its use without obtaining regulatory approval.

Interim, initial, "topline", and preliminary 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 that could result in material changes in the final data.

From time to time, we may publicly disclose initial, preliminary or topline 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 related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the initial, topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, initial, topline and preliminary 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 from clinical trials that we may complete 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 for their disease. Adverse differences between interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

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 or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the initial, interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Even if approved, our product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if our product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, healthcare payors and others in the medical community. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which the product candidate is approved;
- the availability of companion diagnostics for biomarkers associated with our product candidates or any other future product candidates;
- restrictions on the use of our product candidates, such as boxed warnings or contraindications in labeling, or a REMS, or similar risk management measures, if any, which may not be required of alternative treatments and competitor products;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;

- the availability of coverage and adequate reimbursement, as well as pricing, by third-party payors, including government authorities;
- the availability of the approved product candidate for use as a combination therapy;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of sales and marketing efforts;
- unfavorable publicity relating to our products or product candidates or similar approved products or product candidates in development by third parties; and
- the approval of other new therapies for the same indications.

If any of our product candidates is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from that product candidate and our financial results could be negatively impacted.

If we experience delays or difficulties in the enrollment and/or maintenance of patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Patient enrollment is a significant factor in the timing of clinical trials, and the timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow-up periods. 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 to such trial's conclusion as required by the FDA or comparable ex-U.S. regulatory authorities. Additionally, certain clinical trials for future product candidates may be focused on indications with relatively small patient populations, which may further limit enrollment of eligible patients or may result in slower enrollment than we anticipate. The eligibility criteria of our clinical trials, once established, may further limit the pool of available trial participants.

Patient enrollment may also be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' product candidates. Patient enrollment for any of our clinical trials may be affected by other factors, including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the trial in question as defined in the protocol;
- perceived risks and benefits of the product candidate under study;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients;
- continued enrollment of prospective patients by clinical trial sites; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion or, because they may be late-stage cancer patients, will not survive the full terms of the clinical trials.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

We are developing our product candidates in combination with other therapies, which exposes us to additional risks.

We are developing azenosertib and ZN-d5 in combination with one or more other approved or unapproved therapies to treat cancer or other diseases and may in the future develop additional product candidates in combination with other approved or unapproved therapies. Even if any product candidate we develop were to receive marketing approval or be commercialized

for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or comparable ex-U.S. regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or comparable ex-U.S. regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

We also may choose to evaluate our product candidates in combination with one or more cancer therapies that have not yet been approved for marketing by the FDA or comparable ex-U.S. regulatory authorities. We will not be able to market and sell any product candidate we develop in combination with an unapproved cancer therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved cancer therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of regulatory approval.

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

If the market opportunity for any product candidate that we or our strategic partners develop is smaller than we believe, our revenue may be adversely affected and our business may suffer.

Our projections of addressable patient populations that may benefit from treatment with our product candidates are based on our estimates. These estimates, which have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations and market research, may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. Additionally, the potentially addressable patient population for our product candidates may not ultimately be amenable to treatment with our product candidates. Our market opportunity may also be limited by future competitor treatments that enter the market. If any of our estimates proves to be inaccurate, the market opportunity for any product candidate that we or our strategic partners develop could be significantly diminished and have an adverse material impact on our business.

We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be negatively impacted.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. 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 believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates. In addition, our products may need to compete with off-label drugs used by physicians to treat the indications for which we seek approval. This may make it difficult for us to replace existing therapies with our products.

In particular, there is intense competition in the fields of oncology we are pursuing. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, emerging and start-up companies, universities and other research institutions. We also compete with these organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in-licensing new product candidates.

We have chosen to initially address well-validated biochemical targets, and therefore expect to face competition from existing products and products in development for each of our product candidates. There are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. Many of these current and potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources and commercial expertise than we do. Large pharmaceutical and biotechnology companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing biotechnology products. These companies also have significantly greater research and marketing capabilities than we do and

may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical and biotechnology companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result of all of these factors, our competitors may succeed in obtaining approval from the FDA or other comparable ex-U.S. regulatory authorities or in discovering, developing and commercializing products in our field before we do.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe effects, are more convenient, have a broader label, are marketed more effectively, are reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain marketing approval from the FDA or other comparable ex-U.S. regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if the product candidates we develop achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected.

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

Because we have limited financial and managerial resources, we focus on research programs, therapeutic platforms and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other therapeutic platforms or product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs, therapeutic platforms and product candidates for specific indications may not yield any commercially viable products. 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 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.

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

As product candidates progress through preclinical and clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates, if approved, and generate revenue.

Our business entails a significant risk of product liability and if we are unable to obtain sufficient insurance coverage such inability could have an adverse effect on our business and financial condition.

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an FDA or other regulatory authority investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs. FDA or other regulatory authority investigations could potentially lead to a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources and substantial monetary awards to trial participants or patients. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our product candidates, if approved. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a

reasonable cost to protect us against losses caused by product liability claims that could have an adverse effect on our business and financial condition. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics that we or our collaborators may develop.

Any product candidates we develop may become subject to unfavorable third-party coverage and reimbursement practices, as well as pricing regulations.

The availability and extent of coverage and adequate reimbursement by third-party payors, including government health administration authorities, private health coverage insurers, managed care organizations and other third-party payors is essential for most patients to be able to afford expensive treatments. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of our product candidates will be covered and reimbursed by third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize an adequate return on our investment. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, for example, principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within HHS. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor's determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate. As a result, the coverage determination process is often time-consuming and costly. This process will require us to provide scientific and clinical support for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our product candidates may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the member states of the EU, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing authorization. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, product prices under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products, but monitor and control company profits. Additional ex-U.S. price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

If we are unable to establish or sustain coverage and adequate reimbursement for any future product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Additionally, we or our collaborators may develop companion diagnostic tests for use with our product candidates. Companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical products, will apply to companion diagnostics. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize any product candidates that we develop.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

We may be unable to obtain U.S. or ex-U.S. regulatory approvals and, as a result, may be unable to commercialize our product candidates.

Our product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in the United States and in many ex-U.S. jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. We cannot provide any assurance that any product candidate we may develop will progress through required clinical testing and obtain the regulatory approvals necessary for us to begin selling them.

We have not conducted, managed or completed large-scale or pivotal clinical trials nor managed the regulatory approval process with the FDA or any other regulatory authority. The time required to obtain approvals from the FDA and other regulatory authorities is unpredictable, and requires successful completion of extensive clinical trials which typically takes many years, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its ex-U.S. counterparts use when evaluating clinical trial data can and often changes during drug development, which makes it difficult to predict with any certainty how they will be applied. In addition, the FDA and its ex-U.S. counterparts may require approval or clearance of a companion diagnostic for a particular product candidate and may not approve the product candidate for marketing if such regulatory authority does not approve or clear the companion diagnostic. We may also encounter unexpected delays or increased costs due to new government regulations, including future legislation or administrative action, or changes in FDA or ex-U.S. regulatory authorities policy during the period of drug development, clinical trials and FDA or ex-U.S. regulatory authorities regulatory review.

Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from the particular product candidate for which we developing and seeking approval. Furthermore, any regulatory approval to market a drug may be subject to significant limitations on the approved uses or indications for which we may market the drug or the labeling or other restrictions. In addition, the FDA has the authority to require a REMS as part of approving a NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. Similar requirements may exist in ex-U.S. jurisdictions. These requirements or restrictions might include limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may significantly limit the size of the market for the drug and affect reimbursement by third-party payors.

We are also subject to numerous ex-U.S. regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The ex-U.S. regulatory approval process varies among countries, and generally includes all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in ex-U.S. jurisdictions. Moreover, the time required to obtain approval in ex-U.S. jurisdictions may differ from that required to obtain FDA approval.

Our current or future product candidates may cause significant AEs, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could inhibit regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and AEs associated with our product candidates' use. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable ex-U.S. regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

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 investigational new drugs, 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 subjects 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 harm our business, financial condition and prospects significantly.

Patients in our ongoing and planned clinical trials may in the future suffer significant AEs or other side effects not observed in our preclinical studies or previous clinical trials. Some of our product candidates may be used as chronic therapies or be used in pediatric populations, for which safety concerns may be particularly scrutinized by regulatory agencies. In addition, if our product candidates are used in combination with other therapies, our product candidates may exacerbate AEs associated with the therapy. Patients treated with our product candidates may also be undergoing surgical, radiation and chemotherapy treatments, which can cause side effects or AEs that are unrelated to our product candidate, but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses.

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

Further, if any of our product candidates obtains marketing approval, toxicities associated with such product candidates and not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the product or the withdrawal of the product from the market. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or early-stage clinical trials.

The FDA and other comparable ex-U.S. regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction.

We may choose to conduct international clinical trials in the future. The acceptance of study data by the FDA or other comparable ex-U.S. regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. The acceptance of study data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable ex-U.S. regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from ex-U.S. clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of ex-U.S. data alone unless i) the data are applicable to the U.S. population and U.S. medical practice; ii) the trials were performed by clinical investigators of recognized competence and pursuant to current GCP requirements; and iii) the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including the adequacy of the patient population studied and statistical powering, must be met. Furthermore, even where the ex-U.S. study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many ex-U.S. regulatory authorities have similar approval requirements. In addition, such ex-U.S. trials would be subject to the applicable local laws of the ex-U.S. jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable ex-U.S. regulatory authority will accept data from trials conducted outside of its applicable jurisdiction. If the FDA or any comparable ex-U.S. regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval for commercialization in the applicable jurisdiction.

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

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

Obtaining ex-U.S. regulatory approvals and establishing and maintaining compliance with ex-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if our product candidates receive regulatory approval, they will be subject to significant post-marketing regulatory requirements and oversight.

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 ex-U.S. regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with cGMPs or similar ex-U.S. requirements and GCP for any clinical trials that we conduct post-approval. In addition, CMOs and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations or similar ex-U.S. requirements and standards. If we or a regulatory agency 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 agency 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. In addition, failure to comply with FDA and other comparable ex-U.S. regulatory requirements may subject our company to administrative or judicially imposed sanctions, including:

- delays in or the rejection of product approvals;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on the products, manufacturers or manufacturing process;
- warning or untitled letters;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production; 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.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad.

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

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

If we pursue development of companion diagnostic tests to identify patients who are likely to benefit from our product candidates, the failure to obtain required regulatory clearances or approvals for such diagnostic tests may prevent or delay approval of the therapeutic product. Moreover, the commercial success of any of our product candidates that require a companion diagnostic may be tied to the regulatory approval, market acceptance and continued availability of such companion diagnostic.

A key component of our strategy includes the use of companion diagnostics to guide patient selection of our product candidates. Furthermore, if safe and effective use of any of our product candidates depends on an *in vitro* companion diagnostic that is not otherwise commercially available, then the FDA generally will require approval or clearance of that companion diagnostic at the same time that the FDA approves our product candidates if at all. 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 create or obtain one that would be subject to regulatory approval requirements. The process of obtaining or creating such diagnostic is time consuming and costly.

Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical devices by the FDA and comparable regulatory authorities, and, to date, the FDA has generally required premarket approval of companion diagnostics for cancer therapies requiring patient selection. 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.

If the FDA or a comparable regulatory authority requires approval, clearance or certification of, or confirmatory or additional studies with respect to, 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, obtain or maintain regulatory approval, clearance or certification 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 candidate, if approved, on a timely or profitable basis, if at all. Even if a companion diagnostic is approved, we will rely on the continued ability of any third-party collaborator to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies. Market acceptance of the companion diagnostic may be low as a result of the cost and complexity of utilizing such companion diagnostic.

Additionally, approval, clearance or certification of companion diagnostics may be subject to further legislative or regulatory reforms notably in the EU. On May 25, 2017, the In Vitro Medical Devices Regulation (2017/746), or IVDR, entered into force. The IVDR repeals and replaces the EU In Vitro Diagnostic Medical Devices Directive. Unlike directives, which must be implemented into the national laws of the EU member, regulations are directly applicable, i.e., without the need for adoption of EU member states laws implementing them, in all EU member states and are intended to eliminate current differences in the regulation of medical devices among EU member states. The IVDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for medical devices and ensure a high level of safety and health while supporting innovation. The IVDR became applicable on May 26, 2022. However, on October 14, 2021, the European Parliament and Council adopted a "progressive" roll-out of the IVDR to prevent disruption in the supply of *in vitro* diagnostic medical devices, and there is a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation.

The IVDR 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 an EU 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 national competent authorities or the EMA.

These modifications may make it more difficult and costly for us to obtain regulatory clearances or approvals or certifications for our companion diagnostics or to manufacture, market or distribute our products after clearance or approval or certification is obtained.

Disruptions at the FDA, the SEC and other government agencies caused by funding shortages or global health concerns could prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA and other regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA's and ex-U.S. regulatory authorities' ability to perform routine functions. Average review times at the FDA and ex-U.S. regulatory authorities have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies, such as the EMA, following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. Further, in our operations as a public company, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and ex-U.S. manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the entities it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the United States may have adopted similar restrictions and other policy measures in response to the COVID-19 pandemic.

If we are unable to obtain accelerated approval or any other form of expedited development or review from the FDA or comparable ex-U.S. regulatory authorities, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We may in the future seek an accelerated approval or another form of expedited development or review for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product

candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional confirmatory studies to verity and describe the drug's clinical benefit. If such confirmatory studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug on an expedited basis. In addition, in December 2022, the President signed an omnibus appropriations bill to fund the U.S. government through fiscal year 2023. Included in the omnibus bill is the Food and Drug Omnibus Reform Act of 2022, which among other things, introduced reforms intended to expand the FDA's ability to regulate products receiving accelerated approval, including by increasing the FDA's oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear.

In the EU, under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use may perform an accelerated assessment of a marketing authorization application. Applicants requesting an accelerated assessment procedure must justify that the product candidate is expected to be of major public health interest, particularly from the point of view of therapeutic innovation.

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

We may face difficulties from changes to current regulations and future legislation.

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

For example, in March 2010, the ACA was passed, which substantially changes the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures will impact our business. We are continuing to monitor any changes to the ACA that, in turn, may potentially impact our business in the future.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes include the American Rescue Plan Act of 2021, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Moreover, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Most recently, on August 16, 2022, the IRA was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA or ex-U.S. regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Our relationships with healthcare professionals, clinical investigators, CROs and third party payors in connection with our current and future business activities may be subject to fraud and abuse laws and other healthcare laws and regulations.

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

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;
- the federal false claims laws, including the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal Physician Payments Sunshine Act (renamed the Open Payments Act) requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to

CMS information regarding payments and other transfers of value to physicians, as defined by such law, certain non-physician practitioners including physician assistants and nurse practitioners, and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. The information reported is publicly available on a searchable website, with disclosure required annually; and

- analogous state and ex-U.S. 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 non-governmental third-party payors, including private insurers.

Some state laws require biotechnology companies to comply with the biotechnology industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Some state laws require biotechnology companies to report information on the pricing of certain drug products.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and ex-U.S. laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or ex-U.S. laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our business, results of operation, and financial condition.

In the United States, HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. We do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties, but we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA. Certain states have also adopted comparable privacy and security laws and regulations governing the privacy, processing and protection of personal information. For example, the State of California enacted the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with, data breach litigation. Further, the California Privacy Rights Act, or CPRA, generally went into effect on January 1, 2023, and significantly amends the CCPA. The CPRA imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia, Connecticut, Utah and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For instance, the EU General Data Protection Regulation, or GDPR, went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements, administrative penalties and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States. In

July 2020, the Court of Justice of the EU, or CJEU, limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses, or SCCs. In March 2022, the US and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-US Data Privacy Framework has not been implemented beyond an executive order signed on October 7, 2022 on Enhancing Safeguards for Untied States Signals Intelligence Activities. The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs have been required for relevant new data transfers since September 27, 2021; existing standard contractual clauses arrangements had to be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the UK. The UK's Information Commissioner's Office has published new data transfer standard contracts for transfers from the United Kingdom under the UK GDPR. This new documentation has been mandatory for relevant data transfers since September 21, 2022; existing SCCs arrangements must be migrated to the new documentation by March 21, 2024. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international data transfers. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Further, from January 1, 2021, we have had to comply with both the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in United Kingdom national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of £17.5 million or 4% of global turnover. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CMOs, 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, CMOs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA and other ex-U.S. authorities regulations, provide accurate information to the FDA or ex-U.S. regulatory authorities, comply with federal, state and ex-U.S. health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. 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. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

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 our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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

Our research and development activities could be affected or delayed as a result of possible restrictions on animal testing.

Certain laws and regulations require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted, delayed or become more expensive.

Our business activities may be subject to the U.S. Foreign Corrupt Practices Act, or the FCPA, and similar anti-bribery and anti-corruption laws of other countries in which we operate, as well as U.S. and certain ex-U.S. export controls, trade sanctions, and import laws and regulations. Compliance with these legal requirements could limit our ability to compete in ex-U.S. markets and subject us to liability if we violate them.

If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits companies and their employees and third party intermediaries from offering, promising, giving or authorizing the provision of anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, hospitals owned and operated by the government, and doctors and other hospital employees would be considered ex-U.S. officials under the FCPA. Recently the SEC and the U.S. Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents or contractors, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, disgorgement, and other sanctions and remedial measures, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international activities, our ability to attract and retain employees and our business, prospects, operating results and financial condition.

In addition, our products and activities may be subject to U.S. and ex-U.S. export controls, trade sanctions and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U.S. export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments, and persons targeted by U.S. sanctions. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or products targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to existing or potential customers with international operations. Any decreased use of our products or limitation on our ability to export or sell access to our products would likely adversely affect our business.

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

The COVID-19 pandemic has adversely impacted, and we expect will continue to adversely impact, our business, including our preclinical studies and clinical trials.

In 2020, a strain of the novel coronavirus disease, COVID-19, was declared a pandemic and spread across the world, including throughout the United States, Europe and Asia. The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. Our employees are working based on a hybrid work model, in which they work both from our offices and remotely. As a result of the COVID-19 pandemic, we have experienced and we may continue to experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

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

The COVID-19 pandemic continues to evolve. The extent to which the pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the impact of variants, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the adoption, the prolonged efficacy of available vaccines and effectiveness of vaccination efforts and other actions taken in the United States and other countries to contain and treat the disease.

Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. The competition for qualified personnel in the biotechnology field is intense and as a result, we may be unable to continue to attract and retain qualified personnel necessary for the future success of our business. We could in the future have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse

opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed.

If we are unable to establish effective sales or marketing capabilities or enter into agreements with third parties to sell or market our product candidates, we may not be able to successfully sell or market our product candidates that obtain regulatory approval.

We have never commercialized a product candidate. In order to commercialize any product candidates, if approved, for which we retain commercialization rights, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services for each of the territories in which we may have approval to sell or market our product candidates. We may not be successful in accomplishing these required tasks. In addition, for product candidates for which we do not retain commercialization rights, we will rely on the assistance of collaborators to successfully commercialize any product candidates that are approved.

Establishing an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates will be expensive and time-consuming, and will require significant attention of our executives to manage. Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could adversely impact the commercialization of any of our product candidates that we obtain approval to market, especially if we also do not have arrangements in place with third parties to provide such services on our behalf. Alternatively, if we choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration. If we are unable to enter into such arrangements when needed, on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval or any such commercialization may experience delays or limitations. If we are unable to successfully commercialize our approved product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

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.

In order to successfully implement our development and commercialization plans and strategies, and as we continue to operate as a public company, we expect to need additional managerial, operational, sales, marketing, financial, legal, compliance and other personnel. Future growth would impose significant added responsibilities on members of management, including:

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

Our future financial performance and our ability to successfully develop and, if approved, commercialize, our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities. Furthermore, certain of our employees, including members of our management team perform services on behalf of Kalyra Pharmaceuticals, Inc., and Zentera Therapeutics, pursuant to intercompany and collaborative agreements, respectively. As a result, such individuals do not allocate all of their time and resources to us and our other subsidiaries which, coupled with the need to manage growth activities, could further limit their ability to devote a sufficient amount of attention to day-to-day activities of our business.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of clinical development and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third party service providers is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of our product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing third party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our business and operations may suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity.

Despite the implementation of security measures, our information systems and those of our current and any future CROs, CMOs and other contractors, consultants, collaborators and third-party service providers, are vulnerable to attack, damage and interruption from computer viruses and malware (e.g., ransomware), malicious code, natural disasters, terrorism, war, telecommunication and electrical failure, hacking, cyberattacks, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation-state and nation-state-supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization. Attacks upon information technology systems are also increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. If such an event were to occur and cause interruptions in our operations or result in the unauthorized acquisition of or access to our trade secrets, personal information or other proprietary or sensitive information, it could result in a material disruption of our drug discovery and development programs. Some federal, state and ex-U.S. government requirements include obligations of companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Notifications and follow-up actions related to a security breach could impact our reputation, cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal and/or international privacy and security laws.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption, failure or security breach. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

EU pricing, drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the European member states.

We intend to seek approval to market our product candidates in both the United States and in selected ex-U.S. jurisdictions. If we obtain approval in one or more ex-U.S. jurisdictions for our product candidates, we will be subject to rules

and regulations in those jurisdictions. In some ex-U.S. countries, particularly those in the EU, the pricing of drugs is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future healthcare reform measures.

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national laws of EU member states, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

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

The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected.

Unfavorable global, political or economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the recent global economic downturn has caused rising inflation and interest rates and has led to extreme volatility and disruptions in the capital and credit markets. A worsening or prolonged economic downturn or recession could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, and cause the prices of our supplies to increase or cause our customers to delay making payments for our services. In addition, the current military conflict between Russia and Ukraine could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have and may in the future be initiated by nations including the U.S., the EU or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and/or our supply chain, our CROs, CMOs and other third parties with which we conduct business. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our operations are vulnerable to interruption by fire, severe weather conditions, power loss, telecommunications failure, terrorist activity and other events beyond our control, which could harm our business.

