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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021
OR

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

Commission File Number: 001-39263

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, 2021, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $1.76 billion based on the closing price of $53.20 as reported on the Nasdaq Global Select 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 22, 2022 was 45,562,783.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2021 are incorporated herein by reference in Part III.

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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.

The consolidated audited financial statements include the accounts of Zentalis Pharmaceuticals, LLC and its subsidiaries. In connection with our IPO, in April 2020, Zentalis Pharmaceuticals, LLC converted into a Delaware corporation pursuant to a statutory conversion, and changed its name to Zentalis Pharmaceuticals, Inc. All holders of units of Zentalis Pharmaceuticals, LLC became holders of shares of common stock of Zentalis Pharmaceuticals, Inc. In this Annual Report on Form 10-K, we refer to all transactions related to our conversion to a corporation as the Corporate Conversion.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. We intend such forward-looking statements to be covered by 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,” “forecast,” “predict,” “potential” 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 regarding our future results of operations and financial position, the anticipated impact of the COVID-19 pandemic on our business, business strategy, prospective products and product candidates, clinical trial timelines and expected timing for the release of data, research and development costs, future revenue, timing and likelihood of success, potential collaboration opportunities, the sufficiency of our cash, cash equivalents and marketable securities, and plans and objectives of management for future operations and capital expenditures.

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 the sections in this Annual Report on Form 10-K entitled "Summary Risk Factors," “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, 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 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.

TRADEMARKS AND TRADENAMES

Solely for convenience, trademarks, service marks and tradenames referred to in this Annual Report on Form 10-K may appear without the ®, TM or SM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable licensor to these trademarks, service marks and tradenames. This Annual Report on Form 10-K may also contain trademarks, service marks, tradenames and copyrights of other companies, which are the property of their respective owners.

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, have not completed any clinical trials and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and 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 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, ZN-c3 and ZN-c5, which are currently in clinical trials. If we are unable to complete development of, obtain approval for and commercialize ZN-c3 and/or ZN-c5 in a timely manner, our business will be harmed.
- The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities.
- We may face additional risks associated with the development of ZN-c3, ZN-c5, ZN-d5, ZN-e4 and potentially other product candidates in combination with other therapies.
- The clinical trial and regulatory approval processes are lengthy, time-consuming and inherently unpredictable, and we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- 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.

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 use our highly efficient drug discovery engine, which we refer to as our Integrated Discovery Engine, to identify targets and develop small molecule new chemical entities, or NCEs, with properties that we believe could result in potentially differentiated product profiles. Our discovery engine combines our extensive experience and capabilities across cancer biology and medicinal chemistry. 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.

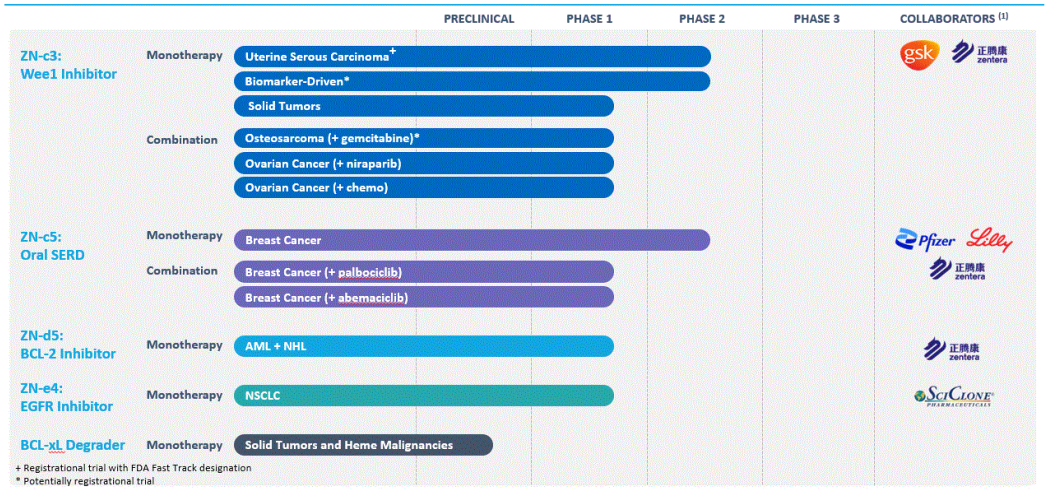
We are developing a broad pipeline of product candidates with an initial focus on validated oncology targets with the potential to address large patient populations. We currently have two lead product candidates: ZN-c3, an inhibitor of Wee1, a protein tyrosine kinase, and ZN-c5, an oral selective estrogen receptor degrader, or SERD. Our other clinical product candidates include ZN-d5, a selective inhibitor of B-cell lymphoma 2, or BCL-2, and ZN-e4, an irreversible inhibitor of mutant epidermal growth factor receptor, or EGFR.

ZN-c3 is currently being evaluated in multiple Phase 1/2 clinical trials for the treatment of advanced solid tumors including uterine serous carcinoma, or USC, as a monotherapy and in combination with chemotherapies in patients with advanced ovarian cancer and osteosarcoma, and in combination with PARP inhibitor in ovarian cancer. ZN-c5 is currently in Phase 1/2 clinical trials for the treatment of estrogen receptor-positive, human epidermal growth factor receptor 2-negative, or ER+/HER2-, advanced or metastatic breast cancer. ZN-d5 is currently in a Phase 1 clinical trial for the treatment of non-Hodgkin's lymphoma, or NHL, and acute myelogenous leukemia, or AML, and ZN-e4 is currently in a Phase 1/2 clinical trial for the treatment of advanced non-small cell lung cancer, or NSCLC.

We plan to initiate combination trials of product candidates across our pipeline in 2022, including a Phase 1/2 combination trial of ZN-d5 and ZN-c3 in acute myeloid leukemia, or AML, and a Phase 1b combination trial of ZN-c5 and ZN-c3 for the treatment of CDK4/6i resistant breast cancer.

We currently own worldwide development and commercialization rights to each of our product candidates, other than in select Asian countries (including China) for each of ZN-c3, ZN-c5 and ZN-d5, for which we have out-licensed these rights to our joint venture, Zentera Therapeutics (Cayman), Ltd., or Zentera, and for ZN-e4, for which we have out-licensed these rights to SciClone Pharmaceuticals International (Cayman) Development Ltd., or SciClone. As of December 31, 2021, we hold a 40.3% equity interest in Zentera.

The following table summarizes our product candidate pipeline.



(1) We are currently evaluating ZN-c5 in combination with palbociclib (Ibrance®), as part of a clinical research collaboration with Pfizer, and are evaluating ZN-c5 in combination with abemaciclib (Verzenio®), as part of clinical research collaboration with Lilly. We are evaluating ZN-c3 in combination with niraparib (ZEJULA®), as part of a clinical research collaboration with GlaxoSmithKline. We maintain full ownership of ZN-c5 and ZN-c3 in each such collaboration. SciClone has development and commercial rights to ZN-e4 in Greater China (including Macau and Hong Kong), South Korea, Taiwan and Vietnam. Our joint venture Zentera has development and commercial rights to ZN-c3, ZN-c5 and ZN-d5 in China, Macau, Hong Kong and Taiwan. Zentera received CTA acceptances in China for ZN-c3, ZN-c3 in combination, ZN-c5 and ZN-d5, and four clinical trials are ongoing. As of December 31, 2021, we hold a 40.3% equity interest in Zentera.

ZN-c3 (Wee1 Inhibitor)

ZN-c3 is currently being evaluated in multiple ongoing clinical trials, including a Phase 2 monotherapy clinical trial for the treatment of women with recurrent or persistent uterine serous carcinoma, or USC. The study was initiated following an end-of-Phase 1 meeting with the U.S. Food and Drug Administration, or FDA, which concurred in principle with the proposal that ZN-c3 has the potential for an accelerated approval pathway based on the proposed global study design. The FDA granted Fast Track designation in November 2021 to ZN-c3 for the treatment of patients with advanced metastatic uterine serous carcinoma who have received at least one prior platinum--based chemotherapy regimen.

In addition, ZN-c3 in combination with chemotherapy has received orphan drug designation and rare pediatric disease designation from the FDA for osteosarcoma. We initiated a Phase 1/2 clinical trial of ZN-c3 in combination with chemotherapy in pediatric and adult patients with osteosarcoma during the third quarter of 2021. We expect to report initial results from this trial in the second half of 2022. If ZN-c3 were to obtain approval for the designated indication, we believe it may be eligible for a rare pediatric disease priority voucher upon approval.

ZN-c3 is also being evaluated in an ongoing Phase 1/2 clinical trial for the treatment of advanced solid tumors as a monotherapy and in an ongoing Phase 1b clinical trial in combination with chemotherapy in patients with platinum resistant ovarian cancer.

In the fourth quarter of 2021, we initiated a Phase 2 monotherapy trial for a tumor agnostic, predictive biomarker, subject to FDA feedback. We also initiated a Phase 1/2 clinical trial evaluating ZN-c3 in combination with GlaxoSmithKline's PARP inhibitor niraparib (ZEJULA®), as part of a clinical research collaboration in ovarian cancer. We also announced plans to initiate a Phase 1/2 combination trial of ZN-d5 + ZN-c3 in AML and a Phase 1b combination trial of ZN-c5 and ZN-c3 in CDK4/6i resistant breast cancer in 2022.

We have agreed to support two planned additional investigator-initiated trials of ZN-c3 that we expect to initiate in 2022: a trial with the Ivy Brain Center in glioblastoma multiforme and a trial in combination with immunotherapy with Dana Farber in triple negative breast cancer.

ZN-c5 (Oral SERD)

In the ongoing Phase 1/2 clinical trial evaluating ZN-c5 in combination with Pfizer's CDK4/6 palbociclib, and the Phase 1b clinical trial evaluating ZN-c5 in combination with Lilly's CDK4/6 abemaciclib, the safety and tolerability data suggested ZN-c5 has the potential to be a promising candidate for further evaluation in combinations. We continue to enroll patients in the two separate combination trials and expect to report initial results in the first half of 2022. In the fourth quarter of 2021, we announced our plans to initiate a Phase 1b combination of ZN-c5 and ZN-c3 in CDK4/6i resistant breast cancer in 2022.

ZN-d5 (BCL-2 Inhibitor)

The ongoing Phase 1 monotherapy dose escalation trial for ZN-d5 is enrolling patients with relapsed/refractory Non-Hodgkin's Lymphoma and additionally began enrolling patients with AML in the third quarter of 2021. We reported initial results from this Phase 1 trial in the fourth quarter of 2021. We also announced plans to initiate a Phase 1/2 combination trial of ZN-d5 and ZN-c3 in AML in 2022.

ZN-e4 (EGFR Inhibitor)

The ongoing Phase 1/2 dose escalation trial for ZN-e4 in patients with advanced non-small cell lung cancer (NSCLC) is enrolling both osimertinib-naïve and experienced patients. We plan to report results from the Phase 1/2 trial in 2022.

BCL-xL Heterobifunctional Degrader

We are developing BCL-xL heterobifunctional degraders based on E3 ligases not expressed in platelets, allowing for the avoidance of dose-limiting thrombocytopenia associated with BCL-xL inhibitors. We believe that our Discovery efforts to select a BCL-xL degrader will lead to an attractive candidate for evaluation as monotherapy and in combination with other therapies, such as ZN-d5 and ZN-c3, for the treatment of hematological and solid malignancies.

Integrated Discovery Engine

We are also currently advancing multiple small molecule programs in preclinical development for other cancer indications, including select solid tumors and hematological malignancies.

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 in a capital efficient manner. 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 target-drug structure activity to design proprietary NCEs 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. We have used our Integrated Discovery Engine to generate a pipeline of four product candidates targeting solid tumors and hematological malignancies. Longer term, we believe our discovery engine has the potential to generate product candidates addressing a wide range of additional therapeutic areas.

Pursuant to a collaboration and license agreement entered into in May 2020, we collaborate with our joint venture Zentera on the development and commercialization of ZN-c3, ZN-c5 and ZN-d5 in China, Macau, Hong Kong and Taiwan. Zentera received clinical trial application, or CTA, acceptances in China for ZN-c3, ZN-c3 in combination, ZN-c5 and ZN-d5, and four clinical trials are ongoing.

Strategy

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

- Discover and develop differentiated small molecule NCEs that address large patient populations with cancer.
- Rapidly advance the development of our lead product candidates, ZN-c3 (Wee1 Inhibitor) and ZN-c5 (oral SERD), toward regulatory approval.

- Advance our additional product candidates, ZN-d5 (BCL-2 Inhibitor) and ZN-e4 (EGFR Inhibitor), across multiple cancer indications.
- Continue to evaluate our product candidate pipeline in combination with internally discovered and third-party compounds.
- Deploy our highly efficient Integrated Discovery Engine to further expand our product candidate pipeline.
- Evaluate strategic opportunities to accelerate development timelines and maximize the value of our product candidate pipeline.

Our Zentalis Approach

We have leveraged our extensive industry experience and know-how, and the guidance of our scientific advisory board, to build our Integrated Discovery Engine that integrates our extensive capabilities across cancer biology and medicinal chemistry. This engine enables us to identify targets for which small molecule NCEs with high potency, high exposure and other optimized drug properties could yield potentially differentiated product profiles. Our approach centers on utilizing our Integrated Discovery Engine with functional screens, preclinical models, machine learning and chemistry, to identify such targets and subsequently develop product candidates with translational science to support ongoing clinical programs that address targets with large cancer patient populations.

Our Integrated Discovery Engine is executed through the following process:

- ***First***, identify fundamental biological pathways of cancers, considering a number of factors, including prior clinical outcomes, input from our scientific and business advisory boards, large unmet medical need and market opportunity.
- ***Second***, identify and analyze key products or compounds targeting these cancer pathways and assess their limitations, including with respect to efficacy, safety, tolerability, PK, patient convenience and their potential to be used in combination.
- ***Third***, use our medicinal chemistry expertise and deep understanding of target-drug structure activity relationships to create proprietary NCEs that are designed to improve upon and address observed limitations of existing products or compounds.
- ***Fourth***, generate strong preclinical data to support our view that such candidates could have potentially differentiated product profiles in our expected lead indications, if approved, before moving a compound into clinical development.

We have initially chosen to focus on targets that have been validated clinically and, in most cases, commercially. This provides us with a clear understanding of the indications we will target and endpoints that have been required for regulatory approval of products for these indications in the past, as well as the potential for clinical adoption and commercial success. This strategy has enabled us to begin our drug discovery and development process at an advanced state relative to where the process would otherwise begin in focusing on uncharacterized targets. We believe this ability provides us with an efficient path to identifying novel drug compounds and advancing them into clinical development in a capital efficient manner.

Our Product Candidates

ZN-c3, an Inhibitor of Wee1 for the Treatment of Solid Tumors and Other Cancers

Overview

We are developing ZN-c3, an oral, small molecule DNA damage response product candidate, targeting Wee1 in cancer. The inhibition of Wee1, a protein tyrosine kinase, aims to generate sufficient DNA damage in cancer cells to undergo apoptosis, thereby preventing tumor growth and potentially causing tumor regression. There is currently no FDA-approved Wee1 inhibitor, and AstraZeneca's adavosertib (AZD1775) is currently one of few other Wee1 inhibitors in clinical development of which we are aware. Despite the observed efficacy of adavosertib in clinical trials, we believe its narrow therapeutic window is a potential limitation affecting its dosing in monotherapy and in combination. We have applied our expertise to design ZN-c3 to have such solubility, selectivity and PK properties that we believe may provide a broad therapeutic window and which, if ZN-c3 is approved, may constitute a differentiated product profile. We believe ZN-c3, if approved, may have broad applicability in a wide range of cancers both as monotherapy and in combination, including with chemotherapy agents, PARP inhibitors and other targeted therapies.

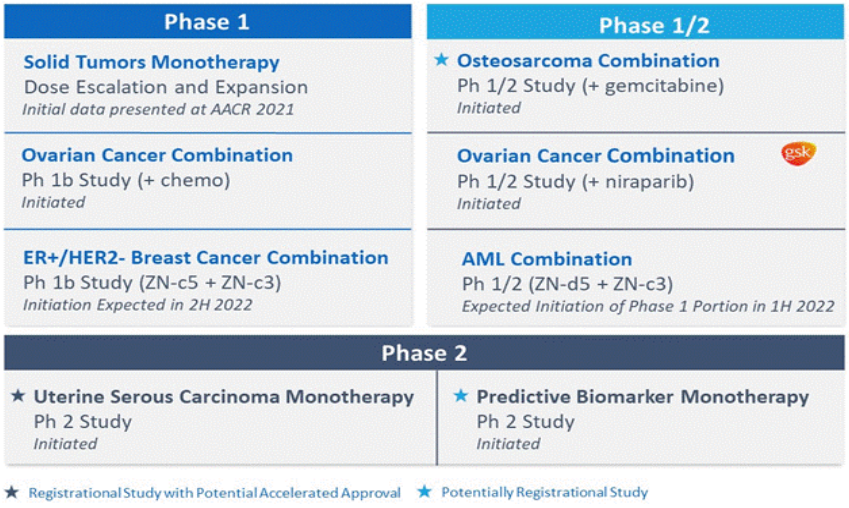
ZN-c3 is currently being evaluated in multiple ongoing clinical trials, including a Phase 2 monotherapy clinical trial for the treatment of women with recurrent or persistent uterine serous carcinoma, or USC. The study was initiated following an end-of-Phase 1 meeting with the FDA, which concurred in principle with the proposal that ZN-c3 has the potential for an accelerated approval pathway based on the proposed global study design. The FDA granted Fast Track designation in November 2021 to ZN-c3 for the treatment of recurrent or persistent USC in adult women. We expect to report an initial enrollment/safety update from this trial in the second half of 2022.

In addition, ZN-c3 in combination with chemotherapy has received orphan drug designation and rare pediatric disease designation from the FDA for pediatric osteosarcoma. We initiated a Phase 1/2 clinical trial of ZN-c3 in combination with chemotherapy in pediatric and adult patients with osteosarcoma during the third quarter of 2021. We expect to report initial results from this trial in the second half of 2022. If ZN-c3 were to obtain approval for the designated indication, we believe it may be eligible for a Rare Pediatric Disease Priority Review Voucher from the FDA upon approval.

ZN-c3 is also being evaluated in an ongoing Phase 1/2 clinical trial for the treatment of advanced solid tumors as a monotherapy and in an ongoing Phase 1b clinical trial in combination with chemotherapy in patients with platinum resistant ovarian cancer.

In the fourth quarter of 2021, we initiated a Phase 2 monotherapy trial for a tumor agnostic, predictive biomarker, subject to FDA feedback. This Phase 2 tumor agnostic trial planned with registrational intent is investigating ZN-c3 in patients with solid tumors that express the identified predictive biomarker. We also initiated a Phase 1/2 clinical trial evaluating ZN-c3 in combination with GlaxoSmithKline's PARP inhibitor niraparib (ZEJULA®), as part of a clinical research collaboration in ovarian cancer. We also announced plans to initiate a Phase 1/2 combination trial of ZN-d5 and ZN-c3 in AML and a Phase 1b combination trial of ZN-c5 and ZN-c3 in CDK4/6i resistant breast cancer in 2022.

ZN-c3 Clinical Program Summary



Background on DNA Damage Repair and Wee1 Inhibitors

The underlying principle behind a number of cancer therapies is to generate sufficient DNA damage in cancer cells, many of which already have deficiencies in DNA damage response, to cause them to undergo apoptosis. Examples of these therapies include alkylating agents, DNA-binding drugs and the use of radiation. However, cancer cells have developed multiple mechanisms of resistance to these therapies, thereby potentially limiting their therapeutic efficacy.

The regulation of DNA damage response mechanisms in cancer cells may therefore play a crucial role in the induction of apoptosis and the ultimate efficacy of DNA damaging cancer therapies. This is particularly true in cancers with specific

mutations in DNA repair proteins that prevent efficient DNA damage response and repair, rendering them particularly vulnerable to any agent that further inhibits the ability of cells to repair DNA damage.

Examples of such cancers are those with mutations in BRCA1 and BRCA2. Inhibitors of PARP, an independent DNA repair protein, work to prevent DNA damage repair, and are FDA approved for the treatment of multiple cancers, such as breast and ovarian cancers associated with BRCA1 and BCRA2 mutations. Sales of FDA-approved PARP inhibitors were approximately $1.6 billion in 2019 and are expected to grow to $6.9 billion in 2026.

Similar to PARP, Wee1 plays a role in cellular regulation and repair, allowing cells with DNA damage to repair and survive. Wee1 is a protein tyrosine kinase that mediates cell cycle arrest by regulating the phosphorylation of cyclin-dependent kinase 1, or CDK1. Inhibition of Wee1 causes dysregulation of DNA replication and inability of DNA response processes to act, leading to an increase in double-strand DNA breaks and subsequently inducing apoptosis. Based on these similar mechanisms of action, we believe the use of Wee1 and PARP, both DNA damage response agents, in combination can have a synergistic effect. In third-party preclinical studies, the combination of PARP and Wee1 has been observed to result in improved anti-tumor activity as compared to the use of each as monotherapy. However, both of these compounds have been associated with bone marrow toxicity, which may limit their concomitant administration.

Wee1 Inhibitor in Clinical Development and Limitations

One of few other Wee1 inhibitors currently in clinical development of which we are aware is adavosertib. Adavosertib has been the subject of many publications in the scientific literature and has been explored in numerous clinical trials across multiple tumor types. Adavosertib is currently being evaluated by third parties in Phase 1 and 2 clinical trials in ovarian cancer and a variety of other solid tumors, both as monotherapy and in combination with other cancer therapies. In earlier third-party clinical trials, multiple patients with advanced or metastatic tumors for whom no standard therapy was available achieved partial responses when dosed with adavosertib in combination with chemotherapy agents. For example, in a Phase 2 clinical trial in 24 patients (21 of such patients were evaluable for efficacy) with relapsed ovarian cancer, the combination of adavosertib and carboplatin, an FDA-approved chemotherapy, demonstrated an overall response rate, or ORR, of 43% and one patient exhibited a complete response, or CR, lasting over 42 months.

In addition, in a recent Phase 2 clinical trial in patients with recurrent USC, an aggressive subtype of endometrial carcinoma characterized by TP53 mutations, adavosertib administered as monotherapy demonstrated an ORR of 30%.

Further, in a recent Phase 1 clinical trial in patients with locally advanced pancreatic cancer, adavosertib in combination with gemcitabine, an FDA-approved chemotherapy, and radiation resulted in a median overall survival of 21.7 months. This overall survival was substantially longer than the 11.9 to 13.6 months observed in a prior clinical trial with a similar population of patients combining gemcitabine with or without erlotinib with radiation.