Our facilities are located in regions that experience severe weather from time to time. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major tornado, flood, fire, earthquake, power loss, terrorist activity or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any

losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

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

As of December 31, 2022, we had available federal and state net operating loss carryforwards, or NOLs, of approximately $390.3 million and $192.4 million, respectively. $369.4 million of our federal NOLs were generated in taxable years beginning after December 31, 2017 and can be carried forward indefinitely, but may only be used to offset up to 80% of our taxable income in future periods. This limitation may require us to pay U.S. federal income taxes in future years despite generating federal NOLs in prior years. Our federal NOLs generated in tax years beginning prior to January 1, 2018 are not subject to this limitation, but are only permitted to be carried forward for 20 taxable years under applicable U.S. federal tax law, and will start to expire in 2033 if not utilized. Our state NOLs begin to expire in 2033.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a cumulative change in its ownership by one or more "5-percent shareholders" that exceeds 50 percentage points over a rolling three-year period), the corporation's ability to use its pre-ownership change federal NOLs and certain other pre-change tax attributes to offset its post-change taxable income and income tax liabilities may be limited. Similar rules may apply under state tax laws. We may have experienced such ownership changes in the past and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. We have not conducted any studies to determine whether any such ownership changes have occurred or the annual limitations, if any, that could result from such ownership changes. Our ability to utilize our NOLs and certain other tax attributes could be limited by an ownership change as described above and consequently, we may not be able to utilize a material portion of our NOLs and certain other tax attributes, which could have a material adverse effect on our cash flows and results of operations.

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

We plan to 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 ex-U.S. countries if we obtain the necessary approvals, including:

- differing regulatory requirements and reimbursement regimes in ex-U.S. countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular ex-U.S. economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- ex-U.S. taxes, including withholding of payroll taxes;
- ex-U.S. currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing ex-U.S. operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable ex-U.S. regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those ex-U.S. countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

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

From time to time, we may evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;

- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

The requirements of being a public company may strain our resources, result in more litigation and divert management's attention.

As a public company, we are and will continue to be subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, the listing requirements of Nasdaq and other applicable securities rules and regulations. Complying with these rules and regulations has increased and will increase our legal and financial compliance costs, make some activities more difficult, time consuming or costly and increase demand on our systems and resources. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and operating results. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are required to disclose changes made in our internal control over financial reporting on a quarterly basis. In order to maintain and, if required, improve our disclosure controls and procedures and internal control over financial reporting to meet this standard, significant resources and management oversight may be required. As a result, management's attention may be diverted from other business concerns, which could adversely affect our business and operating results. We may also need to hire additional employees or engage outside consultants to comply with these requirements, which will increase our costs and expenses.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We have invested and intend to continue to invest in resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us and our business may be adversely affected.

These new rules and regulations may make it more expensive for us to obtain director and officer liability insurance and, in the future, we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our Board of Directors, particularly to serve on our Audit Committee and Compensation Committee, and qualified executive officers. By disclosing information in filings required of us as a public company, our business and financial condition will continue to become more visible, which we believe may result in threatened or actual litigation, including by competitors and other third parties. If those claims are successful, our business could be seriously harmed. Even if the claims do not result in litigation or are resolved in our favor, the time and resources needed to resolve them could divert our management's resources and seriously harm our business.

A portion of our manufacturing of our lead product candidates takes place in ex-U.S. countries, including China, through third-party manufacturers. A significant disruption in the operation of those manufacturers, a trade war or political unrest in such ex-U.S. countries, including China, could materially adversely affect our business, financial condition and results of operations.

We currently contract manufacturing operations to third parties, and clinical quantities of our lead product candidates are manufactured by certain of these third parties outside the United States, including in China, and we expect to continue to use such third-party manufacturers for such product candidates. Any disruption in production or inability of our manufacturers in such ex-U.S. countries, including in China, to produce adequate quantities to meet our needs, whether as a result of a natural disaster or other causes, could impair our ability to operate our business on a day-to-day basis and to continue our development of our product candidates. Furthermore, since these manufacturers are located outside the United States, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the United States or ex-U.S. governments, political unrest or unstable economic conditions in such ex-U.S. countries, including in China. For example, a trade war could lead to tariffs on the chemical intermediates we use that are manufactured in China. Any of these matters could materially and adversely affect our business and results of operations. Any recall of the manufacturing lots or similar action regarding our product candidates used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third-party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currency in the ex-U.S. countries. Future appreciation of the local currency could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in the ex-U.S. countries, including in China.

Risks Related to Our Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary platform.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies and their uses, our and our licensors' ability to operate without infringing the proprietary rights of others, and our and our licensors' ability to successfully defend our patents, including those that we have in-licensed, against third-party challenges. If we or our licensors are unable to protect our intellectual property rights or if our intellectual property rights are inadequate for our technology or our product candidates, our competitive position could be harmed. We and our licensors generally seek to protect our proprietary position by filing patent applications in the United States and outside of the United States related to our product candidates, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications will result in patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents, if issued, will be infringed or will not be designed around, invalidated or rendered unenforceable by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our and our licensors' proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our or our licensors' rights or permit us or our licensors to gain or keep any competitive advantage. These uncertainties and/or limitations in our and our licensors' ability to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

Although we license issued patents in the United States and ex-U.S. countries, we cannot be certain that the claims in our other U.S. pending patent applications, corresponding international patent applications and patent applications in certain ex-U.S. countries will be considered patentable by the United States Patent and Trademark Office, or USPTO, courts in the United States or by the patent offices and courts in ex-U.S. countries, nor can we be certain that the claims in our issued patents will not be found invalid or unenforceable if challenged.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or our licensors or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can

result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we or our licensors do and many of whom have made significant investments in competing technologies, may seek, may have filed patent applications, or may have already obtained patents that will limit, interfere with or block our ability to make, use and sell our product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing ex-U.S. competitors a better opportunity to create, develop and market competing products.

The patent prosecution process is also expensive and time-consuming, and we or our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we or our licensors may not identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, directed to technology that we license, including those from our licensors and from third parties. We also may require the cooperation of our licensors in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors have been or will be conducted in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in-license, and as a result our ability to develop and commercialize products or product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products.

In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, CMOs, consultants, advisors, licensors, and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

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

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we may enter into additional license agreements in the future. For example, our wholly owned subsidiary, ZMI, is party to a license agreement with Recurium IP under which we have an exclusive license to certain intellectual property rights, including certain intellectual property covering azenosertib, ZN-d5, and our BCL-xL product candidate.

This and our other existing license agreements impose on us, and we expect that any future license agreements where we in-license intellectual property will impose on us, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to bankruptcy-related proceedings, the licensors may have the right to terminate the licenses, in which event we would not be able to market products covered by the licenses.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our product candidates in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation. Licensing of intellectual property is of critical importance to our business and involves complex legal,

business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

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

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the affected product candidates, which would have a material adverse effect on our business.

In addition, certain of our agreements may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities. For example, if we choose to sublicense or assign to any third parties certain patent rights exclusively in-licensed under the Recurium Agreement, we may be required to pay to Recurium a specified percentage of certain sublicensing income to be received in connection with such transaction.

If the scope of any patent protection our licensors obtain is not sufficiently broad, or if our licensors lose any of the patent protection we license, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the existence, issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our product candidates or that effectively prevent others from commercializing competitive product candidates.

Moreover, the scope of claims in a patent application can be significantly reduced before any claims in a patent issue, and claim scope can be reinterpreted after issuance. Even if patent applications we license currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we license may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner, which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our in-licensed patents may not cover our product candidates or may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant review, or PGR, and inter partes review, or IPR, or other similar proceedings in the USPTO or ex-U.S. patent offices challenging our patent rights. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity of our patents, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensors and the patent examiner were unaware during prosecution. There is no assurance that all potentially relevant prior art relating to our patents and patent applications or those of our licensors has been found. There is also no assurance that there is not prior art of which we or licensors were or are aware of, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications or those of our licensors, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us. Such loss of in-licensed patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, 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.

The patent protection and patent prosecution for some of our product candidates may be dependent on our licensors and third parties.

We or our licensors may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. It is possible that defects as to form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our licensors, whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our in-licensed patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

As a licensee, we rely on third parties to file and prosecute patent applications and maintain patents and otherwise protect the licensed intellectual property under some of our license agreements. We have not had and do not have primary control over these activities for certain of our patents or patent applications and other intellectual property rights. We cannot be certain that such activities by third parties have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with some of our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. If any of our licensors or any of our future licensors or future collaborators fails to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

In addition, even where we have the right to control patent prosecution of patents and patent applications we have acquired or licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to us assuming control over patent prosecution.

Our technology acquired or licensed from various third parties, including our licensors, 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 use in fields other than the fields licensed to us or for use in 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.

If we are limited in our ability to utilize acquired or licensed technologies, or if we lose our rights to critical licensed technology, we may be unable to successfully develop, out-license, market and sell our products, which could prevent or delay new product introductions. Our business strategy depends on the successful development of licensed and acquired technologies into commercial products. Therefore, any limitations on our ability to utilize these technologies may impair our ability to develop, out-license or market and sell our product candidate.

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

Some of the intellectual property rights we have acquired or licensed or may acquire or license in the future may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any

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

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to develop products that are similar to our product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors might not have been the first to make the inventions covered by the issued patents or patent application that we own or license;
- we or our licensors might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our licensors' pending patent applications will not lead to issued patents;
- issued patents that we own or license may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.
- Should any of these events occur, it could significantly harm our business, results of operations and prospects.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation and administrative proceedings, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent invalidity and infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO, ex-U.S. patent offices and/or in a court of law. Numerous third-party U.S. and ex-U.S. issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates.

As the biopharmaceutical industry expands and more patents issue, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published we may be unaware of third-party patents that may be

infringed by commercialization of any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes these patents. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation that may cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any of our product candidates until the asserted patent expires or is held finally invalid or unenforceable or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- subject us to significant liability to third parties; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

Although no third party has asserted a claim of patent infringement against us as of the date of this periodic report, others may hold proprietary rights that could prevent our product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin activities relating to our product candidates or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or develop our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition and operating results.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we and/or our licensors may be required to file infringement claims, which can be expensive and time-consuming. Further, our licensors may need to file infringement claims, but they may elect not file such claims. In addition, in a patent infringement proceeding, a court may decide that a patent we own or license is not valid, is unenforceable and/or is not infringed. If we or any of our licensors or potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could assert that our patent is invalid and/or unenforceable in whole or in part. In patent litigation, defendant allegations of invalidity and/or unenforceability of asserted patents are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty or written description, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent intentionally withheld material information from the USPTO or made a misleading statement during prosecution.

If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications or those of our licensors is threatened, it could dissuade companies from collaborating with

us to license, develop or commercialize current or future product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

Derivation or interference proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.

Derivation or interference proceedings provoked by third parties or brought by us or our licensors, or declared by the USPTO or similar proceedings in ex-U.S. patent offices may be necessary to determine the priority of inventions with respect to our or our licensors' patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our or our licensors' defense of such proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

In September 2011, the Leahy-Smith America Invents Act, or Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first inventor to file" system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either (1) file any patent application related to our product candidates or (2) invent any of the inventions claimed in our patents or patent applications.

The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications are prosecuted and also affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings,

including PGR, IPR, and derivation proceedings. 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. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' 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.

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.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or other ex-U.S. legislative bodies may pass patent reform legislation that is unfavorable to us.

For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our or our licensors' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO, or similar authorities in ex-U.S. jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our or our licensors' ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

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

We or our licensors may be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we or our licensors are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

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 term of a patent, and the protection it affords, is limited. Even if patents directed to our product candidates are obtained, once the patent term has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of product candidates, patents directed to our product candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we or our licensors do not obtain patent term extension for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration

term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA-approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain ex-U.S. countries upon regulatory approval of our product candidates. However, we or our licensors may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we or our licensors are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

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

Although we have issued patents and pending patent applications in the United States and certain other countries, filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some ex-U.S. countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we or our licensors have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

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

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the USPTO and various ex-U.S. patent offices at various points over the lifetime of our patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on third parties to pay these fees when due. Additionally, the USPTO and various ex-U.S. patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

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

In addition, we rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants, licensors and advisors, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we or our licensors do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biopharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biopharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or 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, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct certain aspects of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, comply with applicable regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators and third-party CROs, to conduct certain aspects of our preclinical studies and clinical trials and to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. 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, including CROs, are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable ex-U.S. regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable ex-U.S. 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 and similar ex-U.S. requirements. 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 adversely affected if any of these third parties violates federal, state or ex-U.S. fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Further, these investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. 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 independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed or precluded entirely.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

The COVID-19 pandemic and government measures taken in response have also had a significant impact on our CROs, and we expect that they will face further disruption which may affect our ability to initiate and complete our preclinical studies and clinical trials.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We contract with third parties for the manufacture of our product candidates for preclinical studies and our ongoing clinical trials, and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. We rely, and expect to continue to rely, on third-party manufacturers for the production of our product candidates for preclinical studies and clinical trials under the guidance of members of our organization. We do not have long-term supply agreements, and we purchase our required supply on a purchase order basis. Furthermore, the raw materials for our product candidates are sourced, in some cases, from a single-source supplier. We currently mitigate potential supply risks for azenosertib and ZN-d5, if any, through inventory management. If we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials.

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third-party manufacturers to manufacture our product candidates according to our schedule, or at all, including if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party manufacturers at a time that is costly or inconvenient for us;
- the breach by the third-party manufacturers of our agreements with them;

- the failure of third-party manufacturers to comply with applicable regulatory requirements;
- the failure of the third-party manufacturers to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our third-party contract manufacturing partners for compliance with cGMP regulations or similar ex-U.S. requirements for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our third-party contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable ex-U.S. regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including 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. Our current and anticipated future dependence upon others for the manufacture of our product candidates or drugs may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

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

Manufacturing drugs, especially in large quantities, is complex and may require the use of innovative technologies. Each lot of an approved drug product must undergo thorough testing for identity, strength, quality, purity and potency. Manufacturing drugs requires facilities specifically designed for and validated for this purpose, and sophisticated quality assurance and quality control procedures are necessary. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturer, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. The use of biologically derived ingredients can also lead to allegations of harm, including infections or allergic reactions, or closure of product facilities due to possible contamination. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization as a result of these challenges, or otherwise, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

If we decide to establish collaborations in the future, but are not able to establish those collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We may continue to seek to selectively form collaborations to expand our capabilities, potentially accelerate research and development activities and provide for commercialization activities by third parties. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We would face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable ex-U.S. regulatory authorities, the potential market for the subject product

candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. Further, we may not be successful in our efforts to establish a collaboration or other alternative arrangements for future product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy.

In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Even if we are successful in entering into a collaboration, the terms and conditions of that collaboration may restrict us from entering into future agreements on certain terms with potential collaborators.

If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Risks Related to Ownership of Our Common Stock

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

The trading price of our common stock is likely to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general, and pharmaceutical and 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.

Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In addition to the factors discussed in this “Risk Factors” section these factors include:

- the timing and results of preclinical studies and clinical trials of our product candidates or those of our competitors;
- the success of competitive products or announcements by potential competitors of their product development efforts;
- regulatory actions with respect to our products or our competitors’ products;
- actual or anticipated changes in our growth rate relative to our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- market conditions in the pharmaceutical and biotechnology sector;
- changes in the structure of healthcare payment systems;
- speculative trading in and short sales of our common stock, as well as trading phenomena such as the "short squeeze";
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- expiration of market stand-off or lock-up agreements; and
- general economic, industry and market conditions.

In addition, the trading prices for common stock of other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. The COVID-19 pandemic continues to evolve and the duration of its impact remains uncertain. The extent to which the pandemic may impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expense related to the ongoing development of our product candidates or future development programs;
- results of clinical trials, or the addition or termination of clinical trials or funding support by us or potential future partners;
- our execution of any collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under potential future arrangements or the termination or modification of any such potential future arrangements;
- any intellectual property infringement, misappropriation or violation lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our product candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such product candidates;
- regulatory developments affecting our product candidates or those of our competitors; and
- changes in general market and economic conditions.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

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

As of December 31, 2022, our executive officers and directors, combined with our stockholders who owned more than 5% of our common stock, together with their respective affiliates, owned a significant percentage of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as matters related to our management and affairs. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. 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.

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

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Outstanding shares of our common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act, or to the extent that such shares have already been registered under the Securities Act and are held by non-affiliates of ours. Moreover, holders of a substantial number of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also register all shares of common stock that we may issue

under our equity compensation plans or that are issuable upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product candidates on unfavorable terms to us.

We may seek additional capital through a variety of means, including through public or private equity, debt financings or other sources, including up-front payments and milestone payments from strategic collaborations. For example, in August 2020, July 2021 and May 2022, we completed underwritten public offerings of our common stock and in April 2022, we completed a direct offering of our common stock. To the extent that we raise additional capital through the sale of equity or convertible debt or equity securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Such financing may result in dilution to stockholders, imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through up-front payments or milestone payments pursuant to strategic 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. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

If securities or industry analysts do not publish research or reports, or if they publish adverse or misleading research or reports, regarding us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. If any of the analysts who cover us issue adverse or misleading research or reports regarding us, our business model, our intellectual property, our stock performance or our market, or if our operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions in our certificate of incorporation and 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 certificate of incorporation and bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions, among other things:

- establish a classified Board of Directors so that not all members of our Board of Directors are elected at one time;
- permit only the Board of Directors to establish the number of directors and fill vacancies on the Board of Directors;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- authorize the issuance of "blank check" preferred stock that our Board of Directors could use to implement a stockholder rights plan (also known as a "poison pill");
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting;
- authorize our Board of Directors to amend the bylaws;
- establish advance notice requirements for nominations for election to our Board of Directors or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and
- require a super-majority vote of stockholders to amend some provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, 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 certificate of incorporation, 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 certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our certificate of incorporation or our bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This exclusive-forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to this provision. If a court were to find this exclusive-forum provision in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business. Nothing in our certificate of incorporation precludes stockholders that assert claims under the Securities Act or the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation of the value of our common stock.

We have never declared or paid any cash dividends on our equity securities. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to any appreciation in the value of our common stock, which is not certain.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. Now that we are no longer an emerging growth company, our independent registered public accounting firm is required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

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

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation

in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our principal executive office is located at 1359 Broadway, Suite 1710, New York, New York, 10018, where we lease approximately 31,300 square feet of office space under a lease that expires in November 2032. We also occupy approximately 56,700 square feet and 17,900 square feet of office and laboratory space, respectively, in San Diego, California, under a lease that expires in September 2032. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

We are not subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

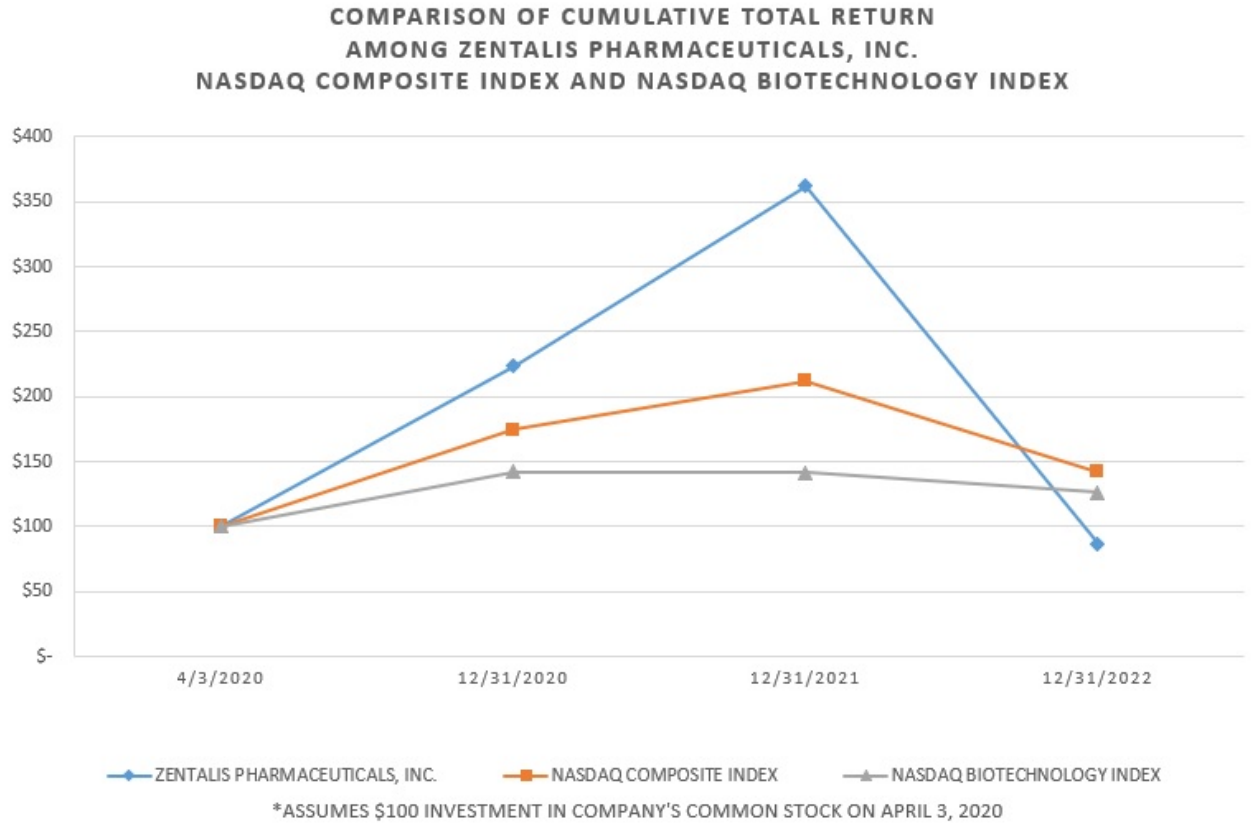
Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

On April 3, 2020, our common stock began trading on The Nasdaq Global Market under the symbol "ZNTL." Prior to that time, there was no public market for our common stock.