Although adavosertib has demonstrated promising efficacy in clinical trials, we believe adavosertib has a narrow therapeutic window, a potential limitation affecting its dosing as monotherapy and in combination. Furthermore, the use of adavosertib in combination with PARP inhibitors in preclinical studies has demonstrated increased bone marrow toxicities, thereby potentially limiting its use in continuous dosing. We believe adavosertib has a number of characteristics that could be improved upon, including selectivity, solubility, PK properties and tumor concentration.

Our Wee1 Solution: ZN-c3

ZN-c3 is our oral Wee1 inhibitor product candidate that we are currently evaluating for the treatment of advanced solid tumors in an ongoing Phase 1/2 clinical trial. We believe ZN-c3 has the potential to provide a wide therapeutic window due to the following observed clinical and preclinical results:

- ***Potency, selectivity and solubility.*** In our preclinical studies, ZN-c3 produced favorable absorption, distribution, metabolism and excretion, or ADME, results. In our in vitro preclinical studies, we observed ZN-c3's potency in inhibiting tumor growth and inducing apoptosis through DNA damage, and ZN-c3 has shown high selectivity for Wee1. In addition, in a series of repeat preclinical studies assessing the solubility of ZN-c3 and adavosertib utilizing a standard in vitro assay and uniform controls, ZN-c3 demonstrated solubility of 2,132,000 nM, approximately 35 times greater than that of adavosertib, which we believe could reduce inter-patient drug exposure variability and limit the toxicity observed in clinical trials of adavosertib.

- ***Preclinical anti-tumor activity***. In head-to-head preclinical studies, ZN-c3 showed anti-tumor activity across a number of cell lines, as well as superior tumor growth inhibition, DNA damage and apoptosis when compared to adavosertib.

Anti-tumor activity was observed in both continuous and intermittent dosing, as well as in the shorter of the dosing periods evaluated.

- ***PK properties.*** In our preclinical studies, ZN-c3 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, which may necessitate lower dose intensity thereby potentially affording a wide therapeutic window. In addition, we observed that ZN-c3 had favorable drug accumulation in tumors.

- ***Well tolerated in preclinical studies and clinical trials.*** In preclinical studies and clinical trials to date, ZN-c3 was observed to be well tolerated across varying dosage levels.

In addition to having a potentially wide therapeutic window, we believe the characteristics of ZN-c3 may allow patients with aggressive solid tumors to be treated with sequential therapy using mechanism of action synergistic multiple agents, including PARP inhibitors. In a third-party preclinical combination study with PARP inhibitors, sequential dosing resulted in favorable tolerability as compared to continuous dosing, while maintaining strong anti-tumor activity.

Preclinical Results

Potency Across Variety of Solid Tumor Cell Lines

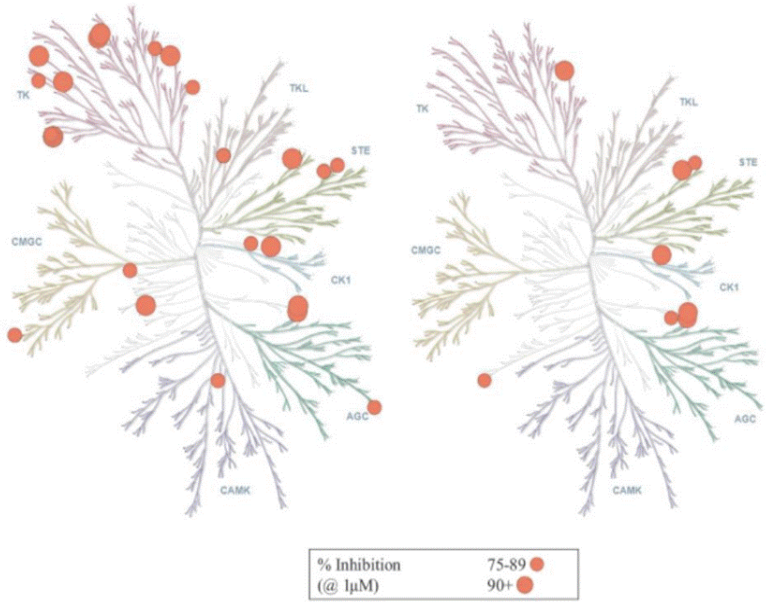
We assessed the potency of ZN-c3 and adavosertib (AZD1775) in repeat in vitro preclinical studies across a variety of solid tumor cell lines, as shown in the table below. We observed ZN-c3's potency in inhibiting tumor growth and inducing DNA damage and apoptosis in each of the solid tumor cell lines studied.

	CTG IC_{50} (nM)[1]								
	Non-Small Cell Lung Cancer		Small Cell Lung Cancer		Triple Negative Breast Cancer		Ovarian Cancer		Squam Cel Carcin
COMPOUND	**A-427**	**NCI-H23**	**DMS-53**	**NCI-H1048**	**MDA-MB-231**	**HCC1806**	**UWB.1.289**	**OVCAR3**	**SK-MI**
AZD1775[2]	94	108	130	97	233	94	57	124	
ZN-c3	**88**	**124**	**118**	**92**	**190**	**95**	**54**	**69**	

(1) Data based on a series of repeat preclinical studies using standard *in vitro* assay and uniform controls.
(2) Data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company developing the compound.

Selectivity of ZN-c3 in Kinase Screening Panel

In our head-to-head in vitro preclinical studies, we assessed the selectivity of ZN-c3, alongside adavosertib. The selectivity profile of each of ZN-c3 (right) and adavosertib (left) was characterized against a broad kinase panel for Wee1 consisting of 485 mammalian serine/threonine and tyrosine, as depicted by the respective kinase dendograms below. ZN-c3 and adavosertib were tested at a single concentration to determine the percentage inhibition at 1 μM. ZN-c3 was observed to have higher selectivity relative to that of adavosertib as depicted by the overall fewer kinases being affected in the ZN-c3 dendogram.



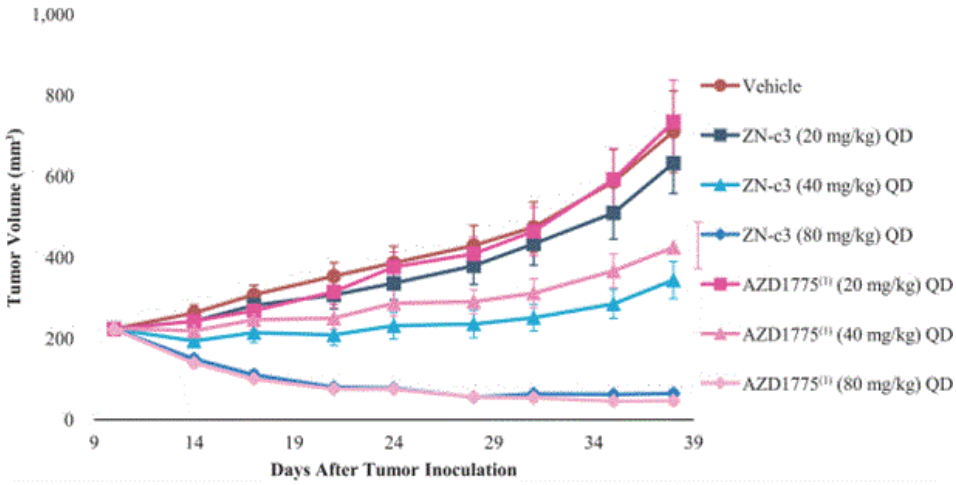
Notes:
Illustration reproduced courtesy of Cell Signaling Technology, Inc. Each branch of the dendogram represents an individual human kinase. Adavosertib data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company developing the compound.

Solubility of ZN-c3

We assessed the relative ADME properties and solubility of ZN-c3 and a proxy chemical compound of adavosertib in a series of repeat preclinical studies. ZN-c3 showed targeted ADME properties, and demonstrated solubility of 2,132 µM, approximately 35 times greater than the 60 µM observed with adavosertib in repeat preclinical studies. We believe greater solubility may reduce interpatient variability, and in turn limit toxicities for ZN-c3.

Anti-Tumor Activity in Human Lung Cancer Model

In a preclinical study, we assessed the anti-tumor potential of ZN-c3 alongside adavosertib, each as a monotherapy, in a lung cancer model using human A-427 cells that contained a KRAS mutation. In this model, doses of 40 mg/kg or 80 mg/kg of ZN-c3 demonstrated tumor shrinkage that was evident at the first post-treatment observation at four days and continued through the end of the experiment. Across dose levels there was no statistical difference between ZN-c3 and adavosertib and each compound produced tumor regression. ZN-c3 was observed to be well tolerated across all doses.

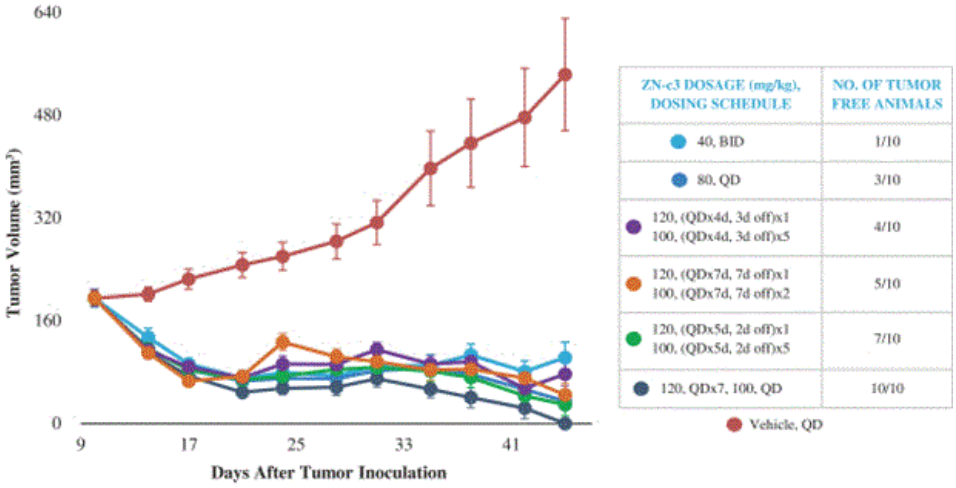


(1) Adavosertib (AZD 1775) data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than he pharmaceutical company developing the compound

Notes:
QD: once daily

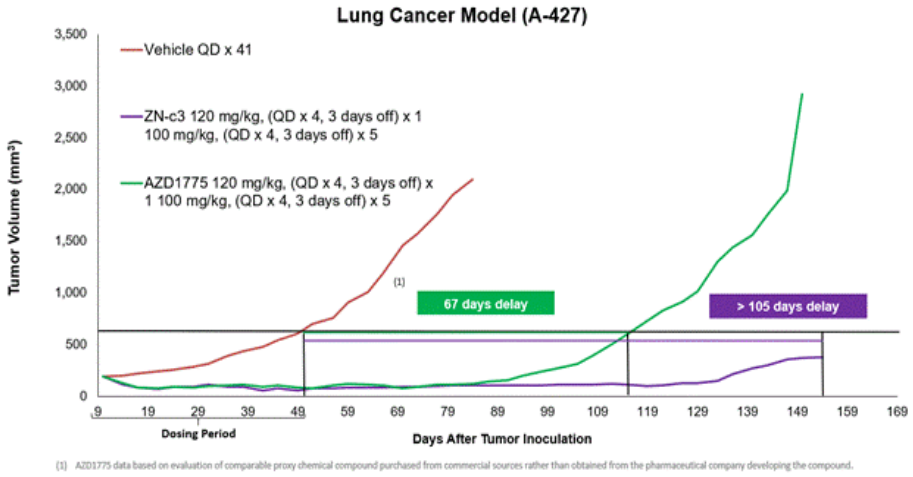
Anti-Tumor Activity in Lung Cancer Model Across Varying Dosage Levels and Intermittent Dosing Regimen

We have explored various dosing regimens of ZN-c3 in preclinical studies. A loading dose of 120 mg/kg daily for seven days followed by once-daily dosing of 100 mg/kg resulted in ten out of ten treated mice being tumor free after five weeks. We also explored the potential of shorter dosing periods or intermittent dosing of ZN-c3 in preclinical studies. A loading dose of 120 mg/kg for five days followed by two days off drug followed by five weeks of 100 mg/kg given five days on, two days off resulted in seven out of ten mice being tumor free as shown in the graph below. A loading dose of 120 mg/kg for seven days followed by seven days off drug followed by two cycles of seven days on 100 mg/kg drug and seven days off drug resulted in five out of ten mice being tumor free as shown in the graph below.



Notes:
QD: Once daily
BID: Twice daily

We also assessed the potential of utilizing an intermittent dosing regimen with ZN-c3 alongside that of adavosertib in a preclinical study. Dosing of ZN-c3 by using a loading dose of 120 mg/kg for four days followed by three days off drug followed by five weeks of 100 mg/kg given four days on, three days off resulted in more prolonged tumor growth delay than that observed with adavosertib at the same dosing regimen.



PK Data Comparison in Animal Models

We assessed the PK properties of ZN-c3 and adavosertib in repeat preclinical animal models, as shown in the table below. For each of the preclinical studies, we observed the respective Cmax, Tmax, AUC and tumor concentration of each compound at doses of 20, 40 and 80 mg/kg/day. Administration of ZN-c3 was observed to result in high drug exposure in animal models and the selective accumulation of ZN-c3 to high levels in tumors. We believe this increased drug exposure may cause the inhibition of Wee1 at low doses, potentially affording a wide therapeutic window.

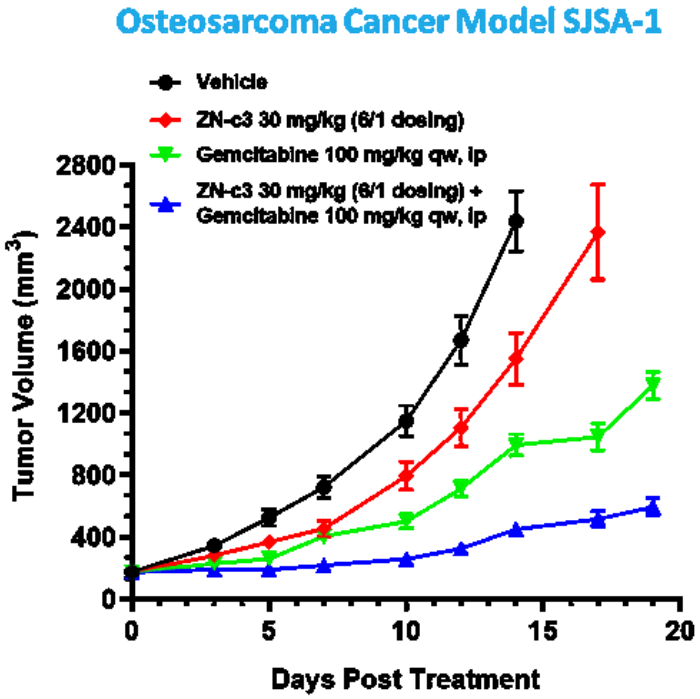
STUDY[1]	**ZN-c3**			**Adavosertib** [2]		
Dose (mg/kg/day)	20	40	80	20	40	80
C_{max} (ng/mL)	1,167	1,997	5,100	635	2,460	4,703
T_{max} (hr)	1	1	1	1	1	1
$AUC_{0\text{-}24hr}$ (ng*hr/mL)	4,863	17,088	39,722	1,494	6,313	13,408
Tumor Concentration (ng/mL)	**10.5**	**48.0**	**811**	**BQL**	**BQL**	**6.95**

(1) Data based on a series of repeat preclinical studies using standard assay and uniform controls.
(2) Data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound.
Note:

BQL: Below Quantifiable Level

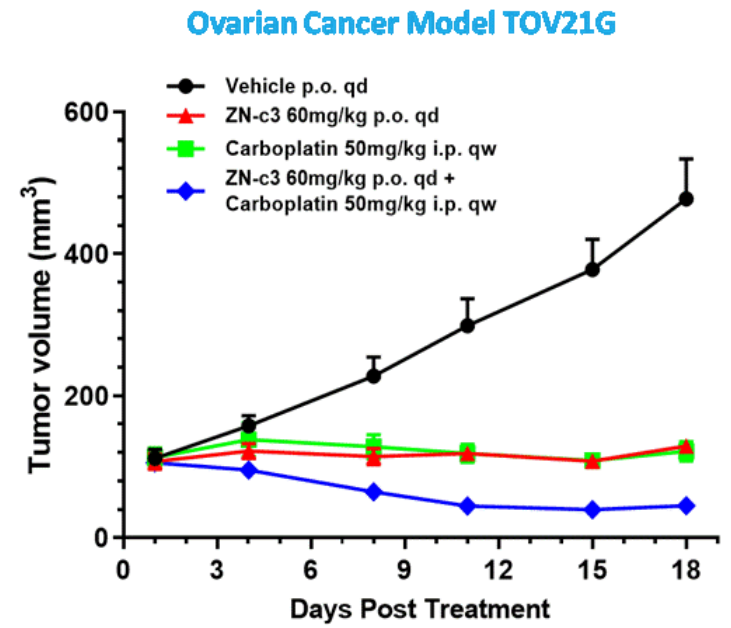
Anti-Tumor Activity in an Osteosarcoma Cancer Model

The anti-tumor activity of ZN-c3 alone and in combination with gemcitabine was assessed in the preclinical osteosarcoma cancer model SJSA-1. ZN-c3 was dosed at 30 mg/kg QD, po six days on, one day off; gemcitabine was dosed at 100 mg/kg, QW, ip and the combination of ZN-c3 and gemcitabine was dosed following the same dosing schedule for each single agent, respectively. The combination treatment resulted in a better anti-tumor effect than each monotherapy treatment (ZN-c3 and gemcitabine) alone.

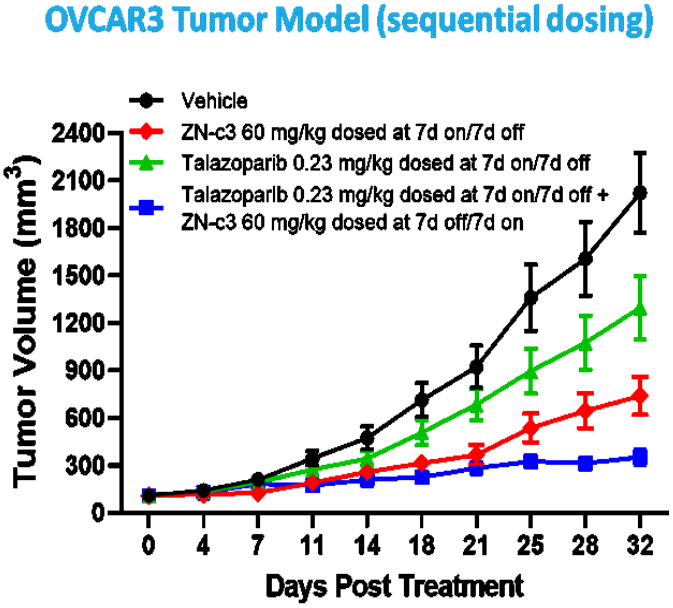


Anti-Tumor Activity in an Ovarian Cancer Models

The anti-tumor activity of ZN-c3 alone and in combination with carboplatin was assessed in the preclinical ovarian cancer model TOV21G. ZN-c3 was dosed at 60 mg/kg QD, po; carboplatin was dosed at 50 mg/kg, QW, ip and the combination of ZN-c3 and carboplatin was dosed following the same dosing schedule for each single agent, respectively. The combination treatment resulted in better anti-tumor effect than each monotherapy treatment (ZN-c3 and gemcitabine) alone.

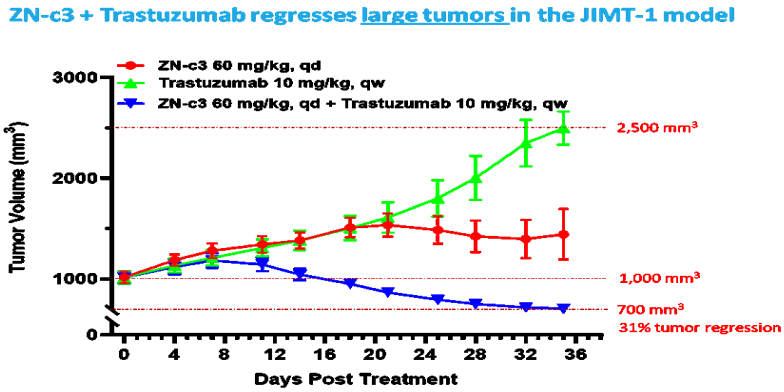


The anti-tumor activity of ZN-c3 alone and in combination with talazoparib was assessed in the preclinical ovarian cancer model OVCAR3. ZN-c3 was dosed at 60 mg/kg QD, seven days on, seven days off, po; talazoparib was dosed at 0.23 mg/kg, QD, seven days on, seven days off, po and the combination of ZN-c3 and talazoparib was dosed following the same dosing schedule for each single agent, respectively. The combination treatment resulted in better anti-tumor effect than each monotherapy treatment (ZN-c3 and talazoparib) alone.



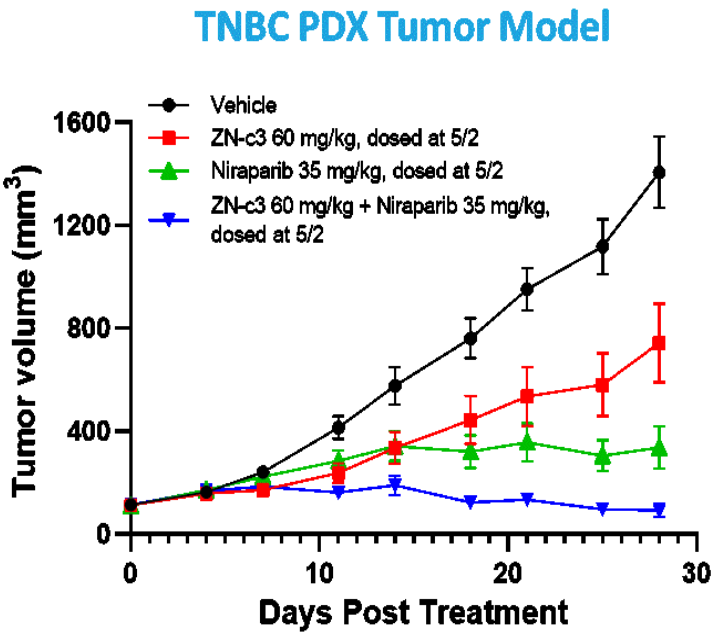
Anti-Tumor Activity in a Breast Cancer Model

The anti-tumor activity of ZN-c3 alone and in combination with trastuzumab was assessed in the preclinical breast cancer model JIMT-1. This model originated from a pleural metastasis of a 62-year old patient with breast cancer who was clinically resistant to trastuzumab. ZN-c3 was dosed at 60 mg/kg QD, po; trastuzumab was dosed at 10 mg/kg, QW, ip and the combination of ZN-c3 and trastuzumab was dosed following the same dosing schedule for each single agent, respectively. Treatment started when tumors reached 1000 mm^3. The combination treatment resulted in better anti-tumor effect than each monotherapy treatment (ZN-c3 and trastuzumab) alone.