Stock Performance Graph

The following graph and table illustrate the total return from April 3, 2020 (the date of our IPO) through December 31, 2022, for (i) our common stock, (ii) the Nasdaq Composite Index, and (iii) the Nasdaq Biotechnology Index. The graph and the table assume that $100 was invested on April 3, 2020 in each of our common stock, the Nasdaq Composite Index, and the Nasdaq Biotechnology Index, and that any dividends were reinvested. The graph assumes our closing sales price on April 3, 2020 of $23.20 per share as the initial value of our common stock and not the initial offering price to the public of $18.00 per share. The comparisons reflected in the graph and table represent past performance and are not intended to forecast the future performance of our stock and may not be indicative of our future performance.



Holders

As of February 27, 2023, there were approximately 15 holders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

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

Recent Sales of Unregistered Securities

The Company did not sell any equity securities during the year ended December 31, 2022 that were not registered under the Securities Act.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12. "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" of this Annual Report on Form 10-K.

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 financial condition and operating results together with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements based upon current plans, expectations and beliefs involving risks and uncertainties. As a result of many factors, including those set forth under "Risk Factors" and elsewhere in this Annual Report on 10-K, our actual results may differ materially from those anticipated in these forward-looking statements. For convenience of presentation some of the numbers have been rounded in the text below.

A discussion regarding our financial condition and results of operations for the years ended December 31, 2022 and 2021, including a year-to-year comparison between 2022 and 2021, is presented below. For a discussion regarding our financial condition and results of operations for the year ended December 31, 2020, including a year-to-year comparison between 2021 and 2020, refer to Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on 10-K for the year ended December 31, 2021 filed on February 24, 2022.

Overview

We are a clinical-stage biopharmaceutical company focused on discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancers. We are developing a focused pipeline of potentially best-in-class oncology candidates. Our product candidates are:

- Azenosertib (ZN-c3), a potentially first-in-class Wee1 inhibitor for advanced solid tumors and hematological malignancies;
- ZN-d5, a B-cell lymphoma 2, or BCL-2, inhibitor for hematological malignancies and related disorders; and
- A heterobifunctional degrader of BCL-xL, a member of the anti-apoptotic BCL-2 proteins, for solid tumors and hematological malignancies.

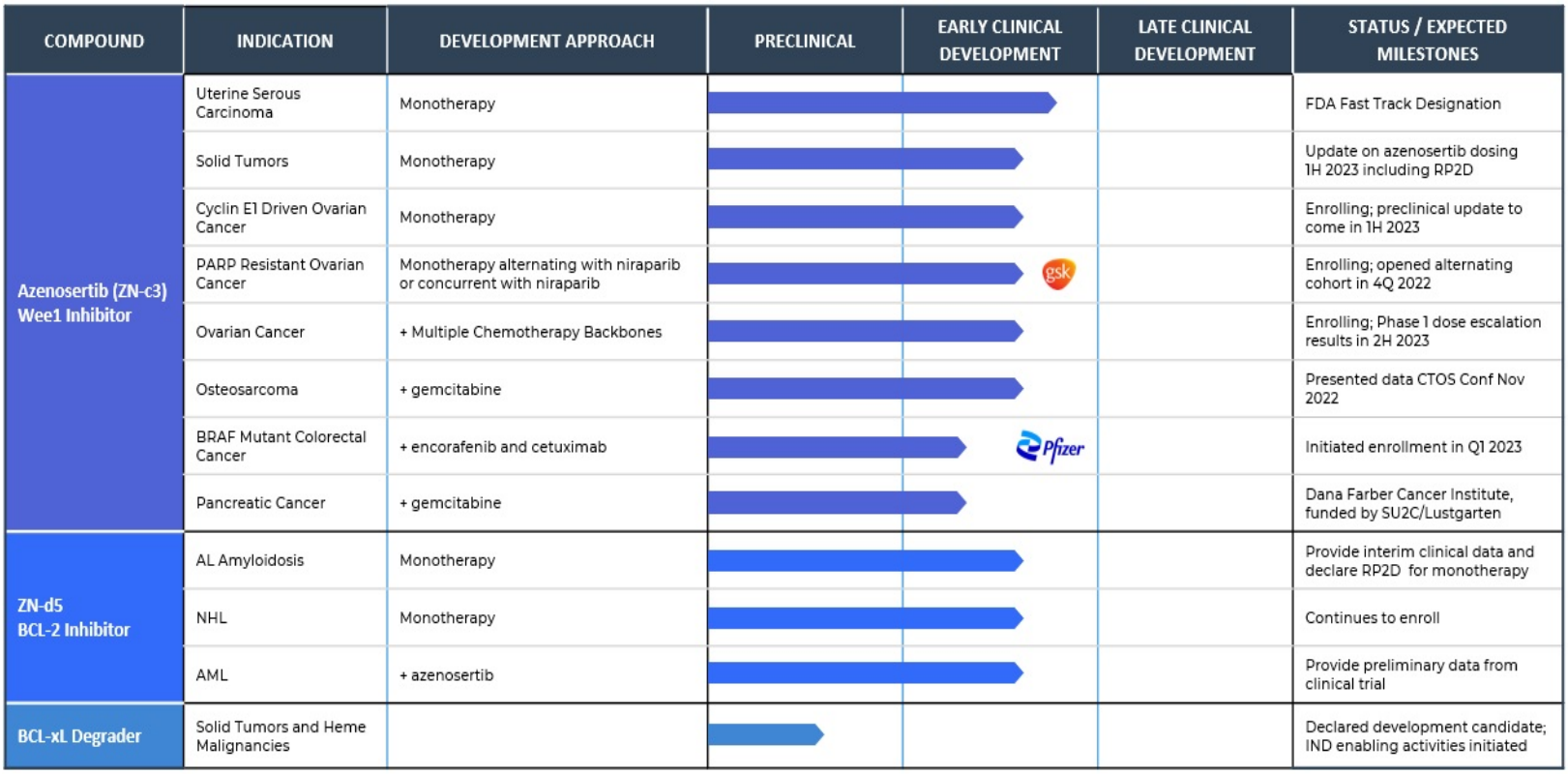
We are currently evaluating azenosertib and ZN-d5 in multiple ongoing clinical trials and conducting studies to enable an Investigational New Drug, or IND, application for our BCL-xL product candidate. We also continue to use our extensive drug discovery experience and capabilities across cancer biology and medicinal chemistry, which we refer to as our Integrated Discovery Engine, to advance our ongoing research on protein degraders of undisclosed targets. We believe our product candidates are differentiated from current programs targeting similar pathways and, if approved, have the potential to significantly impact clinical outcomes of patients with cancer.

Our Pipeline

We are developing a focused pipeline of oncology product candidates with the potential to address significant unmet medical need for cancer patients. Two of our product candidates are currently in multiple ongoing clinical trials: azenosertib, an inhibitor of Wee1, a protein tyrosine kinase, and ZN-d5, a selective inhibitor of BCL-2. To date, azenosertib has been well tolerated and has demonstrated monotherapy anti-tumor activity across multiple tumor types in clinical trials. In addition, ZN-d5 has been well tolerated in clinical trials to date. We have also declared a development candidate for our BCL-xL degrader program, for which we are conducting IND-enabling studies.

We currently exclusively in-license worldwide development and commercialization rights to azenosertib, ZN-d5, and our BCL-xL product candidate. We out-licensed azenosertib and ZN-d5 development and commercialization rights in select Asian countries, including China, to our joint venture, Zentera Therapeutics, or Zentera. As of December 31, 2022, we held a 40.3% equity interest in Zentera. For more information about our joint venture with Zentera, see Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations—License Agreements and Strategic Collaborations" and Note 3 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

The following table summarizes our product candidate pipeline.



Our Development Programs

Azenosertib (Wee1 Inhibitor)

Azenosertib is a potentially best-in-class and first-in-class oral, small molecule Wee1 inhibitor. As illustrated in the figure below, the inhibition of Wee1, a DNA damage response kinase, drives cancer cells into mitosis without being able to repair damaged DNA, resulting in cell death and thereby preventing tumor growth and potentially causing tumor regression. Currently, there are no Wee1 inhibitors approved by the U.S. Food and Drug Administration, or FDA. We have designed azenosertib to have advantages over other investigational therapies targeting Wee1, including superior selectivity and PK properties. Azenosertib is currently being evaluated in the clinic for advanced solid tumors and hematological malignancies in the following three therapeutic settings of high unmet medical need:

- as a monotherapy,
- in combination with traditional chemotherapy and DNA damaging agents, and
- in combination with molecularly targeted agents.

Two key components of our azenosertib clinical development strategy are our dose optimization activities and our pursuit of Cyclin E1 as a patient enrichment strategy.

Azenosertib is being evaluated in multiple current or planned clinical trials, including the following:

- ***Monotherapy - Phase 2 Clinical Trial in Recurrent or Persistent Uterine Serous Carcinoma (USC) (ZN-c3-004).*** Azenosertib is currently being evaluated as a monotherapy in a Phase 2 clinical trial in adult women with USC. As of a September 14, 2022 data cutoff, a total of 43 patients were enrolled and dosed. Azenosertib was well tolerated. The most common treatment related adverse events, or AEs, were nausea (60.5% all grades/9.3% grade 3 or higher), fatigue (46.5% all grades/9.3% grade 3 or higher), diarrhea (37.2% all grades/7.0% grade 3 or higher) and vomiting (32.6% all grades/7.0% grade 3 or higher). We anticipate declaring an azenosertib monotherapy RP2D in the first half of 2023, and we plan to update the timeline of this USC study thereafter. The FDA granted Fast Track designation in November 2021 to azenosertib in patients with advanced or metastatic USC who have received at least one prior platinum-based chemotherapy regimen for management of advanced or metastatic disease. We believe that the study design in this patient population has the potential to support registration in the United States.

- ***Monotherapy - Phase 1 Dose Optimization Clinical Trial in Solid Tumors (ZN-c3-001).*** We are currently evaluating azenosertib as a monotherapy in a Phase 1 dose optimization clinical trial for the treatment of solid tumors. We announced preliminary efficacy data from this trial with a data cutoff of May 15, 2021 from 34 patients, where we showed five confirmed partial responses, or cPRs, to azenosertib in monotherapy across several tumor types, including ovarian cancer (-69% cPR), colorectal cancer (-51% cPR), NSCLC (-49% cPR), and USC (-49% cPR) and (-43% cPR). We announced preliminary safety data from this trial at the 2022 American Association of Cancer Research, or AACR, Annual Meeting in April 2022. As of a January 21, 2022 data cutoff, there were 32 patients evaluated for safety and azenosertib was well tolerated. The most common treatment related AEs were nausea (71.9% all grades/3.1% grade 3 or higher), fatigue (53.1% all grades/18.8% grade 3 or higher), diarrhea (46.9% all grades/6.3% grade 3 or higher) and vomiting (46.9% all grades/0% grade 3 or higher). We also announced preliminary efficacy data from the Phase 1 monotherapy expansion cohort in USC from this trial at the 2022 AACR Annual Meeting. As of a January 21, 2022 data cutoff, there were 11 evaluable patients in the USC cohort, with 27.3% demonstrating an objective response rate, or ORR, and 90.9% demonstrating a disease control rate, or DCR.

- ***Monotherapy - Phase 2 Clinical Trial in Cyclin E1 Driven High-Grade Serous Ovarian Cancer, Fallopian Tube, or Primary Peritoneal Cancer (HGSOC) (ZN-c3-005).*** We are evaluating azenosertib as a monotherapy in a Phase 2 clinical trial in patients with Cyclin E1 driven HGSOC. Our Cyclin E1 enrichment strategy is supported by preclinical data that showed that high Cyclin E1 protein expression sensitized cancer cells to the anti-tumor effects of azenosertib as well as preliminary retrospective clinical data that Cyclin E1 protein levels may be associated with clinical benefit from Wee1 inhibition.

- ***Combination - Phase 1/2 Clinical Trial of Azenosertib and PARPi in Platinum-Resistant Ovarian Cancer (ZN-c3-006).*** We are evaluating azenosertib in combination with GSK's PARP inhibitor, niraparib (ZEJULA®), in a Phase 1/2 clinical trial in platinum-resistant ovarian cancer patients who have failed PARP inhibitor, or PARPi, maintenance treatment as part of a clinical collaboration with GSK. This study is currently enrolling two cohorts — one with concurrent dosing of the two drugs, and one with azenosertib and niraparib administered on a dose escalating, alternating schedule of one week of azenosertib followed by one week of niraparib. This clinical study is supported by preclinical data that showed that combining azenosertib and niraparib resulted in synergistic cell killing in ovarian *in vivo* models.

- ***Combination - Phase 1b Clinical Trial of Azenosertib and Chemotherapy in Platinum-Resistant Ovarian, Peritoneal or Fallopian Tube Cancer (ZN-c3-002).*** Azenosertib is currently being evaluated in combination with each of paclitaxel, carboplatin, pegylated liposomal doxorubicin (PLD) and gemcitabine in four separate cohorts in a Phase 1b clinical trial in patients with platinum-resistant ovarian, peritoneal or fallopian tube cancer. We provided a preliminary efficacy and safety update at the 2022 AACR Annual Meeting in April 2022, highlighting that azenosertib in combination with chemotherapy demonstrated strong anti-tumor activity in a heavily pretreated population and was well tolerated. As of the January 28, 2022 data cutoff, there were 43 evaluable patients for efficacy, with an ORR of 30.2% across all evaluable chemotherapy cohorts (paclitaxel, carboplatin and PLD). In the paclitaxel cohort, there were 8 evaluable patients and an ORR of 62.5%; in the carboplatin cohort, there were 11 evaluable patients and an ORR of 45.5%; and in the PLD cohort, there were 24 evaluable patients and an ORR of 12.5%. As of the January 28, 2022 data cutoff, there were 56 evaluable patients for safety. The most common treatment related AEs were nausea (48.2% all grades/5.4% grade 3 or higher), neutropenia (41.1% all grades/32.1% grade 3 or higher), thrombocytopenia (37.5% all grades/17.9% grade 3 or higher), vomiting (30.4% all grades/7.1% grade 3 or higher) and anemia (26.8 all grades/7.1% grade 3 or higher).

- ***Combination - Phase 1/2 Clinical Trial of Azenosertib and Chemotherapy in Relapsed or Refractory Osteosarcoma (ZN-c3-003).*** Azenosertib is currently being evaluated in combination with gemcitabine, in a Phase 1/2 clinical trial in adult and pediatric patients with R/R osteosarcoma. We reported initial results from this trial at the 2022 Connective Tissue Oncology Society, or CTOS, Annual Meeting in November 2022. As of a October 24, 2022 data cutoff, there were 12 patients evaluable for efficacy, with approximately 33% of patients demonstrating event-free survival, or EFS, at 18 weeks (compared to approximately 12% at 18 weeks for this indication historically). As of the October 24, 2022 data cutoff, there were 17 patients evaluable for safety. Azenosertib demonstrated a manageable safety profile with 82.4% experiencing treatment related AEs of which 52.9% were grade 3 or higher. The most common treatment related AEs were platelet count decreased/thrombocytopenia (47.1% all grades/35.3% grade 3 or higher), fatigue (29.4% all grades/5.9% grade 3 or higher), nausea (29.4% all grades/0% grade 3 or higher) and rash (29.4% all grades/5.9% grade 3 or higher). We received orphan drug designation and rare pediatric disease designation from the FDA for azenosertib in osteosarcoma.

- ***Combination - Phase 1/2 Clinical Trial of Azenosertib with Encorafenib and Cetuximab (BEACON Regimen) in BRAF V600E Mutant Metastatic Colorectal Cancer (mCRC) (ZN-c3-016).*** We are collaborating with Pfizer to evaluate azenosertib in combination with encorafenib and cetuximab, an FDA-approved standard of care known as the

BEACON regimen, in patients with BRAF V600E mutant mCRC in a Phase 1/2 clinical trial. In preclinical studies, Wee1 inhibition has shown synergy with many targeted agents in mutationally driven cancers, and the addition of azenosertib to the BEACON regimen enhanced anti-tumor activity in a cell-line-derived xenograft model. We initiated enrollment in this clinical trial in the first quarter of 2023.

- ***Combination - Phase 1/2 Clinical Trial of Azenosertib and Chemotherapy in Pancreatic Cancer.*** We have also agreed to support the Dana Farber-sponsored Phase 1/2 clinical trial evaluating azenosertib and chemotherapy, gemcitabine, in platinum-resistant pancreatic cancer patients.

ZN-d5 (BCL-2 Inhibitor)

ZN-d5 is a potentially best-in-class selective, oral small molecule inhibitor of BCL-2. BCL-2 is a protein that plays a critical role in the regulation of cell death, known as apoptosis. The overexpression of BCL-2 is frequently detected in numerous cancer types, which prevents apoptosis of cancer cells. Utilizing our medicinal chemistry expertise, we have designed ZN-d5 to have best-in-class potency, selectivity and PK properties. ZN-d5 is currently being evaluated in the clinic in patients with hematological malignancies in both the monotherapy and combination settings.

ZN-d5 is being evaluated in the following monotherapy and combination clinical trials:

- ***Monotherapy - Phase 1/2 Clinical Trial in Relapsed or Refractory Light Chain Amyloidosis (R/R AL Amyloidosis) (ZN-d5-003).*** ZN-d5 is being evaluated as a monotherapy in a Phase 1/2 clinical trial in R/R AL amyloidosis. BCL-2 inhibition has demonstrated clinical activity in R/R AL amyloidosis; however, there are currently no FDA-approved BCL-2 inhibitors for the treatment of R/R AL amyloidosis. This Phase 1/2 study in patients with R/R AL amyloidosis consists of a dose escalation phase to establish the monotherapy RP2D in this setting, and an expansion phase to further assess the safety and efficacy of ZN-d5 in this population. The study is expected to enroll up to approximately 140 patients.

- ***Monotherapy - Phase 1 Clinical Trial in Non-Hodgkin Lymphoma (NHL) (ZN-d5-001).*** We are evaluating ZN-d5 as a monotherapy in a Phase 1 dose escalation clinical trial in patients with NHL. As of the database cutoff date of November 3, 2021, 23 patients with NHL were evaluable for safety. At our R&D Day in December 2021, we reported preliminary interim data from the NHL patients in this study. As of the November 3, 2021 database cutoff date, ZN-d5 was well tolerated, with 73.9% of the NHL patients having experienced AEs (30.4% grade 3 or higher), not all of which were related ZN-d5. Anemia (21.7% all grades/8.7% grade 3 or higher), diarrhea (13.0% all grades/4.3% grade 3 or higher), and nausea and vomiting (8.7% each all grades/0% grade 3 or higher) comprise the most commonly experienced AEs. Investigator-reported responses using the Lugano 2014 classification among 11 patients with diffuse large B-cell lymphoma included a complete response, an unconfirmed PR, and two subjects with stable disease, as of the database cutoff date of November 3, 2021.

- ***Combination - Phase 1/2 Clinical Trial of ZN-d5 and Azenosertib in Relapsed or Refractory Acute Myeloid Leukemia (R/R AML) (ZN-d5-004C).*** ZN-d5 is being evaluated in combination with azenosertib in a Phase 1/2 dose escalation clinical trial in patients with R/R AML. The Phase 1 portion of this trial will escalate the doses of both drugs to identify the RP2D for the combination, which will be assessed in Phase 2 expansion cohort(s). This study is expected to enroll up to approximately 100 patients. This clinical trial is supported by preclinical models that showed that the combination of ZN-d5 with azenosertib yielded a significant enhancement of activity in several indications, including R/R AML, as compared to activity shown with either of these product candidates as a single agent. Preclinical models also showed that the combination of ZN-d5 with azenosertib was well tolerated in mice. We believe we are the only company to have both a Wee1 inhibitor and a BCL-2 inhibitor in clinical development.

BCL-xL Heterobifunctional Degrader

In November 2022, we announced that we identified a BCL-xL protein degrader candidate and initiated IND-enabling studies. We are developing a BCL-xL heterobifunctional degrader based on non-functional or dysfunctional E3 ubiquitin ligase complex in platelets, allowing for the potential mitigation of dose-limiting thrombocytopenia historically associated with BCL-xL inhibitors.

Liquidity Overview

Since our inception, our operations have been limited to organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of our product pipeline. We do not have any products approved for commercial sale and have not generated any revenues from product sales. We will not generate revenue from product sales unless and until we successfully complete clinical development, obtain

regulatory approval for, and commercialize one or more of our product candidates. We will need to raise substantial additional capital to support our continuing operations and pursue our growth strategy.

Since inception, we have incurred significant operating losses. Our net losses were $237.1 million for the year ended December 31, 2022. We had an accumulated deficit of $596.4 million as of December 31, 2022. We had cash, cash equivalents and marketable securities of $437.4 million as of December 31, 2022. We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2022 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2025. We have based these estimates on assumptions that may prove to be imprecise, and we could utilize our available capital resources sooner than we expect.