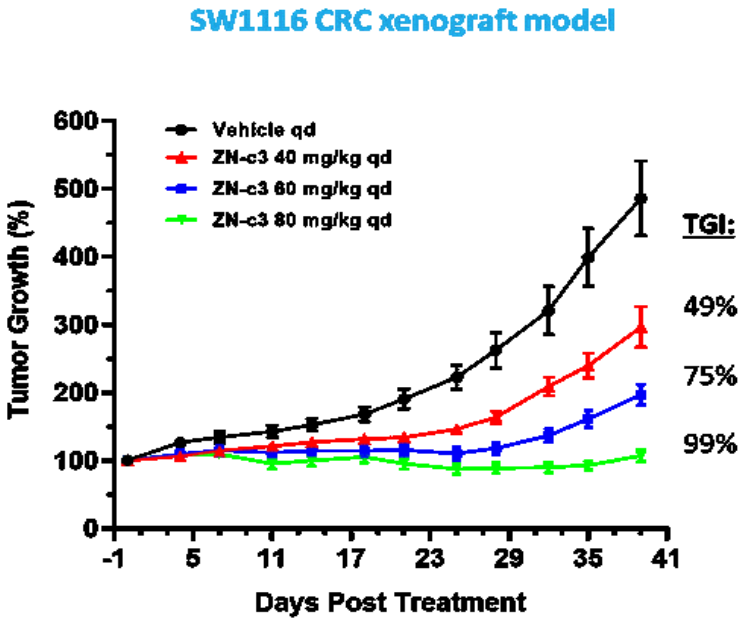
The anti-tumor activity of ZN-c3 alone and in combination with niraparib was assessed in the preclinical triple negative breast cancer (TNBC) patient derived xenograft (PDX). ZN-c3 was dosed at 60 mg/kg QD, five days on, two days off, po; niraparib was dosed at 35 mg/kg, QD, five days on, two days off, po and the combination of ZN-c3 and niraparib was dosed

following the same dosing schedule for each single agent, respectively. The combination treatment resulted in better anti-tumor effect than each monotherapy treatment (ZN-c3 and niraparib) alone.

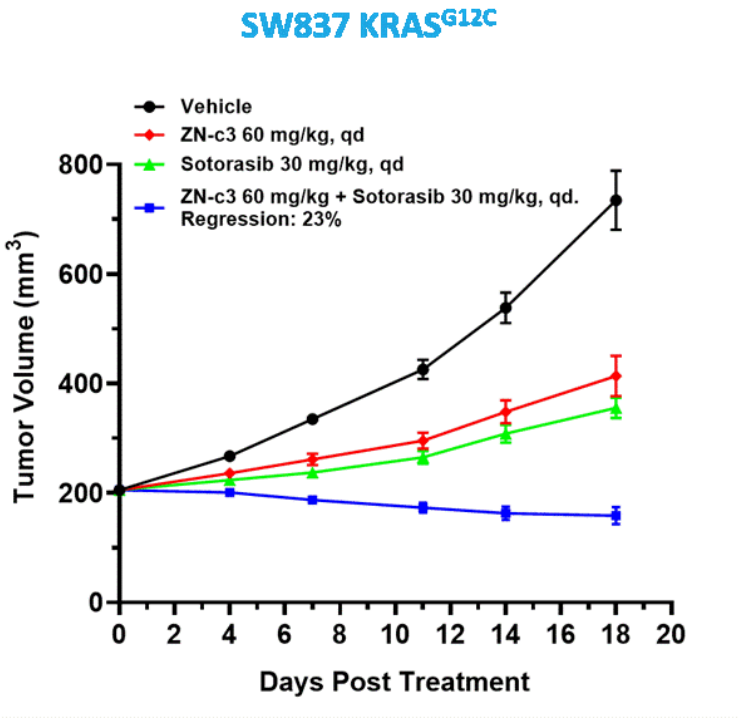


Anti-Tumor Activity in a Colon Cancer Models

The anti-tumor activity of ZN-c3 was assessed in the preclinical colon cancer model SW1116. ZN-c3 was dosed at 40, 60 and 80 mg/kg QD, po. A robust anti-tumor activity was observed.



The anti-tumor activity of ZN-c3 alone and in combination with the $KRAS^{G12C}$ inhibitor sotorasib was assessed in the preclinical colon cancer SW837 model. The SW837 model contains a $KRAS^{G12C}$ mutation. ZN-c3 was dosed at 60 mg/kg QD, po; Sotorasib was dosed at 30 mg/kg, QD, po and the combination of ZN-c3 and sotorasib was dosed following the same dosing schedule for each single agent, respectively. The combination treatment resulted in better anti-tumor effect than each monotherapy treatment (ZN-c3 and $KRAS^{G12C}$) alone.



Toxicology Results

ZN-c3 was evaluated in 28-day repeat dose toxicology studies. Results of these studies showed many of the toxicities associated with other Wee1 inhibitors in development, including those reported for adavosertib.

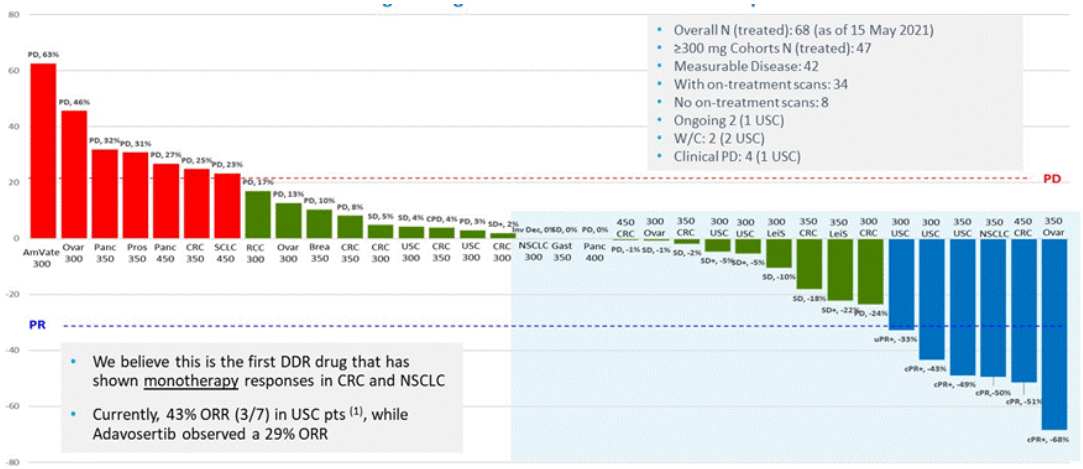
ZN-c3 Interim Clinical Results

On June 28, 2021, we announced clinical and regulatory updates across our pipeline of product candidates, including new interim clinical data from the Phase 1 clinical trial of ZN-c3. Interim data results from the Phase 1 monotherapy trial of ZN-c3 as of a data cut-off date of May 15, 2021 are as follows:

Two unconfirmed Partial Responses, or PRs, previously reported at AACR were confirmed, bringing the total number of confirmed PRs from the ongoing Phase 1 monotherapy trial from three to five. Since reporting initial clinical data at AACR, an additional unconfirmed PR was reported in a patient with USC, resulting in three out of seven USC patients evaluable having responded to treatment. Overall, the objective response rate, or ORR, increased from 40% to 43% based on RECIST criteria. Clinical results were seen across four different tumor types, signaling potential for broad oncology application.

Within the exceptional responder population of the ongoing Phase 1 monotherapy trial, in a patient with an ongoing treatment duration of more than eight months, the Company observed a deepening response of 65% to 69% tumor size decrease based on RECIST criteria. In addition, as of a data cut-off date of May 14, 2021, ZN-c3 was observed to be well-tolerated, with a lower overall rate of severe hematological adverse events relative to the rate previously reported at AACR with respect to the previous data cut-off date of February 12, 2021. The rate of treatment related white blood cell count decrease, or neutropenia, decreased to 2.2% as of the May 14, 2021 data cut-off date from 3.6% as of the February 12, 2021 data cut-off date.

ZN-c3 Dose Escalation and Expansion Study – 300 mg QD and Above Dose Cohorts
Best % Change in Target Lesion Size and Best Overall Response



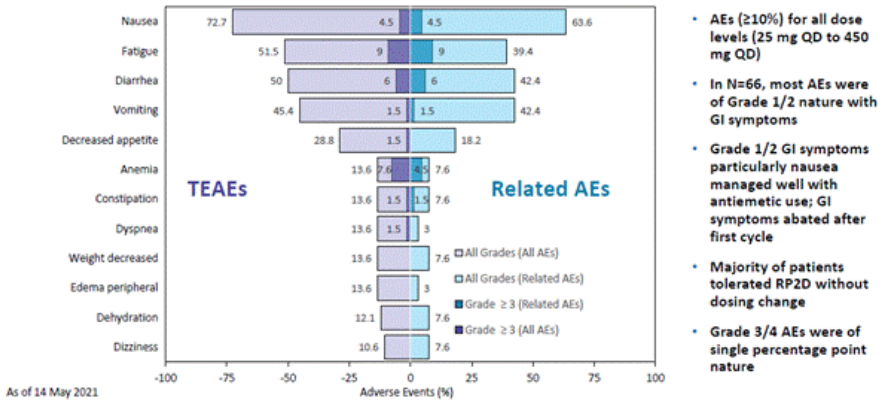
Notes:
3 subjects with no treatment scans (CPC. USC, Pancreas), and experienced clinical progressive disease (CPD) + denotes treatment ongoing Waterfall as of 05/15/2021; both uPRs reported at AACR 2021 in USC are confirmed PRs. Newly reported uPR in USC is included. ORRR based on radiographic responses.

Interim data is subject to change as more data on these patients and additional patients become available and are subject to audit and verification procedures that could result in material changes in the final data.

Safety Results

As of the May 14, 2021 database cutoff, in the ongoing ZN-c3 Phase 1/2 trial in advanced solid tumors, a total of 66 patients were enrolled and had data available in the electronic data capture system. Patients were treated at the following dose levels: 21 at ≤ 200 mg/day, 18 at 300 mg/day and 27 at ≥ 350 mg/day. Enrollment in the Phase 1, monotherapy, dose-escalation portion of this trial was concluded; the maximum tolerated dose, or MTD, was determined to be 350 mg once daily, or QD, and the Recommended Phase 2 dose, or RP2D, was determined to be 300 mg QD. The dose expansion portion of this trial is ongoing.

As of the May 14, 2021, database cutoff in the ongoing Phase 1/2 trial in advanced solid tumors we reported on June 28, 2021, Treatment-emergent adverse events, or TEAEs, and Investigator assessed treatment-related adverse events, or TRAEs, in 65 of 66 and 58 out of 66 patients, respectively, at dose levels from 25mg qd to 450mg qd. Most AEs were of grade 1 and 2, and grade 3 and grade 4 events were of single digit percentage points.



ZN-c3 Pharmacokinetics Results

Following oral administration to cancer patients on the empty stomach, ZN-c3 was absorbed with a median Tmax of 1-4 hours. The peak plasma concentration, or Cmax, and daily exposure, or AUC0-24h, were highly variable and generally increased with escalating doses up to 300 mg. Cmax and AUC appear to reach plateau at daily doses above 300 mg. Based on available data at the RP2D 300 mg QD, the mean ZN-c3 steady-state AUC0-24h was 11,000 ng*h/mL with CV of 52%.

Pharmacodynamic data will be collected in subsequent patients and will be reported in the future.

ZN-c5, an Oral SERD for the Treatment of ER+/HER2- Breast Cancer

Overview

We are developing ZN-c5, an oral, small molecule product candidate targeting the estrogen receptor, or ER, a key driver of tumor growth and survival in ER+/HER2- breast cancer. These tumors are currently treated by a number of hormonal therapies; however, in contrast to most ER binders that simply block or modulate ER activity, ZN-c5 is also designed to cause degradation of the ER. As such, ZN-c5 is known as a selective ER degrader, or SERD. Fulvestrant, marketed as Faslodex® by AstraZeneca, is currently the only FDA-approved SERD. While effective, fulvestrant is limited to its FDA-approved dosing regimen of two painful 5 mL concomitant monthly intramuscular injections, thus restricting the level of ER degradation that can be induced in patients, which we believe limits its efficacy. We have applied our expertise to design ZN-c5 as an oral potent SERD with characteristics which we believe may result in a differentiated product profile. We believe ZN-c5, if approved, has the potential to be used as monotherapy and in combinations and could become the standard of care for hormonal therapy in the treatment of all lines of ER+/HER2- breast cancer.

We are currently conducting a Phase 1/2 clinical trial of ZN-c5 in patients with ER+/HER2- advanced or metastatic breast cancer. ER+/HER2- breast cancer affects approximately 70% of all breast cancer patients in the United States. We continue to enroll patients and collect data for ZN-c5 administered as monotherapy and in combination with palbociclib as part of a clinical research collaboration with Pfizer. Palbociclib, marketed as Ibrance®, is a CDK4/6 inhibitor that is FDA approved for the treatment of ER+/HER2- advanced or metastatic breast cancer in combination with hormonal therapies, such as fulvestrant. In addition, in November 2020, we initiated a Phase 1b open label, multi-center trial evaluating ZN-c5 in combination with abemaciclib in patients with ER+/HER2- advanced or metastatic breast cancer as part of a clinical research collaboration with Lilly. Abemaciclib, marketed as Verzenio®, is a CDK4/6 inhibitor that is FDA approved for the treatment of HR+/HER2- advanced or metastatic breast cancer in combination with fulvestrant, aromatase inhibitors or as a single agent in certain patients with disease progression following treatment with prior endocrine therapy or chemotherapy regimens. We maintain full ownership of ZN-c5 in each collaboration.

We intend to initiate a Phase 1b combination trial of ZN-c5 and ZN-c3 in CDK4/6i resistant breast cancer in 2022.

Background on Breast Cancer and Current Treatments

Breast cancer is the most prevalent cancer in women, accounting for 30% of all female cancers and 13% of cancer-related deaths in the United States. The National Cancer Institute estimated that approximately 275,000 new cases of breast cancer would be diagnosed in the United States in 2020, and approximately 42,000 breast cancer patients would die of the disease.

Most breast cancer tumor growth is dependent on two main protein receptors: estrogen receptor and human epidermal growth factor receptor 2. Approximately 70% of breast cancers in the United States are ER+/HER2-, meaning that they express ER and not HER2, and therefore depend on estrogen signaling for tumor growth and survival. These ER+ tumors are sometimes referred to as hormone receptor positive, or HR+ tumors, and are currently treated using several approaches:

- by blocking receptor function with selective ER modulators, or SERMs;
- by blocking the synthesis of hormones, such as estrogen, with aromatase inhibitors, or AIs; or
- by degrading, and thus potentially eliminating ER receptors with a drug in the SERD class.

AIs have demonstrated superior clinical benefit to SERMs, including tamoxifen, and SERDs have demonstrated superior clinical benefit to AIs.

FDA-Approved SERD, Fulvestrant and its Limitations

Currently, fulvestrant is the only FDA-approved SERD. Fulvestrant, marketed as Faslodex® by AstraZeneca, is FDA-approved for first and second-line treatment for women with HR+/HER2- advanced breast cancer both as monotherapy and as combination therapy with a number of other drug classes. Fulvestrant has demonstrated improved efficacy relative to AIs. In a randomized double-blind, placebo-controlled trial in treatment of naïve advanced and metastatic breast cancer patients, treatment with 500 mg of fulvestrant resulted in median progression free survival, or PFS, of 16.6 months versus 13.8 months for anastrozole, an FDA-approved oral AI marketed as Arimidex® by ANI Pharmaceuticals. However, fulvestrant has a number of pharmacological characteristics that require it to be delivered via two painful 5 mL concomitant monthly intramuscular injections, which we believe may limit its efficacy and tolerability. Despite these limitations, AstraZeneca reported worldwide sales of Faslodex® of over $1.0 billion in 2018, the last year prior to generic competition.

Our SERD Solution: ZN-c5

We believe a conveniently administered oral SERD with superior efficacy could be indicated for monotherapy or in combinations and could become the standard of care for hormonal therapy in the treatment of all lines of ER+/HER2- breast cancer.

ZN-c5 is our oral SERD product candidate, which we believe has the potential to overcome limitations of existing hormonal therapies in the treatment of ER+/HER2- breast cancer due to the following observed preclinical and clinical results:

- ***Potency and Selectivity***. In our *in vitro* preclinical studies, we observed the potency of ZN-c5 as measured by proliferation inhibition and degradation of ERα, and that the combination of ZN-c5 and palbociclib was associated with meaningful shrinkage in MCF-7 tumors. In addition, ZN-c5 has exhibited no agonist effect on uterus in animal models which, if present, may compromise its anti-tumor activity.
- ***Preclinical anti-tumor activity***. In preclinical studies, ZN-c5 demonstrated anti-tumor activity in multiple breast cancer xenograft models in mice, both as monotherapy and in combination with CDK4/6 inhibitors and PI3Ka inhibitors, as well as superior tumor growth inhibition when compared to fulvestrant. In addition, in preclinical studies ZN-c5 administered in combination with BCL-2 inhibitors, including our BCL-2 inhibitor product candidate, ZN-d5, demonstrated increased anti-tumor activity as compared to ZN-c5 as monotherapy.
- ***Preliminary Clinical Activity***. As of the database cutoff date of September 15, 2021, two patients in the Phase 1, monotherapy dose expansion portion of the Phase 1/2 trial, one each at the 150 mg/day and 300 mg/day dose levels, had met the definition of a confirmed partial response, or PR, per RECISTv1.1 criteria. In addition, as of such date, the clinical benefit rate (CBR = PR + SD ≥ 24 weeks) was 38%.
- ***PK characteristics***. In preclinical and clinical studies to date, oral dosing of ZN-c5 has shown high exposure levels.

- ***Tolerability profile***. In preclinical studies, ZN-c5 was well tolerated in one-month repeat dose toxicology studies. In addition, based on results from our Phase 1/2 clinical trial as of the database cutoff date of September 15, 2021, no dose-limiting toxicities have been reported.

- ***Safety profile***. In clinical studies to date, ZN-c5 has demonstrated a favorable tolerability profile, which we believe may be an important differentiating factor for patients who require longer term dosing, particularly patients with earlier stage disease.

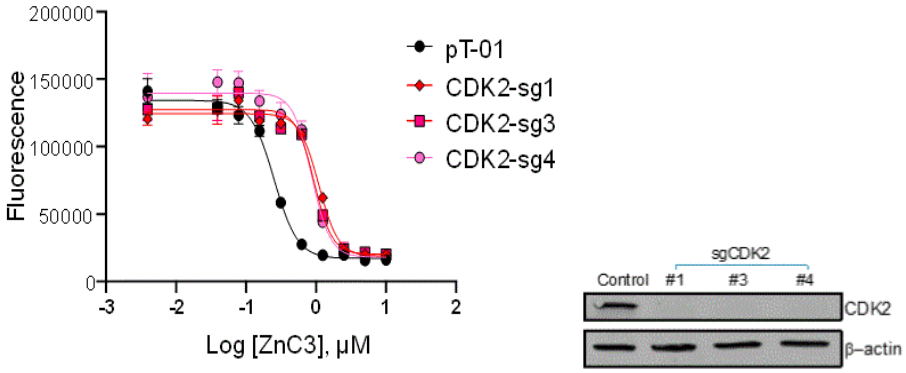
- ***Convenience of administration***. ZN-c5 was designed to be a once-daily oral drug. If approved, we believe this would provide patient convenience and the potential for an all oral dosing regimen as monotherapy and in combination with CDK4/6 inhibitors and other oral targeted therapies.

In our Phase 1/2 clinical trial, we are evaluating the potential of ZN-c5 as monotherapy and in combination with palbociclib, a CDK4/6 inhibitor, as part of a clinical development collaboration with Pfizer. In addition, we initiated a Phase 1b clinical trial evaluating ZN-c5 in combination with abemaciclib as part of a clinical collaboration with Lilly in November 2020, and we plan to initiate a Phase 1b clinical trial evaluating ZN-c5 in combination with ZN-c3 in CDK4/6i resistant breast cancer patients in 2022.

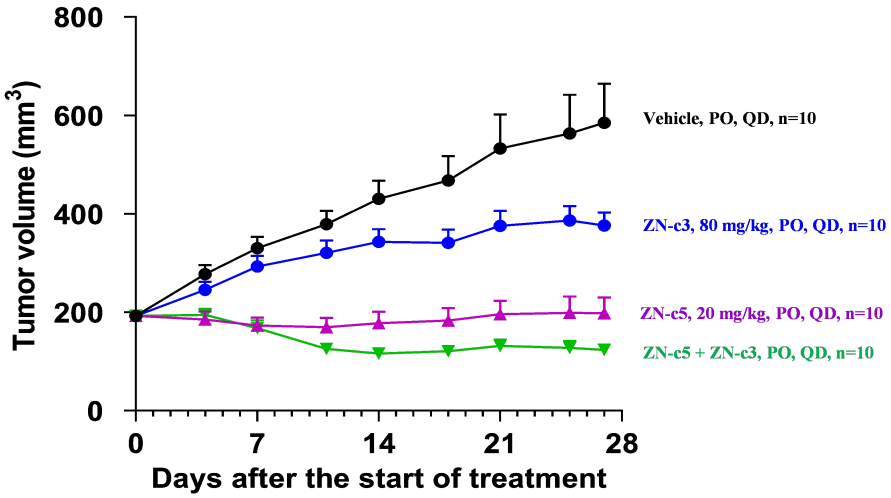
Preclinical Results

Rationale for Combining ZN-c5 with our Wee1 Inhibitor and Anti-tumor Activity in an ER+/HER2- Breast Cancer Model

Current treatment options for ER+/HER2- breast cancer include treatment with CDK4/6 inhibitors, or CDK4/6i, as a single agent and in combination with anti-estrogen treatments, including fulvestrant. However, resistance to CDK4/6i's frequently develops over time through a variety of proposed mechanisms, including but not limited to CDK2 activation due to CCNE1 and/or CDK2 overexpression, loss of RB1, MDM2 overexpression, and WEE1 overexpression. Many of these resistance mechanisms lead to abrogation of the G1/S cell cycle checkpoint, and thus counter the effect of CDK4/6i, i.e., cell cycle blockade at the G1/S checkpoint. Because of this, cancer cells become more reliant on the G2/M checkpoint of the cell cycle to allow for repair of any possible DNA damage before cell division. Wee1 is a tyrosine kinase that controls the G2/M checkpoint, and its inhibition by ZN-c3, our Wee1 inhibitor, leads to abrogation of the G2/M checkpoint, leading to DNA damage due to unchecked replication and apoptosis in cancer cells, thereby preventing tumor growth and potentially causing tumor regression. Interestingly, CRISPR-mediated knockout of CDK2 in cancer cells suggests that expression of CDK2 is associated with increased sensitivity to Wee1 inhibition by ZN-c3. As an example, the figure below shows that 3 different A427 lung cancer cell clones with loss of CDK2 expression, known as CDK2-sg1, 3, and 4, have reduced sensitivity to ZN-c3 in a cell proliferation assay as compared with the original cell line that expresses CDK2, or pT-01.