Impact of COVID-19 Pandemic and Global Macroeconomic Environment

We continue to monitor how the COVID-19 pandemic is affecting our employees, business, preclinical studies and clinical trials. Our employees are working based on a hybrid work model, in which they work both from our offices and remotely. Disruptions caused by the COVID-19 pandemic have resulted in difficulties including delays in initiating new trial sites and certain supply chain activities, suspension of enrollment at some of our existing trial sites, and the incurrence of additional costs as a result of preclinical study and clinical trial delays and adjustments and supply chain delays. Limited operations at our laboratory facilities during quarantine periods resulted in delays in our research-stage programs. As a result, we expect that the COVID-19 pandemic will continue to impact our business, results of operations, clinical development timelines and financial condition. At this time, there is continuing uncertainty relating to the trajectory of the COVID-19 pandemic and impact of related responses. The impact of COVID-19 on our future results will largely depend on future developments, which are highly uncertain and cannot be predicted with confidence. See “Risk Factors — The COVID-19 pandemic has adversely impacted and we expect will continue to adversely impact our business, including our preclinical studies and clinical trials.” in Part I, Item 1A. of this Annual Report on Form 10-K.Further, the global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. All of these factors could impact our liquidity and future funding requirements, including but not limited to our ability to raise additional capital when needed on acceptable terms, if at all. The duration of this economic slowdown is uncertain and the impact on our business is difficult to predict. See “Risk Factors — Unfavorable global, political or economic conditions could adversely affect our business, financial condition or results of operations.” in Part I, Item 1A. of this Annual Report on Form 10-K.

License Agreements and Strategic Collaborations

Recurium IP Holdings, LLC License Agreement

In December 2014, our wholly owned subsidiary, Zeno Pharmaceuticals, Inc., entered into the Recurium Agreement with Recurium IP, which was subsequently amended, under which Zeno Pharmaceuticals, Inc. was granted an exclusive worldwide license to certain intellectual property rights owned or controlled by Recurium IP to develop and commercialize pharmaceutical products for the treatment or prevention of disease, other than for providing pain relief. Following certain corporate restructuring disclosed elsewhere in this Annual Report on 10-K, our wholly owned subsidiary, ZMI, became the Zentalis contracting party to the Recurium Agreement. The intellectual property rights exclusively licensed by ZMI under the Recurium Agreement include certain intellectual property covering azenosertib, ZN-d5 and our BCL-xL product candidate. ZMI has the right to sublicense its rights under the Recurium Agreement, subject to certain conditions. ZMI is required to use commercially reasonable efforts to develop and commercialize at least one product that comprises or contains a compound modulating one of ten specific biological targets and to execute certain development activities.

Under the terms of the Recurium Agreement, ZMI is obligated to make development and regulatory milestone payments, pay royalties on net sales, and make certain sublicensing payments with respect to products that comprise or contain a compound modulating one of ten specific biological targets, including azenosertib, ZN-d5, our BCL-xL product candidate and two licensed products for which we discontinued clinical development in 2022, ZN-c5 and ZN-e4. ZMI is obligated to make development and regulatory milestone payments for each such licensed product of up to $44.5 million. In addition, ZMI is obligated to make milestone payments up to $150,000 for certain licensed products used in animals. ZMI is also obligated to pay royalties on sales of such licensed products at a mid- to high-single digit percentage. In addition, if ZMI chooses to sublicense or assign to any third parties its rights under certain patents exclusively in-licensed under the Recurium Agreement, ZMI must pay to Recurium IP 20% of certain sublicensing income received in connection with such transaction.

The Recurium Agreement will expire on the later of December 21, 2032 and, on a country-by-country basis, on the date of expiration of the last-to-expire royalty term for all licensed products in such country, unless earlier terminated by either party for cause or a bankruptcy event.

Pfizer Development Agreement

In April 2022, we entered into a development agreement with Pfizer to collaborate to advance the clinical development of azenosertib. We did not grant Pfizer any economic ownership or control of azenosertib or the rest of our pipeline. In October 2022, we announced our first clinical development collaboration with Pfizer to initiate a Phase 1/2 dose escalation study of azenosertib, in combination with encorafenib and cetuximab (an FDA-approved standard of care known as the BEACON regimen) in patients with BRAF V600E-mutant mCRC.

GlaxoSmithKline Clinical Trial Collaboration and Supply Agreement

In April 2021, we entered into a clinical trial collaboration and supply agreement with GSK under which we are evaluating the combination of azenosertib and niraparib, GSK's poly (ADP-ribose) polymerase (PARP) inhibitor, in patients with platinum-resistant ovarian cancer. Pursuant to this agreement, we are responsible for the conduct and cost of the relevant studies, under the supervision of a joint development committee made up of our representatives and representatives of GSK that meets quarterly. GSK is supplying niraparib for use in the collaboration, at no cost to us. We are required to provide to GSK clinical data and other reports upon completion of the study.

This agreement does not grant any right of first negotiation to participate in future clinical trials, and neither party granted the other any additional right or ability to evaluate their respective compounds in any other clinical studies, either as monotherapy or in combination with any other product or compound, in any therapeutic area.

The agreement with GSK will expire upon completion of all obligations of the parties thereunder or upon termination by either party. We and GSK each have the right to terminate the agreement for material breach by the other party. In addition, the agreement may be terminated by either party due to safety considerations or if either party decides to discontinue development of its own compound for medical, scientific, legal or other reasons or if a regulatory authority takes any action preventing that party from supplying its compound for the study or in the event the other party is subject to specified bankruptcy, insolvency or similar circumstances. GSK also has the right to terminate this agreement if it notifies us in writing that it reasonably and in good faith believes that niraparib is being used in an unsafe manner, and we fail to incorporate changes to address such issue, and the issue is unable to be resolved following elevation to appropriate parties.

Zentera Therapeutics

In May 2020, each of our wholly owned subsidiaries Zeno Alpha, Inc., K-Group Alpha, Inc. and K-Group Beta, Inc. entered into a collaboration and license agreement with our joint venture, Zentera, which we refer to as the "Zentera Sublicenses", pursuant to which we collaborate with Zentera on the development and commercialization of ZN-c5, ZN-d5 and azenosertib, respectively, whether alone or in a licensed product, which we collectively refer to as the "Collaboration Products", in each case for the treatment or prevention of disease, other than for pain, which is referred to as the "Zentera Field", in the People's Republic of China, Macau, Hong Kong and Taiwan, which is referred to as the "Zentera Collaboration Territory". As disclosed in August 2022, we have discontinued clinical development of ZN-c5. Under each Zentera Sublicense, Zentera will lead development, and upon regulatory approval, the commercialization, of the Collaboration Products in the Zentera Collaboration Territory. On May 19, 2020, Zentera issued an aggregate of 60.2% of its issued shares of common stock to Zeno Alpha, Inc., K-Group Alpha, Inc., K-Group Beta, Inc., Zeno Management, Inc. and Zeno Beta, Inc. In July 2021, Zentera entered into a Series B Preference Shares Purchase Agreement, pursuant to which it raised $75.0 million in gross proceeds. As of December 31, 2022, we hold a 40.3% equity interest in Zentera. Kevin D. Bunker, Ph.D., our Chief Scientific Officer, serves as a member of the Board of Directors of Zentera.

Under each Zentera Sublicense, we granted Zentera an exclusive, royalty-bearing license under certain of our technology, including technology licensed from Recurium IP under the Recurium Agreement, to develop and commercialize the Collaboration Products in the Zentera Field in the Zentera Collaboration Territory, subject to certain rights that we retain, and upon a successful manufacturing transfer, a non-exclusive license under certain of our manufacturing technology to manufacture Collaboration Products in the Zentera Field in the Zentera Collaboration Territory. Zentera has the right to sublicense its rights under the Zentera Sublicenses subject to certain conditions.

Under the terms of the Zentera Sublicenses, Zentera is generally responsible for the costs of developing the Collaboration Products in the Zentera Collaboration Territory, and we are generally responsible for the costs of developing the Collaboration Products outside the Zentera Collaboration Territory, provided that Zentera will reimburse us for a portion of its costs for global data management, pharmacovigilance, safety database management, and chemistry, manufacturing and controls activities with respect to each Collaboration Product. Under the Zentera Sublicenses, we will be eligible to receive future development and regulatory milestones of up to $4.45 million per Collaboration Product. Zentera will pay us royalties on net

sales of Collaboration Products in the Zentera Collaboration Territory at a mid- to high-single digit percentage, subject to certain reductions. In addition, if Zentera or its affiliate chooses to sublicense or assign to any third parties its rights under the Zentera Sublicenses with respect to any Collaboration Product, Zentera must pay to us 20% of certain sublicensing income received by Zentera or its affiliates in connection with such transaction.

Zentera's royalty obligations will expire on a Collaboration Product-by-Collaboration Product and region-by-region basis upon the later of the date on which such product is no longer covered by a valid claim of a licensed patent and the 15th anniversary of the first commercial sale of such product in such region.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue, and we do not expect to generate any revenue in the foreseeable future from product sales. We have generated, and may in the future generate, revenue from payments received under our collaboration agreements, which includes payments of upfront fees, license fees, milestone-based payments and reimbursements for research and development efforts.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, and include:

- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including CROs and other third parties that conduct research, preclinical activities and clinical trials on our behalf as well as CMOs that manufacture drug material for use in our preclinical studies and clinical trials;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- the costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;
- license payments made for intellectual property used in research and development activities; and
- allocated expenses for rent and maintenance of facilities and other operating costs.

We expense research and development costs as incurred. Reimbursed research and development costs under government grants and certain collaborative arrangements are recorded as a reduction to research and development expenses and are recognized in the period in which the related costs are incurred.

We track external development costs by product candidate or development program, but we do not allocate personnel costs, general license payments made under our licensing arrangements or other internal costs to specific development programs or 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,	
	2022	2021
	(in thousands)	
Azenosertib	$ 48,841	$ 42,191
ZN-d5	19,385	16,035
ZN-c5[1]	8,406	24,851
ZN-e4[1]	1,435	1,414
Unallocated research and development expenses	94,667	91,110
Total research and development expenses	$ 172,734	$ 175,601

1

[1] As disclosed previously, in August 2022, we announced that we were discontinuing the clinical development of ZN-c5 and ZN-e4.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have a higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase substantially for the foreseeable future and will comprise a larger percentage of our total expenses as we complete our ongoing clinical trials, initiate new clinical trials, continue to discover and develop additional product candidates and prepare regulatory filings for any product candidates that successfully complete clinical development.

The successful development of our product candidates is highly uncertain. At this time, we cannot determine with certainty the duration and costs of our existing and future clinical trials of our product candidates or any other product candidate we may develop or if, when, or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The duration, costs and timing of clinical trials and development of our product candidates and any other product candidate we may develop in the future will depend on a variety of factors, including:

- per patient trial costs;
- the number of patients who enroll in each trial;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the drop-out or discontinuation rates of patients;
- any delays in clinical trials as a result of the COVID-19 pandemic;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the phase of development of the product candidate;
- the efficacy and safety profile of the product candidate.
- uncertainties in clinical trial design and patient enrollment rates;
- the actual probability of success for our product candidates, including the safety and efficacy, early clinical data, competition, manufacturing capability and commercial viability;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals;
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- our ability to attract and retain skilled personnel.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, business development and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our personnel headcount to support research and development activities relating to our clinical stage programs, and any other product candidate we may develop. We also expect to incur increased expenses associated with being a public company, particularly now that we are no longer an emerging growth company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with Nasdaq and SEC requirements; director and officer insurance costs; and investor and public relations costs.

Interest Income

Interest income consists of interest earned on cash, cash equivalents and available-for-sale marketable securities.

Income Taxes

Since our inception, we and our corporate subsidiaries have generated cumulative federal, state and foreign net operating loss in certain jurisdictions for which we have not recorded any net tax benefit due to uncertainty around utilizing these tax attributes within their respective carryforward periods.

Results of Operations

Comparison of Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021, together with the changes in those items in dollars:

	Year Ended December 31,		
	2022	2021	Increase (Decrease)
		(in thousands)	
Operating Expenses			
Research and development	$ 172,734	$ 175,601	$ (2,867)
General and administrative	54,553	40,941	13,612
Total operating expenses	227,287	216,542	10,745
Loss from operations	(227,287)	(216,542)	(10,745)
Investment and other income, net	5,987	401	5,586
Gain on deconsolidation of Zentera	—	51,582	(51,582)
Net loss before income taxes	(221,300)	(164,559)	(56,741)
Income tax expense (benefit)	(469)	(297)	(172)
Loss on equity method investment	16,282	1,831	14,451
Net loss	(237,113)	(166,093)	(71,020)
Net loss attributable to noncontrolling interests	(307)	(7,368)	7,061
Net loss attributable to Zentalis	$ (236,806)	$ (158,725)	$ (78,081)

Revenue

We did not generate any revenue for the years ended December 31, 2022 and 2021.

Research and Development Expenses

Research and development, or R&D, expenses for the year ended December 31, 2022 were $172.7 million, compared to $175.6 million for the year ended December 31, 2021. The decrease of $2.9 million was primarily due to non-recurring charges incurred in 2021 of $10.0 million for milestone payments and an impairment charge of $8.8 million for in-process R&D. Other reductions in R&D expenses in 2022 as compared to 2021 included $14.0 million of decreased manufacturing costs, $2.7 million of decreased collaborative and consulting costs and a $5.7 million increase in R&D expense reimbursements from Zentera. These reductions were partially offset by increases in clinical trial related expenditures of $19.8 million, increases in personnel costs of $14.4 million and increases in facility, overhead allocations and other costs of $4.1 million.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2022 were $54.6 million, compared to $40.9 million during the year ended December 31, 2021. The increase of $13.6 million was primarily attributable to an increase of $8.5 million in employee-related costs, $5.5 million of which represents non-cash stock-based compensation. Other increases in 2022 as compared to 2021 include $7.2 million of higher facilities, software and supplies costs, $6.0 million of which related to rent and common area maintenance expenses, $1.5 million of higher consulting services and $1.3 million of increased legal

expenses. These amounts were partially offset by a reduction of $1.4 million for permits, fees and other expenses and increased allocations to R&D from G&A of $3.5 million.

Investment and Other Income, Net

Investment and other income was $6.0 million for the year ended December 31, 2022, compared to $0.4 million for the year ended December 31, 2021. The increase of $5.6 million was primarily the result of higher rates of return from our invested marketable securities.

Gain on Deconsolidation of Zentera

During the year ended December 31, 2021, Zentera was deconsolidated, resulting in a gain of $51.6 million. There was no comparable event during the corresponding period in 2022.

Liquidity and Capital Resources

Since our inception, our operations have been limited to organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of our product pipeline. We do not have any products approved for commercial sale and have not generated any revenues from product sales and we have incurred significant operating losses. We expect 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 for our current and future research programs and product candidates, contracting with CMOs to support 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 to raise substantial additional capital to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we plan to finance our operations through the sale of equity, debt financings or other capital sources, which may include collaborations with other companies or other strategic transactions. There are no assurances that we will be successful in obtaining an adequate level of financing as and when needed to finance our operations on terms acceptable to us or at all, particularly in light of the economic downturn and ongoing uncertainty related to the evolving COVID-19 pandemic, the conflict in the Ukraine, ongoing global supply chain issues and increased inflation and interest rates. The COVID-19 pandemic and related global events have resulted in an economic downturn that could adversely affect our operations, our ability to conduct our clinical trials, our ability to raise additional funds through public offerings and the volatility of our stock price and trading in our stock. Even after the COVID-19 pandemic has subsided, we expect we will continue to experience adverse impacts to our business as a result of any economic recession or depression that has occurred or may occur in the future. If we are unable to secure adequate additional funding as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with developing and commercializing therapeutics, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

We do not currently have any approved products and have never generated any revenue from product sales. To date, we have financed our operations primarily through the sale of equity securities. From inception through December 31, 2022, we raised a total of $975.9 million in gross proceeds from the sale of shares of our common stock and convertible preferred units. As of December 31, 2022, we had $43.1 million in cash and cash equivalents, $394.3 million in marketable securities, and an accumulated deficit of $596.4 million. We had no indebtedness as of December 31, 2022.

ATM Program

In May 2021, we entered into a sales agreement, or the Sales Agreement, with SVB Leerink LLC, or SVB Leerink, as sales agent, pursuant to which we may, from time to time, issue and sell common stock with an aggregate value of up to $200.0 million in “at-the-market” offerings, or the ATM, under our Registration Statement on Form S-3 (File No. 333-255769) filed with the SEC on May 4, 2021. Sales of common stock, if any, pursuant to the Sales Agreement, may be made in sales deemed

to be an "at the market offering" as defined in Rule 415(a) of the Securities Act, including sales made directly through The Nasdaq Global Market or any other existing trading market for our common stock. During the quarter ended December 31, 2022, we sold 2,210,500 shares of common stock under the Sales Agreement at a volume weighted-average price of $22.50 per share, raising aggregate gross proceeds of $49.7 million, before fees and expenses of $1.1 million. As of December 31, 2022 there was $140.3 million of our common stock remaining available for sale under the Sales Agreement and our Registration Statement on Form S-3 (File No. 333-255769).

Direct Offering of Common Stock

On April 29, 2022, pursuant to our Registration Statement on Form S-3 (Registration No. 333-255769), we completed a direct offering of our common stock to Pfizer. We issued and sold 953,834 shares of our common stock at an offering price of $26.21 per share. The total gross proceeds for the offering were approximately $25.0 million, before deducting offering expenses of $0.3 million payable by us. We and Pfizer have entered into an agreement to collaborate to advance the clinical development of azenosertib. We did not grant Pfizer any economic ownership or control of azenosertib or the rest of our pipeline of product candidates.

Follow-on Offering of Common Stock

On May 18, 2022, we completed a follow-on offering pursuant to our Registration Statement on Form S-3 (File No. 333-255769), in which we issued and sold 10,330,000 shares of common stock at a public offering price of $19.38 per share. The total gross proceeds for the offering were approximately $200.2 million, before deducting offering expenses of $11.4 million payable by us.

Cash Flows

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

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Net cash used in operating activities	$ (163,751)	$ (154,093)
Net cash used in investing activities	(114,180)	(18,115)
Net cash provided by financing activities	261,043	178,521
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (16,888)	$ 6,313

Operating Activities

We have incurred losses since inception. Net cash used in operating activities for the year ended December 31, 2022 was $163.8 million, consisting primarily of our net loss of $237.1 million as we incurred expenses associated with research activities for our lead product candidates and incurred general and administrative expenses, as well as changes in operating assets and liabilities of $13.3 million, partially offset by non-cash adjustments of $60.1 million.

Net cash used in operating activities for the year ended December 31, 2021 was $154.1 million, consisting primarily of our net loss of $166.1 million as we incurred expenses associated with research activities for our lead product candidates and incurred general and administrative expenses, and partially offset by changes in operating assets and liabilities of $16.6 million and non-cash adjustments of $4.6 million.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2022 of $114.2 million was attributable to the investment of excess cash of $533.2 million and the purchases of property and equipment of $2.5 million, partially offset by proceeds from maturities of marketable securities of $421.5 million.

Net cash used in investing activities for the year ended December 31, 2021 of $18.1 million was attributable to the investment of excess cash of $363.5 million and the purchases of property and equipment of $6.1 million, partially offset by proceeds from marketable securities of $365.8 million and the deconsolidation of Zentera cash of $14.3 million.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2022 of $261.0 million primarily relates to the May 2022 follow-on offering, which provided net cash of $188.8 million, the April 2022 direct offering to Pfizer, which provided net cash of $20.5 million, and shares sold under the Sales Agreement which provided net proceeds of $48.6 million. Of the $25.0 million gross proceeds received from Pfizer, $4.2 million of the proceeds represented a premium in excess of the fair value of our common stock on the date of the investment. An additional $3.1 million was provided from the issuance of common stock under equity incentive plans.

Net cash provided by financing activities in the year ended December 31, 2021 of $178.5 million primarily relates to the July 2021 follow-on offering and shares sold during December 2021 under the Sales Agreement which provided net proceeds of $162.2 million and $9.7 million, respectively. An additional $7.7 million was provided from the issuance of common stock under equity incentive plans.

Funding Requirements

Our operating expenses are expected to increase substantially in the future in connection with our ongoing activities.

Specifically, our expenses will increase as we:

- advance the clinical development of azenosertib and ZN-d5 for the treatment of oncology indications;
- pursue the preclinical and clinical development of other current and future research programs and product candidates and companion diagnostics for biomarkers associated with our product candidates and future product candidates;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel in research, manufacturing and regulatory and clinical development as well as management personnel;
- seek regulatory approval for any product candidates and, if needed, companion diagnostics for biomarkers associated with such product candidates, that successfully complete clinical development; and
- expand our operational, financial and management systems and increase personnel, including personnel to support our operations as a public company.

As of December 31, 2022, we have $2.2 million and $45.2 million in current and long-term lease liabilities, respectively. We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2022 will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2025. We have based these estimates on assumptions that may prove to be imprecise, and we could utilize our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical drugs, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the progress, costs and results of our clinical trials for our programs for azenosertib and ZN-d5;
- the progress, costs and results of additional research and preclinical studies in other research programs we initiate in the future and of companion diagnostics for biomarkers associated with our product candidates and future product candidates;
- the costs and timing of process development and manufacturing scale-up activities associated with our product candidates and other programs as we advance them through preclinical and clinical development;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims.

In addition, the magnitude and duration of the COVID-19 pandemic and its impact on our liquidity and future funding requirements is uncertain as of the filing date of this Annual Report on Form 10-K, as the pandemic continues to evolve

globally. See “Impact of COVID-19 Pandemic” and “Risk Factors — The COVID-19 pandemic has adversely impacted and we expect will continue to adversely impact our business, including our preclinical studies and clinical trials."

Further, our operating results may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Until such time as we can generate significant revenue from product sales, if ever, we plan to finance our operations through the sale of equity, debt financings, or other capital sources, which may include collaborations with other companies or other strategic transactions.