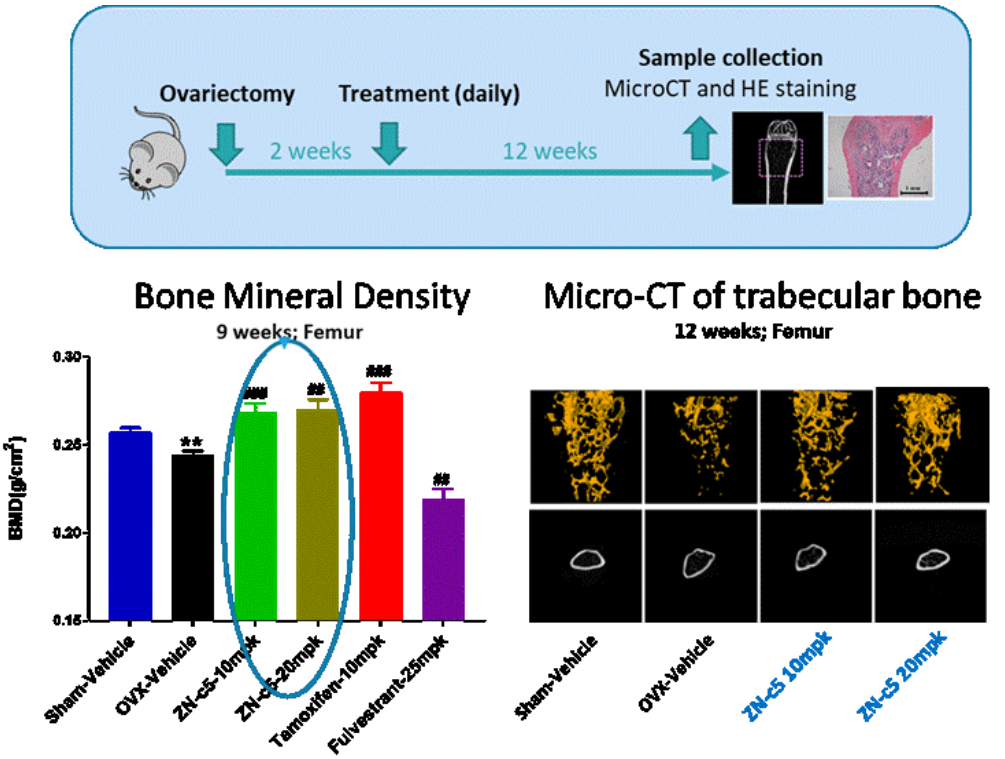


Taken together, these observations led us to investigate the potential for combining ZN-c5 with our Wee1 inhibitor, ZN-c3. In a preclinical study, we assessed the anti-tumor activity of ZN-c5, both as monotherapy and in combination with ZN-c3, in the ER+/HER2- T47D breast cancer xenograft model. As shown in the graph below, the combination of ZN-c5 dosed daily at 20 mg/kg plus ZN-c3 dosed daily at 80 mg/kg had greater anti-tumor activity than ZN-c5 as monotherapy.



ZN-c5 has bone protective effects in a mouse osteoporosis model

Loss of estrogen is associated with osteoporosis in post-menopausal women, and therefore, treatment of female breast cancer patients with a SERD may have similar effects or further aggravate this condition. In addition, patients with advanced breast cancer often suffer from osteolytic bone metastasis. For this reason, we tested our SERD, ZN-c5, in a mouse model of osteoporosis using ovariectomized mice. The schematic of the study is shown in the figure below. In brief, ovariectomized mice were treated with 10 and 20 mg/kg ZN-c5 daily for 12 weeks. Bone mineral density, BMD was measured weekly starting at week 7, and at the end of the study, femurs and tibiae were analyzed using micro computed tomography scans, or micro-CT. As shown in the figure below (bottom, left), ovariectomy, or OVX, led to a reduction in BMD. Interestingly, this loss in BMD was negated by ZN-c5 treatment, and in fact, we observed a significant increase in BMD in mice treated with ZN-c5 as compared to non-ovariectomized mice (Sham-vehicle). Micro-CT scans of the isolated bones (bottom, right figure) showed a significant loss of trabecular bone in OVX control mice (OVX-vehicle). Treatment with ZN-c5 resulted in a dose-dependent reversal of this trabecular bone loss. Taken together, this surprising result suggests that ZN-c5 has bone protective effects.



p < 0.05, **p < 0.01, ***p < 0.001, analyzed by unpaired t-test. All data are presented as mean ± SEM.
**** Compared with sham-vehicle group; # Compared with OVX-vehicle group***

Clinical Results

As of September 15, 2021, we had enrolled 56 patients in the Phase 1, monotherapy portion of this trial, at the following dose levels: 50 mg QD (N=16), 75 mg QD (N=3), 100 mg QD (N=3), 75 mg BID (N=6), 150 mg QD (N=15), 150 mg BID (N=3) and 300 mg QD (N=10). All patients were female, with a median age of 58.5 years (ranging from 38 to 89 years) and an Eastern Cooperative Oncology Group, or ECOG, performance status, a measurement of a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability, of 0 (n = 30) or 1 (n = 25) and not known (n=1).

The median number of prior therapies for advanced disease was two (ranging from zero to nine). 26 of the 56 patients, or 46%, received prior treatment with fulvestrant, and 39, or 70%, received prior therapy with a CDK 4/6 inhibitor. Enrollment in the Phase 1 monotherapy dose escalation portion of this trial has been completed.

As of September 15, 2021, we had enrolled 50 patients in the Phase 1, combination dose escalation portion of this trial, ten patients at the ZN-c5 dose level of 25 mg QD, five at 25 mg BID, 18 at 50 mg QD, two at 50 mg BID, twelve at 100 mg QD, and three at 150 mg QD. 49 patients were female, and one was male, with a median age of 63 years (ranging from 35 to 79 years) and an ECOG performance status of zero (n = 20), one (n = 29) or two (n = 1). The median number of prior therapies for advanced disease was one, with a range from zero to six. 19 of the 50 patients received prior treatments with fulvestrant. Of these 50 patients, 19 are still on treatment and 31 discontinued due to disease progression (n = 24), patient discretion (n=4), investigator discretion (n = 2), and due to intercurrent illness (n=1). Enrollment in the Phase 1, combination dose escalation portion of this trial is ongoing, and a total of up to 62 patients may be enrolled.

Safety Results

Phase 1, Monotherapy Dose Escalation and Monotherapy Dose Expansion

Based on the results as of the database cutoff date of September 15, 2021 for the Phase 1, monotherapy dose escalation and monotherapy dose expansion portions of this trial, ZN-c5 has been observed to be well tolerated with no dose-limiting toxicities reported.

In the Phase 1 monotherapy portion of this trial, a total of 56 patients were enrolled and dosed, with data available in the electronic data capture system as of the September 15, 2021 database cutoff. TEAEs occurred in 54 of the 56 patients, or 96%. Nausea was observed in 17 patients, or 30%; fatigue in 15 patients, or 27%; and hot flush in eight patients, or 15%. Grade 3 TEAEs occurring in ≥ 2 subjects included abdominal pain, hypertension, hyponatremia, pain in extremity (n = 2 each), and gamma-glutamyl transferase (GGT) increase (n = 3). Of these, only 1 TEAE each of abdominal pain and GGT increase were deemed related to ZN-c5. Grade 4 events were not reported.

33 of 56 subjects, or 59%, experienced at least one ZN-c5 TRAE, mainly of Grade 1 or 2 in severity. Grade 3 TRAEs were hypersensitivity, abdominal pain, GGT increase, and dyspnea (n = 1 each). Grade 1 or 2 TRAEs included diarrhea (4%) and nausea (14%). Only one subject had a ZN-c5 dose reduction, due to GGT increase. There were no deaths reported.

Overall, in the Phase 1, monotherapy dose escalation and monotherapy dose expansion portions of the trial, there was no observed increase in severity of adverse events with increasing dosing levels.

Phase 1, Combination Dose Escalation

As of the May 11, 2021 database cutoff date, ZN-c5 in combination with palbociclib was observed to be well tolerated with no dose-limiting toxicities reported. Based on these safety results, we are continuing to enroll patients in ZN-c5 in combination with palbociclib.

Investigator assessed TRAEs to ZN-c5 occurred in 20 of the 41 patients dosed and were all at most, grade 2 in severity. TRAEs with incidence >10% included: hot flush (n = 6), and arthralgia (n = 4).

Investigator assessed TRAEs to palbociclib occurred in 40 of the 41 patients dosed. Adverse events with incidence >10% included: neutrophil count decreased (n = 28), white blood cell count decreased (n = 27), anemia (n = 14), lymphocyte count decreased (n = 12), fatigue (n = 10), platelet count decreased (n = 9), nausea (n = 5), hot flush (n = 4), and arthralgia (n = 4). TRAEs of grade 3 events included: neutrophil count decreased (n = 12), white blood cell count decreased (n = 6), and lymphocyte count decreased (n = 3); there was only one grade 4 lymphocyte count decreased event.

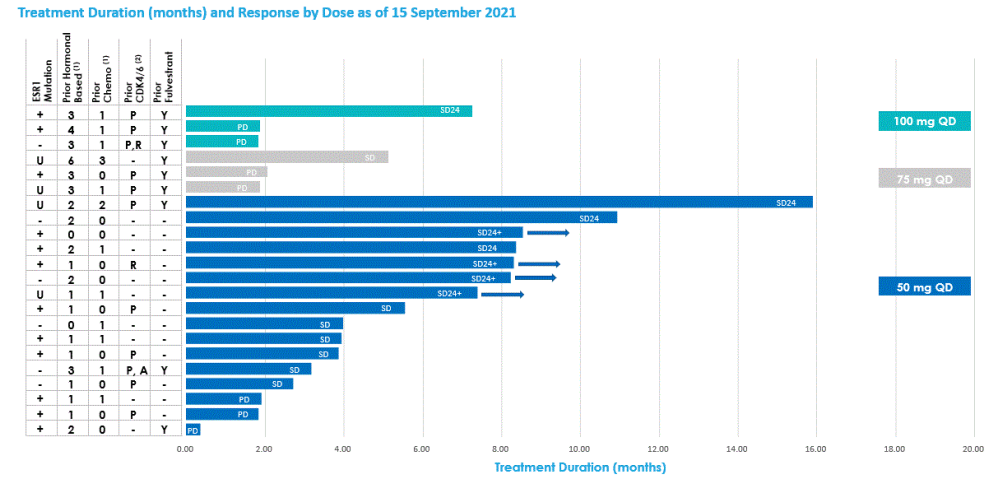
Efficacy Results

Clinical activity in the Phase 1 trial is determined by the CBR, which is the total number or percentage of patients who achieved a CR, PR, or stable disease, or SD, for 24 weeks or longer per RECIST v1.1 criteria.

ZN-c5 achieved a best response of confirmed PR (as per RECIST) in two of 41 subjects, or 5%, with measurable disease. The clinical benefit rate (CBR = PR + SD ≥ 24 weeks) was 38%. In addition, the median progression-free survival (PFS) was 3.8 months (95% CI,3.5-5.4).