We currently have no credit facility or committed sources of capital. 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 of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. 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 or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Critical Accounting Estimates

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

While our significant accounting policies are described in more detail in the notes to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Research and Development Expenses - Clinical Trial Accruals

Methodology	*Judgment and Uncertainties*	*Effect if Actual Results Differ From Assumptions*
All of our clinical trials have been executed with support from CROs and other vendors. We accrue costs for clinical trial activities performed by CROs and other vendors based upon the estimated amount of work completed on each trial.	For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled, the activities to be performed for each patient, the number of active clinical sites, and the duration for which the patients will be enrolled in the trial. We monitor patient enrollment levels and related activities to the extent possible through internal reviews, correspondence with CROs and review of contractual terms.	We base our estimates on the best information available at the time. However, additional information may become available to us, which may allow us to make a more accurate estimate in future periods. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. There were no such significant changes during the years ended December 31, 2022 or 2021.

Share-Based Payments

Methodology	*Judgment and Uncertainties*	*Effect if Actual Results Differ From Assumptions*
We maintain equity incentive plans, which provide for share-based awards, including stock options, restricted stock units, or RSUs, , restricted stock and performance awards. We also maintain an employee stock purchase plan. We determine the fair value of our stock option awards and performance awards at the date of grant using a Black-Scholes model. We determine the fair value of our restricted stock awards at the date of grant using the closing market value of our common stock on the date of grant.	Option-pricing models and generally accepted valuation techniques require management to make assumptions and to apply judgment to determine the fair value of our awards. These assumptions and judgments include estimating the future volatility of our stock price, expected dividend yield and future employee stock option exercise behaviors. Changes in these assumptions can materially affect the fair value estimate. Our performance awards require management to make assumptions regarding the likelihood of achieving long-term Company goals.	We do not currently believe there is a reasonable likelihood that there will be a material change in estimates or assumptions we use to determine stock-based compensation expense. However, if actual results are not consistent with our estimates or assumptions, we may be exposed to changes in share-based compensation expense that could be material. If actual results are not consistent with the assumptions used, the share-based compensation expense reported in our financial statements may not be representative of the actual economic cost of the share-based compensation. A 10% change in our share-based compensation expense for the year ended December 31, 2022, would have affected pre-tax earnings by approximately $4.7 million in 2022.

Recent Accounting Pronouncements

See Note 2 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for further information on certain accounting standards that have been adopted during 2022 or that have not yet been required to be implemented and may be applicable to our future operations.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities and inflation. We held cash and cash equivalents of $43.1 million and $59.7 million as of December 31, 2022 and 2021, respectively. We generally hold our cash in interest-bearing money market accounts. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash equivalents and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures.

Inherent Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on that evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2022.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under the supervision and with the participation of our management, including our principal executive officer and our principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on the evaluation under this framework, our principal executive officer and our principal financial officer have concluded that our internal control over financial reporting was effective as of December 31, 2022.

The effectiveness of our internal control over financial reporting at December 31, 2022 has also been audited by Ernst & Young LLP, our independent registered public accounting firm, as stated in their report included below.

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, 2022 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC)

Opinion on Internal Control Over Financial Reporting

We have audited Zentalis Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), (the COSO criteria). In our opinion, Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC) (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2022 and 2021, the consolidated statements of operations, comprehensive loss, changes in convertible preferred units and members' / stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements") and our report dated March 1, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP
San Diego, California
March 1, 2023

Item 9B. Other Information.

On February 28, 2023, our wholly owned subsidiary, Zeno Management, Inc., and each of Dr. Blackwell, Mr. Gallagher, Dr. Bunker, Dr. Brownstein, Ms. Epperly and Ms. Paul entered into an amended and restated employment agreement primarily to provide that, in the event a change in control occurs and an excise tax is imposed by reason of the application of Sections 280G and 4999 of the Internal Revenue Code as a result of any compensatory payments made to such executive officer in connection with such change in control, such executive will be entitled to an additional payment in an amount that will offset on an after tax basis, the effect of any excise tax imposed upon such executive.

The foregoing description of the amended and restated employment agreements does not purport to be complete and is qualified in its entirety by reference to the complete text of the amendments, copies of which are filed as exhibits to this Annual Report on Form 10-K.

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 included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this item will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this item will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this item will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this item will be included in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and incorporated herein by reference.

Part IV

Item 15. Exhibits and Financial Statement Schedules.

(a)(1) Financial Statements.

The following documents are included on pages F-1 through F-29 attached hereto and are filed as part of this Annual Report on Form 10-K.

Index to Consolidated Financial Statements

(a)(2) Financial Statement Schedules.

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(a)(3) Exhibits.

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Description	Incorporated by Reference				Filed/Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
2.1	Plan of Conversion Converting Zentalis Pharmaceuticals, LLC (a Delaware limited liability company) into Zentalis Pharmaceuticals, Inc. (a Delaware corporation)	10-Q	001-39263	2.1	05/15/2020	
2.2	Certificate of Conversion Converting Zentalis Pharmaceuticals, LLC (a Delaware limited liability company) into Zentalis Pharmaceuticals, Inc. (a Delaware corporation)	10-Q	001-39263	2.2	05/15/2020	
3.1	Certificate of Incorporation of Zentalis Pharmaceuticals, Inc.	S-8	333-237593	4.1	04/07/2020	

Exhibit Number	Description	Incorporated by Reference				Filed/Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
3.2	Bylaws of Zentalis Pharmaceuticals, Inc.	8-K	001-39263	3.1	03/19/2021	
3.3	Second Amended and Restated Limited Liability Company Agreement of Zentalis Pharmaceuticals, LLC	S-1	333-236959	3.3	03/06/2020	
4.1	Amended and Restated Investors' Rights Agreement, dated as of September 6, 2019, by and among Zeno Pharma, LLC and the investors party thereto	S-1	333-236959	4.1	03/06/2020	
4.2	Specimen of Common Stock Certificate evidencing the shares of common stock	S-1	333-236959	4.2	03/06/2020	
4.3	Description of Capital Stock	10-K	001-39263	4.3	03/25/21	
10.1#	Zentalis Pharmaceuticals, LLC 2017 Profits Interest Plan, as amended, and form of profit interest award agreement thereunder	S-1	333-236959	10.1	03/06/2020	
10.2.1#	2020 Incentive Award Plan and form of option agreement and restricted stock unit agreement thereunder	S-1/A	333-236959	10.2	03/30/2020	
10.2.2#	Amendment No. 1 to the Zentalis Pharmaceuticals, Inc. 2020 Incentive Award Plan	10-Q	001-39263	10.3	05/17/2021	
10.3#	Non-Employee Director Compensation Program					*
10.4#	2020 Employee Stock Purchase Plan.	S-8	333-254506	99.1	03/19/2021	
10.5#	Form of Conversion Restricted Stock Award Agreement for former Class B Common Unit Holders	S-1/A	333-236959	10.5	03/30/2020	
10.6.1#	Zentalis Pharmaceuticals, Inc. 2022 Employment Inducement Incentive Award Plan.	8-K	001-39263	10.1	07/22/2022	
10.6.2#	Form of Option Agreement pursuant to the Zentalis Pharmaceuticals, Inc. 2022 Employment Inducement Incentive Award Plan.	8-K	001-39263	10.2	07/22/2022	
10.6.3#	Form of RSU Agreement pursuant to the Zentalis Pharmaceuticals, Inc. 2022 Employment Inducement Incentive Award Plan	8-K	001-39263	10.3	07/22/2022	
10.7#	Form of Indemnification Agreement for Directors and Officers	S-1/A	333-236959	10.6	03/30/2020	
10.8.1	Lease, effective September 30, 2020, between Zentalis Pharmaceuticals, Inc. and TPSC IX, LLC	8-K	001-39263	10.1	10/02/2020	
10.8.2	Partial Lease Termination Agreement and First Amendment to Lease, effective September 16, 2021, by and between Zentalis Pharmaceuticals, Inc. and TPSC IX, LLC	10-Q	001-39263	10.1	11/10/2021	
10.9	Lease, effective March 24, 2021, between Zentalis Pharmaceuticals, Inc. and ESRT 1359 BROADWAY, L.L.C.	10-K	1.39263	10.12	3/25/2021	
10.10.1#	Second Amended and Restated Employment Agreement, effective as of October 1, 2020, between Zeno Management, Inc. and Anthony Y. Sun, M.D.	8-K	001-39263	10.2	10/02/2020	
10.10.2#	Release Agreement, dated May 10, 2022, by and among Zentalis Pharmaceuticals, Inc., Zeno Management, Inc. and Anthony Y. Sun, M.D.	8-K	001-39263	10.2	05/16/2022	
10.11#	Amended and Restated Employment Agreement, effective as of February 28, 2023, between Zeno Management, Inc. and Melissa Epperly					*

Exhibit Number	Description	Incorporated by Reference				Filed/Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
10.12#	Amended and Restated Employment Agreement, dated February 28, 2023, between Zeno Management, Inc. and Kimberly Blackwell, M.D.					*
10.13#	Amended and Restated Employment Agreement, dated February 28, 2023, between Zeno Management, Inc. and Cam S. Gallagher					*
10.14#	Amended and Restated Employment Agreement, dated February 28, 2023, between Zeno Management, Inc. and Carrie Brownstein, M.D.					*
10.15#	Amended and Restated Employment Agreement, dated February 28, 2023, between Zeno Management, Inc. and Kevin Bunker, Ph.D.					*
10.16#	Amended and Restated Employment Agreement, dated February 28, 2023, between Zeno Management, Inc. and Andrea Paul					*
10.17#	Employment Agreement, dated February 8, 2023, between Zeno Management, Inc. and Iris Roth, Ph.D.	8-K	001-39263	10.1	02/13/2023	
10.18.1†	Second Amended and Restated License Agreement, dated September 6, 2019, between the Registrant and Recurium IP Holdings, LLC	S-1	333-236959	10.20	03/06/2020	
10.18.2†	Greater China Amendment to the Second Amended and Restated License Agreement, dated May 19, 2020, by and between Zeno Management, Inc. and Recurium IP Holdings, LLC	10-Q	001-39263	10.3	08/13/2020	
10.18.3†	Compound Specific Patent Rights Amendment to the Second Amended and Restated License Agreement, dated March 17, 2022, by and between Zeno Management, Inc. and Recurium IP Holdings, LLC					*
21.1	List of Subsidiaries of Zentalis Pharmaceuticals, Inc.					*
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.					*
31.1	Certification of Chief Executive Officer pursuant to Exchange Act Rule 13a-14(a).					*
31.2	Certification of Chief Financial Officer pursuant to Exchange Act Rule 13a-14(a).					*
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350.					**
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350.					**
101.INS	Inline XBRL Instance Document - the Instance Document does not appear in the interactive data file because its XBRL tags are embedded within the Inline XBRL document					*
101.SCH	Inline XBRL Taxonomy Extension Schema Document					*
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					*

Exhibit Number	Description	Incorporated by Reference				Filed/Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					*
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					*

* Filed herewith.
** Furnished herewith.
# Indicates management contract or compensatory plan.
† Portions of this exhibit (indicated by asterisks) have been redacted in compliance with Regulation S-K Item 601(b)(10)(iv).

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, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ZENTALIS PHARMACEUTICALS, INC.

Date: March 1, 2023

By: /s/ Kimberly Blackwell, M.D.
Kimberly Blackwell, M.D.
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, 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/ Kimberly Blackwell, M.D. **Kimberly Blackwell, M.D.**	Chief Executive Officer and Director *(principal executive officer)*	March 1, 2023
/s/ Melissa B. Epperly **Melissa B. Epperly**	Chief Financial Officer *(principal financial and accounting officer)*	March 1, 2023
/s/ David M. Johnson **David M. Johnson**	Chairperson	March 1, 2023
/s/ Cam S. Gallagher **Cam S. Gallagher**	President and Director	March 1, 2023
/s/ Enoch Kariuki **Enoch Kariuki**	Director	March 1, 2023
/s/ Jan Skvarka **Jan Skvarka**	Director	March 1, 2023
/s/ Karan S. Takhar **Karan S. Takhar**	Director	March 1, 2023

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC)

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC) (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, changes in convertible preferred units and members' / stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated March 1, 2023 expressed an unqualified opinion thereon.

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

Critical Audit Matter

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

Accrued clinical trial expenses

Description of the Matter	During 2022, the Company incurred $172.7 million for research and development expenses and as of December 31, 2022, the Company accrued $32.3 million for research and development expenses, which includes clinical trial expenses and accruals. As described in Note 2 of the financial statements, the Company records accruals for estimated costs of research and development activities that include costs for clinical trials. The Company records costs based on estimates and/or representations from contract research organizations ("CROs") and other vendors regarding work performed, level of patient enrollment, completion of patient studies and progress of the clinical trials. The Company monitors patient enrollment levels and related activities through internal reviews, correspondence with CROs and reviews of contractual terms. Auditing management's accounting for accrued clinical trial expenses was especially challenging as the evaluation is dependent upon a high volume of data received from third-party service providers and internal clinical personnel, which is tracked in spreadsheets. The accrued amounts are determined based on an evaluation of the unique terms and conditions set forth in each respective agreement.
How We Addressed the Matter in Our Audit	We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over management's accounting for accrued clinical trial expenses. To test the adequacy of the Company's accrued clinical trial expenses, our substantive audit procedures included, among others, testing the accuracy of data and assumptions used in management's clinical trial accrual models by inspecting invoices paid to date, agreeing terms and conditions to a sample of contracts and performing inquiries with clinical staff to corroborate progress and level of expended effort incurred by the Company's CROs and other third-party vendors. We further obtained the clinical trial agreements for a sample of active clinical sites and compared the costs and number of patient visits to the Company's clinical trial accrual models. We also tested a sample of expenses against the related invoices and contracts and examined a sample of subsequent payments to evaluate the completeness of the accrued clinical trial expenses.

/s/ Ernst & Young LLP

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

San Diego, California
March 1, 2023

Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC)
Consolidated Balance Sheets
(In thousands, except share amounts and par value)

	December 31,	
	2022	2021
ASSETS		
Current assets		
Cash and cash equivalents	$ 43,069	$ 59,714
Marketable securities, available for sale	394,302	280,173
Prepaid expenses and other current assets	14,562	10,640
Restricted cash	—	243
Total current assets	451,933	350,770
Property and equipment, net	7,705	8,148
Operating lease right-of-use assets	42,373	44,691
Prepaid expenses and other assets	9,723	7,040
Goodwill	3,736	3,736
Investment in Zentera Therapeutics	21,213	37,495
Restricted cash	2,627	2,627
Total assets	$ 539,310	$ 454,507
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 11,247	$ 11,590
Accrued expenses	45,400	32,354
Total current liabilities	56,647	43,944
Deferred tax liability	853	1,622
Long-term lease liability	45,166	44,459
Other long-term liabilities	2,620	—
Total liabilities	105,286	90,025
Commitments and contingencies (see Note 10)		
EQUITY		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, no shares issued and outstanding at December 31, 2022 and 2021	—	—
Common stock, $0.001 par value; 250,000,000 shares authorized; 59,280,247 and 45,490,764 shares issued and outstanding at December 31, 2022 and 2021, respectively	59	45
Additional paid-in capital	1,031,462	723,593
Accumulated other comprehensive loss	(1,353)	(125)
Accumulated deficit	(596,365)	(359,559)
Total stockholders' equity	433,803	363,954
Noncontrolling interests	221	528
Total equity	434,024	364,482
Total liabilities and stockholders' equity	$ 539,310	$ 454,507

See accompanying notes to consolidated financial statements.

Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC)
Consolidated Statements of Operations
(In thousands, except per share amounts)

	Year ended December 31,		
	2022	2021	2020
Operating Expenses			
Research and development	$ 172,734	$ 175,601	$ 84,901
General and administrative	54,553	40,941	33,886
Total operating expenses	227,287	216,542	118,787
Loss from operations	(227,287)	(216,542)	(118,787)
Other Income (Expense)			
Investment and other income, net	5,987	401	683
Gain on deconsolidation of Zentera	—	51,582	—
Net loss before income taxes	(221,300)	(164,559)	(118,104)
Income tax expense (benefit)	(469)	(297)	444
Loss on equity method investment	16,282	1,831	—
Net loss	(237,113)	(166,093)	(118,548)
Net loss attributable to noncontrolling interests	(307)	(7,368)	(707)
Net loss attributable to Zentalis	$ (236,806)	$ (158,725)	$ (117,841)
Net loss per common share outstanding, basic and diluted	$ (4.48)	$ (3.72)	$ (4.19)
Common shares used in computing net loss per share, basic and diluted	52,857	42,688	28,113

See accompanying notes to consolidated financial statements.

Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC)
Consolidated Statements of Comprehensive Loss
(In thousands)

	Year ended December 31,		
	2022	2021	2020
Net loss	$ (237,113)	$ (166,093)	$ (118,548)
Other comprehensive income (loss):			
Unrealized gain (loss) on marketable securities, net	(1,228)	(161)	36
Total comprehensive loss	(238,341)	(166,254)	(118,512)
Comprehensive loss attributable to noncontrolling interests	(307)	(7,368)	(707)
Comprehensive loss attributable to Zentalis	$ (238,034)	$ (158,886)	$ (117,805)

See accompanying notes to consolidated financial statements.

Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC)
Consolidated Statements of Changes in Convertible Preferred Units and Members'/Stockholders' Equity (Deficit)
(In thousands, except per unit amounts)

	Year Ended December 31, 2020														
	Zentalis Stockholders														
	Convertible Preferred Units		Convertible Preferred Units		Class A Common Units		Class B Common Units		Common		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Noncontrolling Interests	Total Equity (Deficit)
	Units	Amount	Units	Amount	Units	Amount	Units	Amount	Shares	Amount					
Balance at December 31, 2019	9,950	$141,706	—	$ —	5,601	$ 709	2,671	$ 2,178	—	$ —	$ —	$ —	$ (82,993)	$ 6,821	$ (73,285)
Issuance of Series C convertible preferred units at $17.50 per unit net of issuance costs	867	14,228	—	—	—	—	—	—	—	—	—	—	—	—	—
Cancellation of profit interest awards, net	—	—	—	—	—	—	(64)	—	—	—	—	—	—	—	—
Issuance of common stock in connection with an initial public offering, net of underwriting discounts, commissions and offering costs	—	—	—	—	—	—	—	—	10,589	11	172,354	—	—	—	172,365
Contributions from noncontrolling interest owners	—	—	—	—	—	—	—	—	—	—	—	—	—	18,424	18,424
Share-based compensation expense	—	—	—	—	—	—	—	329	—	—	22,817	—	—	—	23,146
Conversion of convertible preferred units to common stock	(10,817)	(155,934)	—	—	—	—	—	—	15,011	15	155,919	—	—	—	155,934
Conversion of common and incentive units to common and restricted stock	—	—	—	—	(5,601)	(709)	(2,607)	(2,507)	10,278	10	3,206	—	—	—	—
Issuance of common stock in connection with an equity offering, net of underwriting discounts, commissions, and offering costs	—	—	—	—	—	—	—	—	4,744	5	155,300	—	—	—	155,305
Issuance of common stock in connection with restricted stock unit vesting	—	—	—	—	—	—	—	—	426	—	—	—	—	—	—
Cancellation of restricted stock awards	—	—	—	—	—	—	—	—	(8)	—	—	—	—	—	—
Other comprehensive income	—	—	—	—	—	—	—	—	—	—	—	36	—	—	36
Net loss attributable to noncontrolling interest	—	—	—	—	—	—	—	—	—	—	(257)	—	—	(450)	(707)
Net loss attributable to Zentalis	—	—	—	—	—	—	—	—	—	—	—	—	(117,841)	—	(117,841)
Balance at December 31, 2020	—	$ —	—	$ —	—	$ —	—	$ —	41,040	$ 41	$ 509,339	$ 36	$ (200,834)	$ 24,795	$ 333,377

	Year Ended December 31, 2021						
	Zentalis Stockholders						
	Common		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Noncontrolling Interests	Total Equity
	Shares	Amount					
Balance at December 31, 2020	41,040	$ 41	$ 509,339	$ 36	$ (200,834)	$ 24,795	$ 333,377
Share-based compensation expense	—	—	35,737	—	—	—	35,737
Issuance of common stock in connection with an equity offering, net of underwriting discounts, commissions and offering costs	3,691	4	171,969	—	—	—	171,973
Issuance and withholding of common stock in connection with restricted stock unit vesting, net	517	—	(1,146)	—	—	—	(1,146)
Deconsolidation event	—	—	—	—	—	(16,899)	(16,899)
Issuance of common stock upon exercise of options	232	—	7,149	—	—	—	7,149
Issuance of common stock under employee stock purchase plan	15	—	545	—	—	—	545
Cancellation of restricted stock awards	(4)	—	—	—	—	—	—
Other comprehensive income (loss)	—	—	—	(161)	—	—	(161)
Net loss attributable to non-controlling interest	—	—	—	—	—	(7,368)	(7,368)
Net loss attributable to Zentalis	—	—	—	—	(158,725)	—	(158,725)
Balance at December 31, 2021	45,491	$ 45	$ 723,593	$ (125)	$ (359,559)	$ 528	$ 364,482

	Year Ended December 31, 2022						
	Zentalis Stockholders						
	Common		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Noncontrolling Interests	Total Equity
	Shares	Amount					
Balance at December 31, 2021	45,491	$ 45	$ 723,593	$ (125)	$ (359,559)	$ 528	$ 364,482
Share-based compensation expense	—	—	46,840	—	—	—	46,840
Issuance of common stock in connection with an equity offering, net of underwriting discounts, commissions and offering costs	13,495	13	257,909	—	—	—	257,922
Issuance of common stock in connection with restricted stock unit vesting, net	159	1	—	—	—	—	1
Issuance of common stock upon exercise of options	122	—	2,246	—	—	—	2,246
Issuance of common stock under employee stock purchase plan	30	—	874	—	—	—	874
Cancellation of restricted stock awards	(17)	—	—	—	—	—	—
Other comprehensive income (loss)	—	—	—	(1,228)	—	—	(1,228)
Net loss attributable to non-controlling interest	—	—	—	—	—	(307)	(307)
Net loss attributable to Zentalis	—	—	—	—	(236,806)	—	(236,806)
Balance at December 31, 2022	59,280	$ 59	$ 1,031,462	$ (1,353)	$ (596,365)	$ 221	$ 434,024

See accompanying notes to consolidated financial statements.

Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC)
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2022	**2021**	**2020**
Operating activities:			
Net loss	$ (237,113)	$ (166,093)	$ (118,548)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,426	544	160
IPR&D impairment	—	8,800	—
Recognized tax gain on IPR&D impairment	—	(2,462)	—
Gain on deconsolidation of Zentera, net of tax	—	(49,930)	—
Share-based compensation	46,840	35,737	23,146
Loss on disposal of equipment	56	15	—
(Accretion of discounts)/amortization of premiums on marketable securities, net	(3,725)	908	556
Loss on equity method investment	16,282	1,831	—
Deferred income taxes	(769)	(48)	17
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(6,605)	1,294	(5,796)
Accounts payable and accrued liabilities	15,527	13,964	14,307
Operating lease right-of-use assets and liabilities, net	4,330	1,347	(667)
Net cash used in operating activities	(163,751)	(154,093)	(86,825)
Investing activities:			
Purchases of marketable securities	(533,161)	(363,508)	(400,984)
Proceeds from maturities of marketable securities	421,529	365,820	116,910
Deconsolidation of Zentera cash	—	(14,320)	—
Purchases of property and equipment	(2,548)	(6,107)	(758)
Net cash used in investing activities	(114,180)	(18,115)	(284,832)
Financing activities:			
Proceeds from issuance of common stock in initial public offering, net	—	—	172,482
Proceeds from issuance of common stock under equity incentive plans	3,121	7,694	—
Net-settlement of restricted stock unit vesting	—	(1,146)	—
Contributions from noncontrolling interest owners, net	—	—	18,424
Proceeds from issuance of common stock, net	257,922	171,973	155,305
Proceeds from the issuance of Series C convertible preferred units, net	—	—	14,228
Net cash provided by financing activities	261,043	178,521	360,439
Net (decrease) increase in cash, cash equivalents and restricted cash	(16,888)	6,313	(11,218)
Cash, cash equivalents and restricted cash at beginning of year	62,584	56,271	67,489
Cash, cash equivalents and restricted cash at end of year	$ 45,696	$ 62,584	$ 56,271
Supplemental disclosure of cash flow information:			
Income taxes paid	$ 12	$ 20	$ 18
Supplemental disclosure of non-cash investing and financing activities:			
Right-of-use assets obtained in exchange for operating lease liabilities	$ —	$ 44,613	$ 300
Accrued capital expenditures	$ —	$ (1,510)	$ —

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported in the Consolidated Statements of Cash Flows for the periods presented:

	Year Ended December 31,		
	2022	2021	2020
Cash and cash equivalents	$ 43,069	$ 59,714	$ 54,951
Restricted cash, current	—	243	—
Restricted cash, non-current	2,627	2,627	1,320
Total cash, cash equivalents and restricted cash reported in the Consolidated Statement of Cash Flows	$ 45,696	$ 62,584	$ 56,271

See accompanying notes to consolidated financial statements.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Business

Organization

Zentalis Pharmaceuticals, Inc. ("Zentalis", "We" or the "Company") is a clinical-stage biopharmaceutical company focused on discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancer. The Company is developing a focused pipeline of potentially best-in-class oncology candidates. The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. All of the Company's tangible assets are held in the United States.

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements have been prepared in conformity with U.S. generally accepted accounting principles ("U.S. GAAP") and include our wholly-owned subsidiaries and variable interest entities ("VIEs") for the periods in which we determined we were the primary beneficiary. All intercompany transactions and balances have been eliminated in consolidation.

We evaluate our ownership, contractual and other interests in entities that are not wholly-owned to determine if these entities are VIEs, and, if so, whether we are the primary beneficiary of the VIE. In determining whether we are the primary beneficiary of a VIE and therefore required to consolidate the VIE, we apply a qualitative approach that determines whether we have both (1) the power to direct the activities of the VIE that most significantly impact the VIE's economic performance and (2) the obligation to absorb losses of, or the rights to receive benefits from, the VIE that could potentially be significant to that VIE.

We will continuously assess whether we are the primary beneficiary of a VIE, as changes to existing relationships or future transactions may result in the consolidation or deconsolidation of such VIE. During the periods presented, we have not provided any other material financial or other support to our VIE that we were not contractually required to provide.

Noncontrolling Interests

Noncontrolling interests represent interests held by third parties in our consolidated subsidiaries. We reflect noncontrolling interest attributable to the other owners in a separate line in our consolidated statements of operations and a separate line within stockholders' equity in our consolidated balance sheets.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. On an ongoing basis, we evaluate our estimates and judgments, which are based on historical and anticipated results and trends and on various other assumptions that management believes to be reasonable under the circumstances. By their nature, estimates are subject to an inherent degree of uncertainty and, as such, actual results may differ from management's estimates.

Though the impact of the COVID-19 pandemic to our business and operating results presents additional uncertainty, we continue to use the best information available to inform our critical accounting estimates.

Cash and Cash Equivalents

Cash equivalents are comprised of short-term, highly-liquid investments with maturities of 90 days or less at the date of purchase. As of December 31, 2022 and 2021, our cash equivalents consisted of money market funds and corporate debt securities.

Marketable Securities

Marketable securities are investments with original maturities of more than ninety days from the date of purchase that we have the ability to liquidate to fund current operations. Accordingly, those investments with contractual maturities greater than

one year from the date of purchase are classified as short-term investments on the accompanying consolidated balance sheets. Marketable securities are considered available-for-sale and are carried at fair value with unrealized gains and losses recorded in other comprehensive income (loss) and included as a separate component of stockholders' equity. The cost of marketable securities is adjusted for amortization of premiums or accretion of discounts to maturity, and such amortization or accretion is included in investment and other income, net through an allowance account. We use the specific identification method for calculating realized gains and losses on marketable securities sold. Realized gains and losses on marketable securities, if any, are included in investment and other income, net in the consolidated statements of operations.

Restricted Cash

Under the terms of our office leases, we are required to maintain a letter of credit as a security deposit during the term of such leases. At December 31, 2022 and 2021, restricted cash of $2.6 million and $2.9 million, respectively, was pledged as collateral for the letters of credit.

Fair Value of Financial Instruments

The authoritative guidance defines fair value and requires us to establish a framework for measuring fair value and disclosure about fair value measurements using a three-tier approach. These tiers include: Level 1, defined as observable inputs such as quoted prices in active markets; Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions.

Our financial instruments include cash equivalents, marketable securities, prepaid expenses and other assets, accounts payable and accrued expenses. Fair value estimates of these instruments are made at a specific point in time, based on relevant market information. These estimates may be subjective in nature and involve uncertainties and matters of significant judgement and therefore cannot be determined with precision.

The fair value of marketable securities is determined using proprietary valuation models and analytical tools, which utilize market pricing or prices for similar instruments that are both objective and publicly available, such as matrix pricing or reported trades, benchmark yields, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities and bids and offers.

The carrying amount of cash equivalents, prepaid expenses and other assets, accounts payable and accrued expenses are generally considered to be representative of their respective values because of the short-term nature of those instruments.

Concentrations of Credit Risk and Sources of Supply

We are subject to credit risk from our portfolios of cash equivalents and marketable securities. We maintain our cash and cash equivalent and marketable securities balances with major commercial banks. Deposits held with the financial institutions exceed the amount of insurance provided on such deposits. We are exposed to credit risk in the event of a default by the financial institutions holding our cash and cash equivalents and marketable securities to the extent recorded on the consolidated balance sheets. We have also established guidelines to limit our exposure to credit risk by diversifying our marketable securities portfolio and placing them in investments with maturities that maintain safety and liquidity.

We rely on third-party manufacturers for the supply of active pharmaceutical ingredients.

Property and Equipment, Net

Property and equipment are recorded at cost, less accumulated depreciation and amortization. Equipment is depreciated using the straight-line method over its estimated useful life ranging from three to five years and leasehold improvements are amortized using the straight-line method over the estimated useful life of the asset or the lease term, whichever is shorter. Repair and maintenance costs are expensed as incurred.

Leases

We have entered into operating leases for real estate. We determine if an arrangement is a lease at inception and evaluate each lease agreement to determine whether the lease is an operating or finance lease. For leases where we are the lessee, right-of-use (“ROU”) assets represent the Company’s right to use an underlying asset for the lease term and lease liabilities represent

an obligation to make lease payments arising from the lease. Liabilities from operating leases are included in accrued expenses and long-term lease liabilities on our consolidated balance sheet. ROU assets and lease liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. As our leases do not provide an implicit interest rate, we use our incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The operating lease ROU asset also includes any prepaid lease payments, lease incentives received, and costs which will be incurred in exiting a lease. Our leases often include options to extend or terminate the lease. These options are included in the lease term when it is reasonably certain that we will exercise that option. As of December 31, 2022, it is not reasonably certain that these options will be exercised and they are not included within the lease term. Short-term leases with an initial term of 12 months or less are not recorded on the balance sheet. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. We have lease agreements with lease and non-lease components which are accounted for as a single lease component for all of our leases.

Impairment of Long-Lived Assets

We account for long-lived assets in accordance with authoritative guidance for impairment or disposal of long-lived assets. Long-lived assets are reviewed for events or changes in circumstances, which indicate that their carrying value may not be recoverable.

Goodwill

Our goodwill, which has an indefinite useful life, represents the excess of the cost over the fair value of net assets acquired from its business combination. The determination of the value of goodwill and intangible assets arising from business combinations and asset acquisitions requires extensive use of accounting estimates and judgments to allocate the purchase price to the fair value of the net tangible and intangible assets acquired, including capitalized in-process research and development ("IPR&D").

Goodwill is reviewed for impairment at least annually, or more frequently if an event occurs indicating the potential for impairment. During the impairment review process, we consider qualitative factors to determine whether it is more likely than not that the fair value of the reporting unit is less than the carrying amount, including goodwill. If we determine that it is not more likely than not that the fair value of our reporting unit is less than the carrying amount, then no additional assessment is deemed necessary. Otherwise, we proceed to compare the estimated fair values of the reporting units with the carrying values, including goodwill. If the carrying amounts of the reporting units exceed the fair values, we record an impairment loss based on the difference. We completed our most recent annual evaluation for impairment for goodwill as of December 31, 2022 using the qualitative assessment and determined that no impairment existed, and no charges were recorded.

Equity Method Accounting

We have significant influence, but not a controlling interest, in our affiliate Zentera. From the deconsolidation of Zentera during July 2021 prospectively, this investment is accounted for using the equity method. Our share of earnings or losses of the investment entity are reported on the consolidated statement of operations, with a corresponding increase or decrease to the equity investment carried on the statement of financial position. This information is generally not received sufficiently timely for us to record our portion of earnings or loss in the current financial statements, and therefore we report our portion of earnings or loss on a one quarter lag. The maximum exposure to loss as a result of our investment in Zentera is directly associated with the carrying amount of the equity method investment on our consolidated balance sheet.

Research and Development Expenses

Research and development expenses include salaries and benefits, facilities and other overhead expenses, external clinical trial expenses, research-related manufacturing services, contract services and other outside expenses. Research and development expenses are charged to operating expenses as incurred when these expenditures relate to our research and development efforts and have no alternative future uses. Reimbursed research and development costs under government grant arrangements are recorded as a reduction to research and development expenses and are recognized in the period in which the related costs are incurred.

We are obligated to make upfront payments upon execution of certain research and development agreements. Advance payments, including nonrefundable amounts, for goods or services that will be used or rendered for future research and development activities are deferred. Such amounts are recognized as expense as the related goods are delivered or the related services are performed, or such time when we do not expect the goods to be delivered or services to be performed.

Clinical Trial Expenses

We make payments in connection with our clinical trials under contracts with contract research organizations that support conducting and managing clinical trials. The financial terms of these agreements are subject to negotiation and vary from contract to contract and may result in uneven payment flows. Generally, these agreements set forth the scope of work to be performed at a fixed fee, unit price or on a time and materials basis. A portion of our obligation to make payments under these contracts depends on factors such as the successful enrollment or treatment of patients or the completion of other clinical trial milestones.

Expenses related to clinical trials are accrued based on our estimates and/or representations from service providers regarding work performed, including actual level of patient enrollment, completion of patient studies and progress of the clinical trials. Other incidental costs related to patient enrollment or treatment are accrued when reasonably certain. If the amounts we are obligated to pay under our clinical trial agreements are modified (for instance, as a result of changes in the clinical trial protocol or scope of work to be performed), we adjust our accruals accordingly. Revisions to our contractual payment obligations are charged to expense in the period in which the facts that give rise to the revision become reasonably certain.

Share-Based Compensation

We record share-based compensation expense associated with equity instruments in accordance with the authoritative guidance for stock-based compensation. The cost of employee services received in exchange for an award of an equity instrument is measured at the grant date based on the estimated fair value of the award and is recognized as expense on a straight-line basis over the requisite service period of the award. Share-based compensation expense for an award with a performance condition is recognized when the achievement of such performance condition is determined to be probable. If the outcome of such performance condition is not determined to be probable or is not met, no compensation expense is recognized, and any previously recognized compensation expense is reversed. Forfeitures are recognized as a reduction of share-based compensation expense as they occur.

Income Taxes

Deferred income taxes are recognized for the tax consequences in future years of differences between the tax basis of assets and liabilities and their financial reporting amounts at each year end based on enacted tax laws and statutory tax rates applicable to the periods in which the differences are expected to affect taxable income. A provision has been made for income taxes due on taxable income and for the deferred taxes on temporary differences. Deferred tax assets and liabilities are adjusted for the effects of changes in tax laws and rates on the date of enactment. Realization of the deferred income tax asset is dependent on gathering sufficient taxable income in future years.

Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized. Income tax expense is the combination of the tax payable for the period and the change during the period in deferred tax assets and liabilities. We follow the accounting guidance on accounting for uncertainty in income taxes. The guidance prescribes a recognition threshold and measurement attribute criteria for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities based on the technical merits of the position.

Accumulated Other Comprehensive Income

Accumulated other comprehensive income is the result of unrealized gains and losses on marketable securities.

Net Loss per Common Share Outstanding

Basic net loss per common share outstanding is computed by dividing net loss, after adjusting for dividends, if declared, by the weighted-average number of common shares outstanding during the period. Diluted net loss per common share outstanding is computed using the weighted-average number of common shares outstanding during the period and, if dilutive, the weighted average number of potential common shares. Potential common shares consist of unvested restricted stock awards, unvested restricted stock units and common shares issuable upon the exercise of stock options.

3. Significant Transactions

Zentera Therapeutics

In May 2020, we became a majority common shareholder of Zentera Therapeutics a Shanghai-based clinical-stage biopharmaceutical company focused on developing cancer therapeutics (“Zentera”), concurrent with its Series A convertible preferred stock offering. The financial position and results of operations of Zentera were included in our consolidated financial statements from the date of the initial investment as a result of our control of the entity and our determination that we were the primary beneficiary of Zentera. In July 2021, Zentera completed a Series B convertible preferred stock offering which diluted our investment to a position of less than majority owned. Upon review of the facts and circumstances, together with the authoritative accounting literature, we determined that while Zentera is a variable interest entity ("VIE"), consolidation of Zentera is no longer appropriate. After the July 2021 Series B convertible preferred offering in which we did not participate, our review concluded that we ceased to be the primary beneficiary of Zentera as our equity ownership was reduced to 40.3% and changes were made to the corporate governance of Zentera. As a result, we no longer individually have the ability to direct the activities that most significantly impact Zentera's economic performance.

Beginning in July 2021, the financial position and results of operations of Zentera are no longer included in our consolidated financial statements. During the period of deconsolidation we measured the fair value of our retained investment in Zentera using the backsolve method with consideration for a lack of marketability. An equity method investment of $21.2 million is recorded on our balance sheet at December 31, 2022. This amount represents our maximum exposure to loss as a result of our investment in Zentera. A deferred tax liability of $4.5 million representing the tax impact of the unrealized gain on deconsolidation is recorded on our balance sheet at December 31, 2022. A gain of $51.6 million, measured as the difference between the fair value of our retained noncontrolling interest together with the carrying amount of the Zentera noncontrolling interest, and the carrying amount of Zentera’s assets and liabilities was recognized during the year ended December 31, 2021. The difference between the carrying amount of our investment in Zentera and our portion of the Zentera net assets was $5.1 million as of December 31, 2022. This difference is accounted for in our equity method investment analogous to in-process research and development.

In May 2020, each of our subsidiaries Zeno Alpha, Inc., K-Group Alpha, Inc. and K-Group Beta, Inc. entered into a collaboration and royalty-bearing license agreement with Zentera, which we refer to as the “Zentera Sublicenses,” pursuant to which we collaborate with Zentera on the development and commercialization of ZN-c5, ZN-d5 and azenosertib, respectively (each a "Collaboration Product"), in the People’s Republic of China, Macau, Hong Kong and Taiwan, which is referred to as the “Zentera Collaboration Territory.” Under each Zentera Sublicense, Zentera will lead development, and upon regulatory approval, the commercialization, of the Collaboration Products in the Zentera Collaboration Territory.

Under the terms of the Zentera Sublicenses, Zentera is generally responsible for the costs of developing the Collaboration Products in the Zentera Collaboration Territory, and we are generally responsible for the costs of developing the Collaboration Products outside the Zentera Collaboration Territory, provided that Zentera will reimburse us for a portion of the costs for global data management, pharmacovigilance, safety database management, and chemistry, manufacturing and controls activities with respect to each Collaboration Product. Prior to the deconsolidation of Zentera, these costs were eliminated in consolidation. For the years ended December 31, 2022 and 2021, the amounts incurred under this arrangement totaled $11.0 million and $5.3 million, respectively and are presented as contra-research and development expense in the consolidated statement of operations. A corresponding receivable is recorded within prepaid expenses and other current assets on the consolidated balance sheet.

4. Business Combinations

Kalyra Pharmaceuticals, Inc.

On December 21, 2017, we acquired $4.5 million of Kalyra Pharmaceuticals, Inc.’s ("Kalyra") Series B Preferred Stock representing a 25% equity interest in Kalyra for purposes of entering the analgesics therapeutic research space. The acquisition price was paid entirely in cash.

In accordance with the authoritative guidance, we concluded that Kalyra is a business consisting of inputs, employees, intellectual property and processes capable of producing outputs. Additionally, we have concluded that Kalyra is a VIE, we are the primary beneficiary and have the power to direct the activities that most significantly affect Kalyra’s economic performance through common management and our board representation. Prior to December 21, 2017, the Company and Kalyra transacted for the delivery of research and development services and support. The financial position and results of operations of Kalyra have been included in our consolidated financial statements from the date of the initial investment.

Pursuant with authoritative guidance, we have recorded the identifiable assets, liabilities and noncontrolling interests in the VIE at their fair value upon initial consolidation. The identified goodwill is comprised of the workforce and expected

synergies from combining the entities. During the year ended December 31, 2021, Kalyra determined that they will no longer pursue the development of Kalyra's lead product candidate and ceased the associated clinical trial. The in-process research and development costs ("IPR&D") recorded on Kalyra's balance sheet exclusively relates to this candidate. Management recorded an impairment charge of $8.8 million within the research and development expense line item on the consolidated statement of operations during the year ended December 31, 2021, which resulted in a reduction of the IPR&D asset from $8.8 million to zero. The impairment of IPR&D resulted in a reversal of the associated deferred tax liability of $2.5 million during the year ended December 31, 2021. Total assets and liabilities of Kalyra as of December 31, 2022 and 2021 are immaterial.

The liabilities recognized as a result of consolidating Kalyra do not represent additional claims on our general assets. Pursuant to the authoritative guidance, the equity interest in Kalyra not owned by Zentalis is reported as a noncontrolling interest on our consolidated balance sheets.

The following is a reconciliation of equity (net assets) attributable to the noncontrolling interest (in thousands):

	December 31,	
	2022	2021
Noncontrolling interest at beginning of period	$ 528	$ 24,795
Net loss attributable to noncontrolling interest	(307)	(7,368)
Deconsolidation of Zentera	—	(16,899)
Noncontrolling interest at end of period	$ 221	$ 528

5. Fair Value Measurement

Available-for-sale marketable securities consisted of the following (in thousands):

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Commercial paper	$ 296,309	$ 71	$ (587)	$ 295,793
Corporate debt securities	7,472	—	(26)	7,446
US government agencies	23,970	—	(182)	23,788
US Treasury securities	67,904	—	(629)	67,275
	$ 395,655	$ 71	$ (1,424)	$ 394,302

As of December 31, 2022, fifty-three of our available-for-sale debt securities with a fair market value of $280.1 million were in a gross unrealized loss position of $1.4 million. When evaluating an investment for impairment, we review factors such as the severity of the impairment, changes in underlying credit ratings, forecasted recovery, our intent to sell or the likelihood that we would be required to sell the investment before its anticipated recovery in market value and the probability that the scheduled cash payments will continue to be made. Based on our review of these marketable securities, we believe none of the unrealized loss is as a result of a credit loss as of December 31, 2022, because we do not intend to sell these securities, and it is not more-likely-than-not that we will be required to sell these securities before the recovery of their amortized cost basis.

Contractual maturities of available-for-sale debt securities are as follows (in thousands):

	December 31, 2022
	Estimated Fair Value
Due within one year	$ 394,302
After one but within five years	—
	$ 394,302

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at

the measurement date. Fair value should maximize the use of observable inputs and minimize the use of unobservable inputs. The Company determines the fair value of financial assets and liabilities using three levels of inputs as follows:

Level 1—Inputs which include quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Inputs (other than quoted market prices included in Level 1) that are either directly or indirectly observable, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the instrument's anticipated life.

Level 3—Unobservable inputs for assets or liabilities and include little or no market activity.

A financial instrument's categorization within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement. The following table summarizes, by major security type, our cash equivalents and available-for-sale marketable securities that are measured at fair value on a recurring basis and are categorized using the fair value hierarchy (in thousands):

	December 31, 2022			December 31, 2021		
	Level 1	Level 2	Total estimated fair value	Level 1	Level 2	Total estimated fair value
Cash equivalents:						
Money market funds	$ 26,811	$ —	$ 26,811	$ 43,653	$ —	$ 43,653
Commercial paper	1,998	—	1,998	—	—	—
Total cash equivalents:	28,809	—	28,809	43,653	—	43,653
Available-for-sale marketable securities:						
Commercial paper	—	295,793	295,793	—	199,277	199,277
Corporate debt securities	—	7,446	7,446	—	10,078	10,078
US government agencies	—	23,788	23,788	—	20,033	20,033
US Treasury securities	67,275	—	67,275	50,785	—	50,785
Total available-for-sale marketable securities:	67,275	327,027	394,302	50,785	229,388	280,173
Total assets measured at fair value	$ 96,084	$ 327,027	$ 423,111	$ 94,438	$ 229,388	$ 323,826

There were no transfers between Level 1 and Level 2 of the fair value hierarchy during the year ended December 31, 2022. We had no instruments that were classified within Level 3 as of December 31, 2022 or 2021.

6. Prepaid Expenses and Other Assets

Prepaid expenses and other assets consisted of the following (in thousands):

	December 31,	
	2022	2021
Prepaid insurance	$ 1,018	$ 990
Prepaid software licenses and maintenance	958	403
Foreign R&D credit refund	659	1,808
Prepaid research and development expenses	15,002	11,204
Interest receivable	508	258
Zentera receivable	5,874	2,373
Other prepaid expenses	266	644
Total prepaid expenses and other current assets	24,285	17,680
Less long-term portion	9,723	7,040
Total prepaid expenses and other assets, current	$ 14,562	$ 10,640

7. Property and Equipment, net

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

	December 31,	
	2022	2021
Lab equipment	$ 2,622	$ 2,057
Leasehold improvements	4,891	4,515
Office equipment and furniture	2,065	2,123
Computer equipment	150	211
Construction in process	37	34
Subtotal	9,765	8,940
Accumulated depreciation and amortization	(2,060)	(792)
Property and equipment, net	$ 7,705	$ 8,148

Depreciation and amortization expense was approximately $1.4 million and $0.5 million for the years ended December 31, 2022 and 2021, respectively.

8. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2022	2021
Accrued research and development expenses	$ 32,310	$ 18,531
Accrued employee expenses	11,246	9,250
Accrued general and administrative expenses	662	1,480
Lease liability	2,162	1,453
Income taxes payable	384	971
Accrued legal expenses	1,256	669
Total accrued expenses	48,020	32,354
Less long-term portion	2,620	—
Total accrued expenses, current	$ 45,400	$ 32,354

9. Stockholders' Equity

Direct Offering of Common Stock

On April 29, 2022, pursuant to our Registration Statement on Form S-3 (Registration No. 333-255769), filed with the SEC on May 4, 2021, we completed a direct offering of common stock to Pfizer Inc. (“Pfizer”). We issued and sold 953,834 shares of our common stock at an offering price of $26.21 per share. The total gross proceeds for the offering were approximately $25.0 million, before deducting offering expenses of $0.3 million payable by us. The parties have entered into an agreement to collaborate to advance the clinical development of azenosertib (ZN-c3), a selective Wee1 inhibitor designed to induce synthetic lethality in cancer cells. We did not grant Pfizer any economic ownership or control of azenosertib or the rest of our pipeline. The gross offering proceeds received from Pfizer exceeded the fair value of our common stock on the date of the investment. As of December 31, 2022, $3.8 million has been recorded as accrued research and development expense on the consolidated balance sheet and will be recognized as a reduction of research and development expense over the term of the collaboration agreement.

Follow-on Offering of Common Stock

On May 18, 2022, pursuant to our Registration Statement on Form S-3 (Registration No. 333-255769), we completed a follow-on offering in which we issued and sold 10,330,000 shares of common stock at a public offering price of $19.38 per share. The total gross proceeds for the offering were approximately $200.2 million, before deducting offering expenses of $11.4 million payable by us.

In May 2021, the Company entered into a sales agreement, or the Sales Agreement, with SVB Leerink LLC, or SVB Leerink, as sales agent, pursuant to which the Company may, from time to time, issue and sell common stock with an aggregate value of up to $200.0 million in “at-the-market” offerings, or the ATM, under the Company's Registration Statement on Form S-3 (File No. 333-255769). Sales of common stock, if any, pursuant to the Sales Agreement, may be made in sales deemed to be an “at the market offering” as defined in Rule 415(a) of the Securities Act, including sales made directly through The Nasdaq Global Market or any other existing trading market for the Company's common stock. During the quarter ended December 31, 2022, the Company sold 2,210,500 shares of common stock under the Sales Agreement at a volume weighted-average price of $22.50 per share, raising aggregate gross proceeds of approximately $49.7 million before fees and expenses of approximately $1.1 million. As of December 31, 2022 there was $140.3 million of common stock remaining available for sale under the Sales Agreement.

Share-based Compensation

In April 2020, the Company’s Board of Directors adopted, and the Company’s stockholders approved the 2020 Incentive Award Plan (the "2020 Plan"), which allows for grants to selected employees, consultants and non-employee members of the Board of Directors. We currently grant stock options and restricted stock units (“RSUs”), under the 2020 Plan. Awards may be made under the 2020 Plan covering up to the sum of (1) 5,600,000 shares of common stock; plus (2) any shares forfeited from the unvested restricted shares of our common stock issued upon conversion of unvested Class B common units (up to 1,250,000 shares); plus (3) an annual increase on the first day of each fiscal year beginning with the fiscal year ending December 31, 2021 and continuing to, and including, the fiscal year ending December 31, 2030, equal to the lesser of (a) 5% of the shares of

common stock outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of shares as determined by our Board of Directors.

In July 2022, the Company's Board of Directors approved the Zentalis Pharmaceuticals, Inc. 2022 Employment Inducement Incentive Award Plan (the "2022 Inducement Plan"), which is used exclusively for the grant of equity awards to new employees as an inducement material to the employees' entering into employment with the Company. The Board of Directors has initially reserved 1,500,000 shares of the Company's common stock for issuance pursuant to awards granted under the 2022 Inducement Plan.

As of December 31, 2022, 7,517,610 shares were subject to outstanding awards under the 2020 Plan and 980,553 shares were available for future grants of share-based awards under the 2020 Plan. As of December 31, 2022, 1,456,750 shares were subject to outstanding awards under the 2022 Inducement Plan and 43,250 shares were available for future grants of share-based awards under the 2022 Inducement Plan.

In connection with the corporate conversion, each outstanding profits interest award unit was converted into a number of shares of common stock and restricted common stock based upon the IPO price. The restricted common stock issued in respect of profits interest award units continues to be subject to vesting in accordance with the vesting schedule that was applicable to such profits interest award units. In conjunction with our IPO on April 2, 2020, all unvested profit interest awards were converted into restricted stock awards ("RSAs").

During 2022, we issued an aggregate of 122,082 shares of common stock in connection with the exercises of stock options for cash in the aggregate amount of approximately $2.2 million. We did not issue any shares of common stock in connection with grants of RSA's. We issued 158,671 shares of common stock, upon vesting of RSU's.

Total share-based compensation expense related to share-based awards was comprised of the following (in thousands):

	Year ended December 31,		
	2022	2021	2020
Research and development expense	$ 20,439	$ 14,879	$ 7,296
General and administrative expense	26,401	20,858	15,850
Total share-based compensation expense	$ 46,840	$ 35,737	$ 23,146

Share-based compensation expense by type of share-based award (in thousands):

	Year ended December 31,		
	2022	2021	2020
Profits interest award units	$ —	$ —	$ 329
Stock options	36,338	20,773	6,925
RSAs and RSUs	10,075	14,643	15,892
Employee Stock Purchase Plan	427	321	—
	$ 46,840	$ 35,737	$ 23,146

Prior to the deconsolidation of Zentera during the third quarter of 2021, total share-based compensation expense includes $138 thousand of share-based compensation expense for employees, consultants and directors of Zentera, for the twelve months ended December 31, 2021, compared to $187 thousand for the same period in 2020.

Total unrecognized estimated compensation cost by type of award and the weighted average requisite service period over which such expense is expected to be recognized (in thousands, unless otherwise noted):

	December 31, 2022	
	Unrecognized Expense	Remaining Weighted-Average Recognition Period (Years)
Stock options	$ 95,906	3.1
RSAs	330	0.7
RSUs	18,880	2.5

Stock Options: The following table summarizes option activity for the year ended December 31, 2022. The amounts include stock options granted to both employees and non-employees:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	4,243,482	$ 33.97		
Granted	5,329,020	$ 31.16		
Exercised	(122,082)	$ 18.40		
Cancelled	(1,398,961)	$ 47.68		
Outstanding at December 31, 2022	8,051,459	$ 29.97	8.2	$3,431
Vested and expected to vest at December 31, 2022	7,524,257	$ 30.38	8.1	$3,431
Exercisable at December 31, 2022	2,037,706	$ 30.94	6.6	$2,307

The weighted average grant date fair value of stock options granted during the years ended December 31, 2022 and 2021 was $20.45 and $33.27, respectively. The total intrinsic value of options exercised during the years ended December 31, 2022 and 2021 was approximately $2.0 million and $8.8 million, respectively.

The exercise price of stock options granted is equal to the closing price of the Company's common stock on the date of grant. The fair value of each option award is estimated on the date of grant using the Black-Scholes model. Due to the Company's limited operating history and a lack of company specific historical and implied volatility data, the Company estimates expected volatility based on the historical volatility of a group of similar companies that are publicly traded. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company uses the "simplified method" for estimating the expected term of employee options, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option (generally 10 years). The risk-free interest rate is based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. The Company has not issued any dividends and does not expect to issue dividends over the life of the options. As a result, the Company has estimated the dividend yield to be zero. The fair value of the stock options granted during the year ended December 31, 2022 was determined with the following assumptions:

	Year ended December 31,	
	2022	2021
Expected volatility	73.6% - 80.5%	73.2% - 76.6%
Average expected term (in years)	6.0 - 6.5	5.2 - 6.1
Risk-free interest rate	1.5% - 4.2%	0.5% - 1.3%
Expected dividend yield	—%	—%

Restricted Stock Awards: RSAs are shares of our common stock subject to forfeiture restrictions that lapse based on the awardee's continued employment or service. The shares covered by a RSA cannot be sold, pledged or otherwise disposed of until the awards vest, and any unvested shares will be forfeited following the awardee's termination of service.

The following table summarizes RSA activity for the year ending December 31, 2022. The amounts include RSAs granted to both employees and non-employees:

	Number of Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2021	361,832	$ 3.47
Vested	(220,891)	$ 4.48
Forfeited	(15,435)	$ 2.84
Outstanding at December 31, 2022	125,506	$ 5.45

The fair value of RSAs issued upon conversion of the unvested profit interest award units was based on a Black-Scholes pricing model. The estimated fair value of the RSAs for any future grants will be based on the closing market value of our common stock on the date of grant. The total grant date fair value of RSAs vested during the years ended December 31, 2022, 2021 and 2020 was approximately $1.0 million, $1.7 million and $1.1 million, respectively. The fair value of RSAs vested during the years ended December 31, 2022, 2021 and 2020, was approximately $8.3 million, $21.0 million and $14.3 million, respectively.

Restricted Stock Units: A RSU is a promise by us to issue a share of our common stock upon vesting of the unit.

The following table summarizes RSU activity for the year ending December 31, 2022. The amounts include RSUs granted to both employees and non-employees:

	Number of Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2021	274,195	$ 33.06
Granted	929,083	$ 27.99
Vested	(158,671)	$ 28.84
Forfeited	(121,706)	$ 37.13
Outstanding at December 31, 2022	922,901	$ 27.48

The estimated fair value of the RSUs was based on the closing market value of our common stock on the date of grant. The total grant date fair value of RSUs vested during the years ended December 31, 2022, 2021 and 2020 was approximately $4.6 million $12.7 million and $10.1 million, respectively. The fair value of RSUs vested during the years ended December 31, 2022, 2021 and 2020 was approximately $7.3 million, $26.4 million and $21.8 million, respectively.

Employee Stock Purchase Plan

In April 2020, the Company's Board of Directors adopted, and the Company's stockholders approved the 2020 Employee Stock Purchase Plan (the "2020 ESPP"), which became effective upon the corporate conversion. The number of common shares initially available for issuance under the 2020 ESPP was the sum of (1) 450,000 shares of common stock; plus (2) an annual increase on the first day of each fiscal year beginning with the fiscal year ending December 31, 2021 and continuing to, and including, the fiscal year ending December 31, 2030, equal to the least of (a) 1% of the shares of common stock outstanding on the final day of the immediately preceding calendar year, (b) 1,500,000 shares and (c) such smaller number of shares as determined by our Board of Directors. The 2020 ESPP was amended and restated effective March 15, 2021 to provide for a share reserve of 2,000,000 shares and the elimination of the evergreen provision.

The weighted average assumptions used to estimate the fair value of stock purchase rights under the 2020 ESPP are as follows:

	Year ended December 31,	
	2022	2021
ESPP		
Volatility	74.0 %	48.2 %
Expected term (years)	0.5	0.5
Risk free rate	1.6 %	0.1 %
Expected dividend yield	— %	— %

Under the terms of the 2020 ESPP, the Company's employees may elect to have up to 20% of their compensation, up to a maximum of $21,250 per calendar year, withheld to purchase shares of the Company's common stock for a purchase price equal to 85% of the lower of the fair market value per share (at closing) of the Company's common stock on (i) the first trading day of a six-month offering period, or (ii) the applicable purchase date, defined as the last trading day of the six-month offering period.

10. Commitments and Contingencies

Legal Contingencies

From time to time, we may be involved in various disputes, including lawsuits and claims arising in the ordinary course of business, including actions with respect to intellectual property, employment, and contractual matters. Any of these claims could subject us to costly legal expenses. The Company records a liability in its consolidated financial statements for these matters when a loss is known or considered probable and the amount can be reasonably estimated. The Company reviews these estimates each accounting period as additional information is known and adjusts the loss provision when appropriate. If a matter is both probable to result in a liability and the amounts of loss can be reasonably estimated, the Company estimates and discloses the possible loss or range of loss to the extent necessary to make the consolidated financial statements not misleading. If the loss is not probable or cannot be reasonably estimated, a liability is not recorded in our consolidated financial statements. While we do generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, or our policy limits may be inadequate to fully satisfy any damage awards or settlement. If this were to happen, the payment of any such awards could have a material adverse effect on our consolidated results of operations and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business. We are currently not a party to any legal proceedings that require a loss liability to be recorded.

Operating Leases

In September 2020, we entered into a lease for approximately 117,900 square feet of laboratory and office space in San Diego. This lease was partially terminated and amended during September 2021. This amendment reduced the rentable square feet by approximately 43,200. The lease commenced in December 2021 and continues through September 2032. The lease also included access to a temporary space of 13,200 square feet of laboratory and office space in San Diego. This lease component commenced in November 2020 and continued through January 2022. The lease is subject to approximately 3.0% annual increases throughout the lease term. We also pay for various operating costs, including utilities and real property taxes. The agreement includes two options to extend the lease for a period of five years each. When we determined our lease term for our operating lease right-of-use assets and lease liabilities for these leases, we did not include the extension options for this lease.

In March 2021, we entered into a lease for approximately 31,362 square feet of office space in New York, New York. The lease commenced in December 2021 and continues through November 2032. The lease is subject to one increase in per annum rent of approximately 8.1% commencing on the sixth anniversary of the commencement date. We received lease incentives under the agreement , including tenant allowances and free rent periods. We also pay for various operating costs, including utilities and real property taxes. The agreement contains one option to extend the lease for a period of five years. When we determined our lease term for our operating lease right-of-use assets and lease liabilities, we did not include the extension options for the lease.

Rent expense recorded by the Company under the leases was approximately $7.0 million and $2.6 million for the years ended December 31, 2022 and 2021, respectively. We paid approximately $2.5 million and $1.3 million of lease payments, respectively, during the years ended December 31, 2022 and 2021.

The following table presents the weighted average remaining lease term and weighted average discount rates related to our operating leases as of December 31, 2022:

Weighted average remaining lease term (in years)	9.8
Weighted average discount rate	9.0%

Approximate annual future minimum operating lease payments as of December 31, 2022 are as follows (in thousands):

Year	Amount
2023	$ 6,340
2024	6,486
2025	6,799
2026	7,278
2027	7,451
Thereafter	38,778
Total minimum lease payments:	73,132
Less: imputed interest	25,804
Total operating lease liabilities	47,328
Less: current portion	2,162
Lease liability, net of current portion	$ 45,166

11. Income Taxes

Zentalis Pharmaceuticals, Inc. is a corporation for tax purposes and is subject to income taxes which have been included in the consolidated financial statements.

The amount of net loss before income taxes and loss on equity method investment for the years ended December 31, 2022, 2021 and 2020 is as follows (in thousands):

	Year ended December 31,		
	2022	2021	2020
U.S. net loss before income taxes	$ (237,926)	$ (171,053)	$ (112,827)
Foreign net income (loss) before income taxes	344	4,663	(5,277)
Net loss before income taxes, including loss on equity method investment	$ (237,582)	$ (166,390)	$ (118,104)

The following table presents the current and deferred income tax provision (benefit) for federal, state and foreign income taxes (in thousands):

	Year ended December 31,		
	2022	2021	2020
Current tax provision:			
Federal	$ —	$ —	$ —
State	11	11	16
Foreign	298	550	410
Total current tax provision	309	561	426
Deferred tax provision:			
Federal	(683)	(120)	—
State	(41)	(736)	—
Foreign	(54)	(2)	18
Total deferred tax provision	(778)	(858)	18
Total provision for income taxes:	$ (469)	$ (297)	$ 444

The following table is a reconciliation of the expected tax computed at the U.S. statutory federal income tax rate to the total provision for income taxes (in thousands):

	Year ended December 31,					
	2022		2021		2020	
Expected tax at 21%	$ (49,892)	21.0 %	$ (34,941)	21.0 %	$ (24,802)	21.0 %
State income tax, net of federal tax	(4,222)	1.8 %	(931)	0.6 %	273	(0.3)%
Research credits	(12,558)	5.3 %	(6,938)	4.2 %	(4,025)	3.4 %
Share-based compensation	1,245	(0.5)%	(3,307)	2.0 %	(1,718)	1.5 %
Other	(2,799)	1.2 %	939	(0.6)%	146	(0.1)%
Section 162(m) limitations	3,950	(1.7)%	3,982	(2.4)%	2,956	(2.5)%
Change in valuation allowance	63,807	(26.9)%	40,899	(24.6)%	27,614	(23.4)%
Provision for income taxes	$ (469)	0.2 %	$ (297)	0.2 %	$ 444	(0.4)%

Deferred income taxes as of each of the following periods reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes.

Significant components of our net deferred tax asset or liability are as follows (in thousands):

	December 31,	
	2022	2021
Deferred tax assets		
Net operating loss	$ 95,392	$ 82,117
Compensation	1,937	1,553
Share-based compensation	7,735	4,123
ASC 842 lease liability	9,967	9,740
Intangibles	1,745	2,004
Capitalized research and experimental expenditures	30,776	—
Accrued liabilities	476	675
Research credits	27,024	14,466
Other	62	—
Total gross deferred tax assets	175,114	114,678
Valuation allowance	(160,967)	(97,160)
Net deferred tax assets	14,147	17,518
Deferred tax liabilities		
Depreciable assets	(1,609)	(1,699)
ASC 842 right of use asset	(8,924)	(9,481)
Equity method investment	(4,467)	(7,954)
Other	—	(6)
Deferred tax liabilities	(15,000)	(19,140)
Net deferred tax liabilities	$ (853)	$ (1,622)

Realization of a portion of our deferred tax assets is dependent upon our generating sufficient taxable income in future years to obtain benefit from the reversal of temporary differences. Management considered all available evidence under existing tax law and anticipated expiration of tax statutes and determined that a valuation allowance of $161.0 million and $97.2 million was required as of December 31, 2022 and 2021, for those deferred tax assets that are not expected to provide future tax benefits. The increase in valuation allowance was primarily related to the federal and states losses incurred and tax credits generated during the period ended December 31, 2022.

At December 31, 2022, we have federal and state net operating loss ("NOL") carryforwards of approximately $390.3 million and $192.4 million, respectively. The federal NOL carryforwards generated in taxable years beginning prior to January 1, 2018 begin to expire in 2033. The federal NOL carryforwards generated in taxable years beginning after December 31, 2017 of $369.4 million can be carried forward indefinitely but may only be used to offset up to 80% of taxable income in future periods. The state NOL carryforwards begin to expire in 2033.

At December 31, 2022, we have federal and state research tax credit carryforwards, net of reserves, of approximately $20.5 million and $8.3 million, respectively. The federal credit carryforwards begin to expire in 2033, and the state credit carryforwards do not expire and can be carried forward indefinitely until utilized.

We have not completed a study to determine whether an ownership change per the provisions of Sections 382 or 383 of the Code, as well as similar state provisions, has occurred. Utilization of our NOL and income tax credit carryforwards may be subject to a substantial annual limitation due to ownership changes that may have occurred or that could occur in the future. These ownership changes may limit the amount of the net operating loss and income tax credit carryover that can be utilized annually to offset future taxable income. In general, an “ownership change” as defined by Section 382 of the Code results from a transaction or series of transactions over a rolling three-year period resulting in an ownership change of more than 50 percentage points of the outstanding stock of a company by certain stockholders.

Uncertain Tax Positions

In accordance with authoritative guidance, the impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more-likely-than-not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained.

The following table summarized the activity related to our unrecognized tax benefits (in thousands):

	December 31,		
	2022	2021	2020
Gross unrecognized tax benefits at the beginning of the year	$ 2,835	$ 1,932	$ 1,124
Increase related to current year tax positions	1,112	969	661
Increase related to prior year tax positions	350	—	197
Decrease related to prior year tax positions	—	(66)	(50)
Gross unrecognized tax benefits at end of the year	$ 4,297	$ 2,835	$ 1,932

Included in the balance of unrecognized tax benefits at December 31, 2022 is $4.0 million that, if recognized, would not impact our income tax benefit or effective tax rate as long as our deferred tax asset remains subject to a valuation allowance. We do not expect any significant increases or decreases to our unrecognized tax benefits within the next 12 months.

We recognize interest and penalties related to unrecognized tax positions within the income tax expense line in the accompanying consolidated statements of operations. There were no accrued interest and penalties associated with uncertain tax positions as of December 31, 2022 and 2021.

The Company files federal and state income tax returns in the United States and Australia. Due to the Company's unutilized NOLs and credits, all years remain subject to income tax examination by authorities. The Company is not currently under examination by federal, state or foreign jurisdictions.

12. Net Loss Per Common Share

Basic and diluted net loss per common share were calculated as follows (in thousands except per share amounts):

	Year ended December 31,		
	2022	2021	2020
Numerator:			
Net loss attributable to Zentalis	$ (236,806)	$ (158,725)	$ (117,841)
Denominator:			
Weighted average number of common shares outstanding, basic and diluted	52,857	42,688	28,113
Net loss per common share	$ (4.48)	$ (3.72)	$ (4.19)

Our potential and dilutive securities, which include outstanding stock options, unvested RSAs and unvested RSUs have been excluded from the computation of diluted net loss per common share as the effect would be anti-dilutive.

The following common stock have been excluded from the calculations of diluted net loss per common share because their inclusion would be antidilutive (in thousands).

	Year ended December 31,		
	2022	2021	2020
Outstanding stock options	8,051	4,243	3,121
Unvested RSAs	126	361	742
Unvested RSUs	923	274	675
	9,100	4,878	4,538

13. Employee Savings Plan

We have an employee savings plan pursuant to Section 401(k) of the Internal Revenue Code. All employees are eligible to participate provided that they meet the requirements of the plan. The Company began making matching contributions under the plan during 2021. The Company has recorded as expense $1.4 million and $991.5 thousand in matching contributions for the years ended December 31, 2022 and 2021, respectively.

14. Related Party Disclosures

Recurium

Kevin D. Bunker, Ph.D, our Chief Scientific Officer, and Cam S. Gallagher, our President and a member of our Board of Directors, currently serve as managing members of Recurium IP Holdings, LLC, or Recurium IP. Each of Dr. Bunker and Mr. Gallagher maintains an ownership interest in Recurium IP. Accordingly, the Company identifies Recurium IP as a related party. In December 2014, our wholly owned subsidiary, Zeno Pharmaceuticals, Inc., entered into a license agreement, or the Recurium Agreement, with Recurium IP, which was subsequently amended, under which Zeno Pharmaceuticals, Inc. was granted an exclusive worldwide license to certain intellectual property rights owned or controlled by Recurium IP to develop and commercialize pharmaceutical products for the treatment or prevention of disease, other than for providing pain relief. Following certain corporate restructuring disclosed elsewhere in this Annual Report on 10-K, our wholly owned subsidiary, ZMI, became the Zentalis contracting party to the Recurium Agreement. The intellectual property rights exclusively licensed by ZMI under the Recurium Agreement include certain intellectual property covering azenosertib, ZN-d5 and our BCL-xL product candidate. For the years ended December 31, 2022 and 2021, the amounts incurred under the Recurium Agreement totaled zero and $10.0 million.

Kalyra Pharmaceuticals, Inc.

On December 21, 2017, we acquired 17,307,692 shares of Series B preferred stock of Kalyra Pharmaceuticals, Inc. for a per share price of twenty-six cents ($0.26) or approximately $4.5 million. The management team and stockholders of Kalyra are also stockholders of the Company.

We entered into a Master Services Agreement ("MSA") with Kalyra in January 2015 which states that Kalyra may provide research and development services to us and that we shall reimburse such expenses on a time and materials basis based on the initial statements of work. For the years ended December 31, 2022 and 2021, we incurred an immaterial amount of expense with Kalyra that was eliminated in consolidation for research and development services provided. As of December 31, 2022, there was an immaterial balance due to Kalyra that eliminated in consolidation. As of December 31, 2021, there was no balance due to Kalyra.

We entered into an Intercompany Services Agreement ("ISA") with Kalyra in January 2018 which states that we may provide research and development services to Kalyra and that Kalyra shall reimburse such expenses on a time and materials basis. For the years ended December 31, 2022 and 2021, we provided an immaterial amount of research and development services to Kalyra that was eliminated in consolidation. As of December 31, 2022 and 2021, an immaterial amount was due from Kalyra that eliminated in consolidation.

Tempus

Kimberly Blackwell, M.D., our Chief Executive Officer and a member of our Board of Directors, was previously employed by Tempus Labs, Inc., or Tempus, and now serves as an advisor of Tempus. The Company entered into a Master Services Agreement with Tempus in December 2020 to provide data licensing and research services. For the years ended December 31, 2022 and 2021, the fees incurred for services performed by Tempus were $0.2 million and $1.0 million, respectively.

Zentera

Dr. Bunker serves as a member of the board of directors of Zentera. Accordingly, the Company identifies Zentera as a related party.

In May 2020, each of our wholly owned subsidiaries, Zeno Alpha, Inc., K-Group Alpha, Inc. and K-Group Beta, Inc., entered into the Zentera Sublicenses, pursuant to which we collaborate with Zentera on the development and commercialization

of ZN-c5, ZN-d5 and azenosertib, respectively, in the Zentera Collaboration Territory. Under the terms of the Zentera Sublicenses, Zentera is responsible for the costs of developing the Collaboration Products in the Zentera Collaboration Territory, and we are responsible for the costs of developing the Collaboration Products outside the Zentera Collaboration Territory, provided that Zentera will reimburse us for a portion of its costs for global data management, pharmacovigilance, safety database management, and chemistry, manufacturing and controls activities with respect to each Collaboration Product. Prior to the deconsolidation of Zentera during July 2021, these costs were eliminated in consolidation. For the years ended December 31, 2022 and 2021, the amounts incurred under this arrangement totaled $11.0 million and $5.3 million, respectively and are presented as contra-research and development expense in the consolidated statement of operations.

During the three months ended March 31, 2022, we divested an early stage asset to Zentera for $0.2 million.

Director Biographical Information

Kimberly Blackwell, M.D.

Kimberly Blackwell, M.D., has served as our Chief Executive Officer since May 2022 and as a member of our Board since July 2020. Prior to joining Zentalis as Chief Executive Officer, Dr. Blackwell served as the Chief Medical Officer of Tempus Labs, Inc., a technology company advancing precision medicine through the practical application of artificial intelligence in healthcare, a position she held from March 2020 to May 2022. From March 2018 to March 2020, Dr. Blackwell served as the Vice President of Early-Stage Oncology and Immuno-oncology at Eli Lilly and Company (NYSE: LLY), where she led clinical teams advancing early phase therapeutics. From June 2000 to March 2018, Dr. Blackwell was a Professor at Duke University, where she oversaw the women's cancer program. Dr. Blackwell has been serving as a member of the Board of Directors of Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE) since May 2020, as a member of the Board of Directors of Century Therapeutics, Inc. (Nasdaq: IPSC) since June 2021, and as a member of the Board of Directors of Fore Biotherapeutics, Inc., a private precision oncology company, since September 2021. Dr. Blackwell received an M.D. from Mayo Medical School and a B.A. in Bioethics from Duke University. We believe Dr. Blackwell's extensive experience in life sciences, including advancing oncology in academic and commercial institutions and in preclinical and clinical settings, qualifies her to serve on our Board.

David Johnson

David Johnson has served as a member of our Board since January 2020 and as our Chairperson since May 2022. Mr. Johnson also served as our Lead Independent Director from April 2020 to May 2022. Mr. Johnson currently serves as Chief Executive Officer and a member of the Board of Directors of Solve Therapeutics, Inc., a venture backed start-up focused on developing next generation mAb based oncology therapeutics, a position he has held since July 2021. In addition, Mr. Johnson is currently serving as a general partner at Velosity Capital, a position he has held since January 2022. Previously, Mr. Johnson served as the Chairman of Lengo Therapeutics, Inc., or Lengo, a precision oncology company, from March 2021 until it was acquired by Blueprint Medicines Corporation (Nasdaq: BPMC) in December 2021. Prior to Lengo, Mr. Johnson served as Chief Executive Officer of VelosBio Inc., an oncology-focused biopharmaceutical company that he founded in 2017, which was acquired by Merck & Co., Inc. (NYSE: MRK) in December 2020. From 2013 to 2016, Mr. Johnson served as Chief Executive Officer of Acerta Pharma, LLC, an oncology-focused pharmaceutical company, which is now a member of the AstraZeneca Group (Nasdaq: AZN). Mr. Johnson has served as a member of the Board of Directors of Aura Biosciences, Inc., or Aura, a biopharmaceutical company, since January 2021, and as Chairman of Aura since March 2021, as a member of the Board of Directors of Palleon Pharmaceuticals Inc., a biopharmaceutical company, since August 2021, and as a member of the Board of Directors of Sudo Biosciences, Inc., a biopharmaceutical company, since January 2021. Mr. Johnson received a Bachelor's Degree in Economics from Indiana University. We believe Mr. Johnson's extensive and diverse expertise in the life sciences industry, including as an experienced executive of clinical-stage companies, qualifies him to serve on our Board.

Cam Gallagher

Cam Gallagher has served as our President since May 2022 and as a member of our Board since our founding in December 2014. Mr. Gallagher served as the Chief Business Officer at Immusoft Corp, a preclinical gene therapy company, from April 2018 to May 2022, and has been serving as a member of its Board of Directors since December 2022. From October 2016 to June 2019, Mr. Gallagher served as the Head of Corporate Development and as a member of the Board of Directors of Oncternal Therapeutics, Inc. (Nasdaq: ONCT), a clinical stage, oncology biopharmaceutical company, and from 2014 to 2016, he served as the Chief Business Officer and as a member of the Board of Directors of RetroSense Therapeutics, LLC, a gene therapy company, until its acquisition by Allergan plc. Mr. Gallagher has served as the Chief Business Officer of Kalyra Pharmaceuticals, Inc., or Kalyra, since July 2013. Mr. Gallagher has been a member of the Board of Directors of Ocuphire Pharma, Inc. (Nasdaq: OCUP), a clinical stage ophthalmology company, since November 2020 and currently serves as Chairman of the Board of Directors. Mr. Gallagher has also served as a member of the Board of Directors of Healios K.K. (TSE: 4593) from March 2022 to March 2023, as a member of the Board of Directors of selectIon, Inc. since July 2018, as a managing member of Recurium IP Holdings, LLC, or Recurium IP, since October 2017, and as managing director of Nerveda, LLC, a life

science seed fund he co-founded, since September 2007. He also served as a member of the Board of Directors of Ray Therapeutics, Inc., a biotechnology company specializing in optogenetics gene therapies, since February 2021, and as a member of the Board of Directors of VelosBio Inc., an oncology-focused biopharmaceutical company, from December 2017 until its acquisition by Merck & Co., Inc. (NYSE: MRK) in December 2020. In addition, Mr. Gallagher has served on the Board of the Moores Cancer Center at UC San Diego Health since May 2019. Mr. Gallagher received an M.B.A. from the University of San Diego and a B.S. in Business Administration from Ohio University. We believe Mr. Gallagher's deep operational and transactional experience and expertise in the life sciences industry qualifies him to serve on our Board.

Enoch Kariuki, Pharm.D.

Enoch Kariuki, Pharm.D., has served as a member of our Board since February 2021. Dr. Kariuki is currently serving as a general partner at Velosity Capital, a position he has held since March 2021. Previously, from June 2021 to January 2022, Dr. Kariuki served as Chief Executive Officer of Lengo Therapeutics, Inc., or Lengo, a precision oncology company that was acquired by Blueprint Medicines Corporation (Nasdaq: BPMC). Prior to Lengo, Dr. Kariuki served as Chief Financial Officer of VelosBio Inc., an oncology-focused biopharmaceutical company, from July 2020 until its acquisition by Merck & Co., Inc. (NYSE: MRK), or Merck, in December 2020. From June 2018 to February 2020, Dr. Kariuki served as Senior Vice President, Corporate Development at Synthorx, Inc., a clinical stage biotechnology company that was acquired by Sanofi (Nasdaq: SNY). From 2014 to April 2018, Dr. Kariuki served as Vice President at H.I.G. Capital, a private equity and alternative assets investment firm. Dr. Kariuki served as a member of the Board of Directors and Chairperson of the Audit Committee of Imago Biosciences, Inc., a biopharmaceutical company, from February 2021 until it was acquired by Merck in January 2023. Dr. Kariuki received an M.B.A. from the Tuck School of Business at Dartmouth and a Pharm.D. from Texas Southern University. We believe Dr. Kariuki's experience as a senior financial executive at large and small commercial and clinical-stage life sciences companies qualifies him to serve on our Board.

Jan Skvarka, Ph.D.

Jan Skvarka, Ph.D., has served as a member of our Board since September 2022. From September 2019 to November 2021, Dr. Skvarka was the President, Chief Executive Officer, and a member of the Board of Directors of Trillium Therapeutics Inc., a publicly traded, clinical-stage immuno-oncology company, which was acquired by Pfizer Inc. (NYSE: PFE) in November 2021. From 2014 to January 2019, Dr. Skvarka served as the President, Chief Executive Officer, and a member of the Board of Directors of Tal Medical Inc., a clinical-stage neuroscience company. Previously, Dr. Skvarka was a partner in the life sciences practice at Bain & Company in Boston, Massachusetts, and a manager at Price Waterhouse, Corporate Finance in London, United Kingdom, and Vienna, Austria. Dr. Skvarka has served as Executive Chairman of DEM Biopharma, Inc. since March 2022, as a member of the Board of Directors of Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE) since March 2023, and as Executive Chairman of GentiBio, Inc. from June 2022 to November 2022. Dr. Skvarka holds an M.B.A. from Harvard Business School and a Ph.D. in Economics from the University of Economics in Slovakia. We believe Dr. Skvarka is qualified to serve on our Board due to his operational, strategic, and financial experience in the biopharmaceutical industry.

Karan Takhar

Karan Takhar has served as a member of our Board since December 2017. Mr. Takhar currently serves as Senior Managing Director and head of Life Sciences investing at Matrix Capital Management Company, L.P., or Matrix, an investment fund focused on technology and life sciences, a position he has held since February 2021. From August 2013 to January 2021, Mr. Takhar held roles of increasing responsibility at Matrix, including the role of Managing Director from January 2017 to January 2021. Mr. Takhar has served as a member of the Board of Directors of Aura Biosciences, Inc. (Nasdaq: AURA) since March 2021. Mr. Takhar also currently serves as a member of the Boards of Directors of numerous private companies, including Bardavon Health Innovations LLC, Encoded Therapeutics Inc., ElevateBio LLC, Koneksa Health Inc., Palleon Pharmaceuticals Inc. and Kalyra. Mr. Takhar received a B.S. in Economics and Mathematics from the Massachusetts Institute of Technology. We believe Mr. Takhar's broad operational and transactional experience as an investor in the life sciences industry qualifies him to serve on our Board.

Information About Our Executive Officers

Kimberly Blackwell, M.D.

See biography under "Director Biographical Information."

Cam Gallagher

See biography under "Director Biographical Information."

Carrie Brownstein, M.D.

Carrie Brownstein, M.D., has served as our Chief Medical Officer since October 2022. Prior to joining Zentalis, Dr. Brownstein served as the Chief Medical Officer of Cellectis S.A. (Nasdaq: CLLS) from April 2020 to September 2022. From March 2017 to April 2020, she held roles of increasing responsibility at Celgene Corporation, a pharmaceutical company, serving as the Executive Director Strategy Lead for Myeloid Disease from March 2017 to July 2017, and as the Vice President of Global Clinical Research and Development from July 2017 to April 2020. Celgene Corporation was acquired by Bristol-Myers Squibb Company (NYSE: BMY) prior to Dr. Brownstein's departure in April 2020. From August 2012 to March 2017, Dr. Brownstein served as the Executive Director of Clinical Sciences, Oncology at Regeneron Pharmaceuticals, Inc. (Nasdaq: REGN) Dr. Brownstein currently serves as a member of the Board of Directors of Shattuck Labs, Inc. (Nasdaq: STTK), a position she has held since October 2021. Prior to her career in the biopharmaceutical industry, Dr. Brownstein practiced medicine as a pediatric oncologist within notable institutions, including New York Presbyterian Columbia University, Memorial Sloan Kettering Cancer Center and Mount Sinai Medical Center. She received her B.A. from the University of Michigan and her M.D. from Tufts University School of Medicine.

Kevin Bunker, Ph.D.

Kevin Bunker, Ph.D., has served as our Chief Scientific Officer since September 2022, and served as our Chief Operating Officer from 2015 to September 2022. Dr. Bunker serves as Chief Scientific/Operations Officer of Kalyra, a small molecule drug discovery and development company, a position he has held since founding the company in 2011. Dr. Bunker also currently serves as a member of the Boards of Directors of Kalyra and Zentera Therapeutics, our joint venture in China, or Zentera, and has served as a managing member of Recurium IP Holdings, LLC, or Recurium IP, since 2017. From 2006 to 2011, prior to founding Kalyra, Dr. Bunker was part of the medicinal chemistry department at Pfizer Inc. (NYSE: PFE), including as a Senior Scientist, where he made meaningful contributions to Pfizer Inc.'s drug discovery research group in La Jolla, California. Dr. Bunker received his B.S. in chemistry from Arizona State University and his Ph.D. in Organic Chemistry from the University of California, San Diego under the direction of Professor Joseph O'Connor. He also held a post-doctorate position as a research associate at The Scripps Research Institute under the direction of Professor Dale Boger.

Melissa Epperly

Melissa Epperly has served as our Chief Financial Officer and Treasurer since September 2019. From June 2018 to August 2019, Ms. Epperly served as Chief Financial Officer at PsiOxus Therapeutics Ltd (now known as Akamis Bio Ltd), a clinical-stage gene therapy cancer company, where she led the company's financial operations. Prior to joining Akamis Bio Ltd, Ms. Epperly served as Chief Financial Officer and head of Business Development at R-Pharm US LLC, a commercial-stage oncology company, from October 2015 to June 2018, where she led the company's financial operations and business development activities. From 2012 to 2015, Ms. Epperly served as a Director at Anchorage Capital Group, L.L.C., a credit-focused hedge fund. Previously, Ms. Epperly was a Vice President at Goldman Sachs in equity research in New York and London, a management consultant with Bain & Company, and a healthcare investment banker at Morgan Stanley. Ms. Epperly currently serves on the Boards of Directors of publicly traded companies, Kinnate Biopharma Inc. (Nasdaq: KNTE), Nautilus Biotechnology, Inc. (Nasdaq: NAUT) and Roivant Sciences Ltd. (Nasdaq: ROIV). She received an M.B.A. from Harvard Business School and a B.A. in Biochemistry and Economics from the University of Virginia.

Andrea Paul

Andrea Paul has served as our General Counsel and Corporate Secretary since August 2022. From May 2021 to July 2022, Ms. Paul served as General Counsel and Corporate Secretary of LogicBio Therapeutics, Inc., a genomic medicine company that was acquired by AstraZeneca plc (Nasdaq: AZN) in November 2022. From December 2017 to May 2021, she held positions of increasing responsibility at Akebia Therapeutics, Inc. (Nasdaq: AKBA), or Akebia, where she was Vice President, Legal from November 2020 to May 2021, Vice President, Legal—Corporate & Securities from February 2020 to November 2020, and Senior Corporate and Securities Counsel from December 2017 to February 2020. Prior to Akebia, Ms. Paul served as Senior Corporate Counsel at Momenta Pharmaceuticals, Inc., a publicly traded biotechnology company that was acquired by Johnson & Johnson (NYSE: JNJ) in 2020. Ms. Paul began her legal career as an associate at Sullivan and Cromwell LLP and Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. Ms. Paul currently chairs the Securities Law Committee of the Boston Bar Association. She received her J.D. from Harvard Law School, where she was the Managing Editor of Vol. 121 of The Harvard Law Review, and her B.A. in Art History from Columbia University.

Iris Roth, Ph.D.

Iris Roth, Ph.D., has served as our as Chief Operating Officer since February 2023. Prior to joining Zentalis, Dr. Roth served as Vice President, Medicine Development Leader, Immuno-Oncology of GlaxoSmithKline (NYSE: GSK) from March 2019 to February 2023. From January 2019 to April 2019, she served as the Chief Operating Officer of Kartos Therapeutics, Inc., a privately held, clinical stage biopharmaceutical company. From 2016 to January 2019, Dr. Roth served as the Vice President, Global Medicine Leader of AstraZeneca plc (Nasdaq: AZN). Prior to AstraZeneca, Dr. Roth served as the Vice President, Program Team Leader of MyoKardia, Inc., a biopharmaceutical company that was acquired by Bristol-Myers Squibb Company (NYSE: BMY) in 2020, and also held roles of increasing responsibility at Genentech, Inc., culminating in the role of Senior Disease Area Director, Oncology. She received her B.S. in Genetics from the University of California, Berkeley and her Ph.D. in Biomedical Sciences from the University of California, San Francisco.