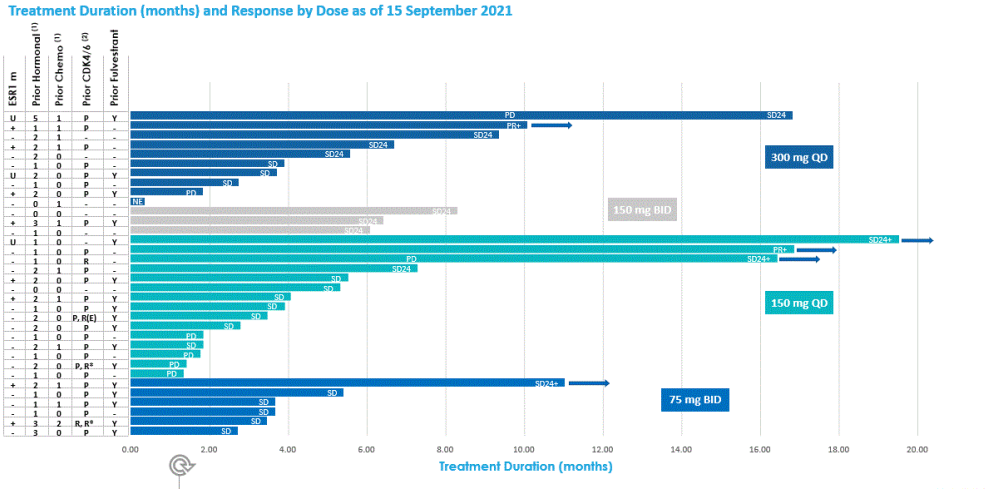
The following figures illustrate treatment duration and best overall response for the Phase 1, monotherapy dose escalation portion of the trial as of the database cutoff date of September 15, 2021.

Updated Interim Clinical Data: ZN-c5-001 Monotherapy 50-100 mg



(1) Number of treatments reflect advanced or metastatic setting, not neo/adjuvant; also reflect combinations with targeted therapies CDK4/6, mTOR, PI3Ki
(2) P-palbociclib, A-abemaciclib, R-ribociclib, E-experimental treatment (could be placebo)
+ ESR1 mutation detected
U Unknown

Updated Interim Clinical Data: ZN-c5-001 Monotherapy 150-300 mg



(1) Number of treatments reflect advanced or metastatic setting, not neo/adjuvant; also reflect combinations with targeted therapies CDK4/6, mTOR, PI3Ki
(2) P-palbociclib, A-abemaciclib, R-ribociclib, E-experimental treatment (could be placebo)
+ ESR1 mutation detected
U Unknown

ZN-c5 Pharmacokinetics Results

PK analyses were conducted for 54 of 56 subjects, or 96%, in fasted conditions during Cycle 1 of the Phase 1 monotherapy dose escalation and expansion. (Table 4)

The preliminary PK was characterized by fast absorption with median Tmax values of 1 to 2 hrs. The exposures were approximately dose-proportional at the dose levels of 50 to 100 mg and less than dose-proportional between 100 and 300 mg. No accumulation of ZN-c5 was observed after 15 days of QD dosing.

Preliminary Pharmacokinetic Data for ZN-c5 Monotherapy

ZN-c5 monotherapy was administered at doses 50–300 mg QD or 75–150 mg BID. ZN-c5 is absorbed with median Tmax of 2–4 hours, independent of dose level. Exposure and Cmax on Day 1 and Day 15 were less than dose proportional. No significant accumulation in exposure was observed for doses up to 100 mg.

Table 4. Preliminary Pharmacokinetic Data for ZN-c5 (Mean ± SD)

Dose and Number of Subject (Day1/Day15)	Day 1			Day 15			Day 15/ Day 1 AUC Ratio
	C_{max} (ng/mL	T_{max}* (hr)	AUC_{0-24hr} (ng•h/mL	C_{max} (ng/mL	T_{max}* (hr)	AUC_{0-24hr} (ng•h/mL	
50 mg (N = 16/14)	5,790 ± 1,260	2 (0.5-4)	75,700 ± 20,800	5,270 ± 803	1 (1-4)	64,300 ± 13,800	0.88 ± 0.22
75 mg (N = 3/3)	6,700 ± 4,080	2 (1-4)	77,300 ± 47,800	6,700 ± 1,040	2 (1-2)	64,400 ± 16,000	1.1 ± 0.66
100 mg (N = 3/3)	7,120 ± 2,550	4 (2-6)	103,000 ± 42,100	9,250 ± 5,350	2 (1-2)	107,000 ± 75,700	0.97 ± 0.31
150 mg (N = 15/13)	10,100 ± 2,530	2 (1-6)	129,000 ± 29,600	9,320 ± 2,880	2 (1-8)	110,000 ± 28,700	0.86 ± 0.22
75 mg BID† (150 mg/day) (N = 4/4)	7,800 ± 3,200	1.5 (1-2)	NA	7,360 ± 3,030	2 (1-2)	101,000 ± 29,900	NA
300 mg (N = 10/9)	13,600 ± 5,380	3 (2-6)	192,000 ± 81,800	11,500 ± 4,570	2 (2-6)	126,000 ± 36,700	0.68 ± 0.11
150 mg BID† (300 mg/day) (N = 3/3)	10,100 ± 3,320	2 (1-2)	NA	8,170 ± 1,430	2 (2-2)	127,000 ± 30,800	NA

*Tmax: median and range
AUC 0-24hr on Day 15 estimated as 2xAUC 0-12 hr

ZN-c5 human drug exposure at all dose levels, ranging from 50 mg to 300 mg, exceeds the ZN-c5 effective concentration, 100%, or EC100, observed in our preclinical mouse studies at 10 mg/kg/day, the dose level associated with a 100% tumor growth inhibition in an MCF-7 mouse model. Based on the activity observed in mouse models, the exposures observed in human patients may translate into once daily, oral dosing.

Phase 1b Trial of ZN-c5 in combination with abemaciclib

In November 2020, we dosed the first patient in our Phase 1b open label, multi-center trial of ZN-c5 in combination with abemaciclib in patients with ER+/HER2- advanced or metastatic breast cancer, which we refer to as our ZN-c5-003 Trial. This trial aims to assess the safety, tolerability, PK, pharmacodynamics, and anti-tumor activity of ZN-c5 in combination with abemaciclib. The ZN-c5-003 Trial will be conducted at several sites in the United States and Europe. We plan to enroll approximately 18 patients in this trial.

Phase 1b Trial of ZN-c5 in combination with ZN-c3

In December 2021 at our R&D Day, we announced our intent to initiate a Phase 1b combination trial of ZN-c5 with ZN-c3 in CDK4/6i resistant breast cancer in 2022. This trial aims to assess the safety, tolerability, PK, pharmacodynamics, and anti-tumor activity of ZN-c5 in combination with ZN-c3. This trial will be conducted at several sites in the United States and Europe. We plan to enroll approximately 18 patients in this trial.

ZN-d5, an Inhibitor of BCL-2 for the Treatment of Hematologic Cancers

Overview

We are developing ZN-d5, an oral selective inhibitor of BCL-2, an intracellular protein that suppresses apoptosis for the treatment of cancers, with an initial focus on hematologic malignancies. We have applied our expertise to design ZN-d5 as an oral BCL-2 inhibitor and to have optimized potency, selectivity and PK.

We began enrolling subjects in a Phase 1 clinical trial evaluating ZN-d5 in patients with relapsed or refractory NHL and AML, in October 2020. This trial initially enrolled subjects with NHL and enrollment of subjects with AML began in the third quarter of 2021. This dose-escalation study is designed to assess the safety, efficacy and PK of ZN-d5, and to determine the MTD and RP2D in NHL and AML. Based on the unmet medical need, we will initiate a Phase 1 monotherapy clinical trial to evaluate ZN-d5 in patients with relapsed or refractory amyloidosis, in the first quarter of 2022. In 2022, we also intend to initiate a Phase 1/2 clinical trial evaluating ZN-d5 in combination with ZN-c3, our Wee1 inhibitor product candidate, in patients with AML.

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, 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, SLL, AML, 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 will restore the normal apoptosis process in cancer cells. This new cancer therapeutic strategy has been validated through the recent approval of venetoclax.

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 PPIs also makes BCL-2 family proteins difficult targets for small molecule drugs. Currently, venetoclax 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.

Our BCL-2 Inhibitor: ZN-d5

We have designed ZN-d5 to have the following characteristics:

- ***Potency***. In our preclinical studies, ZN-d5 was observed to be potent in cell lines and xenograft models across a variety of hematological malignancies.

- ***Selectivity***. In our *in vitro* studies, ZN-d5 showed more than 600 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. 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 that are associated with a high rate of thrombocytopenia..

- ***Tolerability profile***. In our animal toxicity studies, ZN-d5 was observed to be well tolerated across various dosage levels.

We believe the observed properties of ZN-d5 make it an attractive candidate for evaluation as monotherapy and in combination with other therapies, initially for the treatment of hematological malignancies. As noted above, ZN-d5 is in an ongoing Phase 1 dose escalation study in relapsed and refractory NHL and AML patients. Our plans for 2022 for ZN-d5 include opening enrollment in a Phase 1 study to patients with relapsed or refractory amyloidosis in the first quarter and launching a Phase 1/2 trial in combination with ZN-c3, our Wee1 inhibitor product candidate, in relapsed or refractory AML in the first half of the year.

Preclinical Results

Potency and Selectivity Across Hematological Malignancies

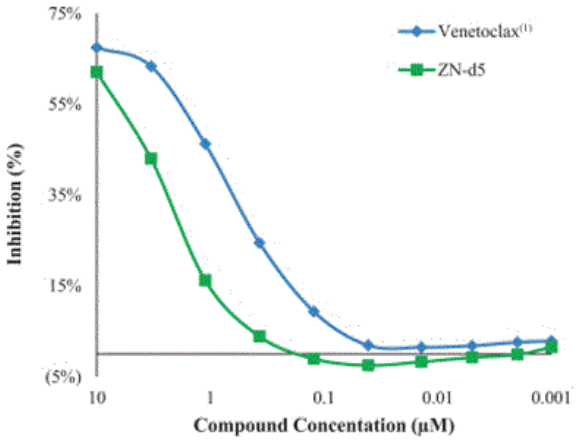
In an in vitro preclinical study, we assessed the selectivity and potency of ZN-d5 alongside venetoclax. As shown in the table below, we assessed the affinity of each agent as measured in nM in a biochemical assay. Based on these measurements, ZN-d5 showed 600 times greater selectivity for BCL-2 than BCL-xL, and we believe such selectivity may limit the incidence of thrombocytopenia observed in third-party clinical trials as a result of BCL-xL inhibition. We also observed that ZN-d5 was potent across hematological malignancy cell lines as measured by CellTiter-Glo, or CTG, a cell viability assay, shown in the table below.

			CTG IC_{50} (nM)						
	AFFINITY (nM)		ALL	MCL	DLBCL		AML		
COMPOUND	BCL-2 Kd	BCL-XL Kd	RS4;11	GRANTA-519	DOHH-2	TOLEDO	HL-60	MOLM-13	M11
Venetoclax[1]	0.41	28	2.9	161	43	191	26	18	
ZN-d5	0.29	190	5.1	89	50	92	21	39	

(1) Data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company commercializing the compound.

In a preclinical study, we also assessed the platelet toxicity of ZN-d5 against venetoclax, as measured by mM in a platelet viability assay. In each assay, ZN-d5 was observed to be less toxic to platelets than venetoclax, which we believe may limit the incidence of thrombocytopenia.

ZN-d5 Toxicity Compared to Venetoclax In *In Vitro* Assay



	CTG IC_{50} (µM)
Venetoclax(1)	0.6
ZN-d5	2.4

Potency for BCL-2 Mutations

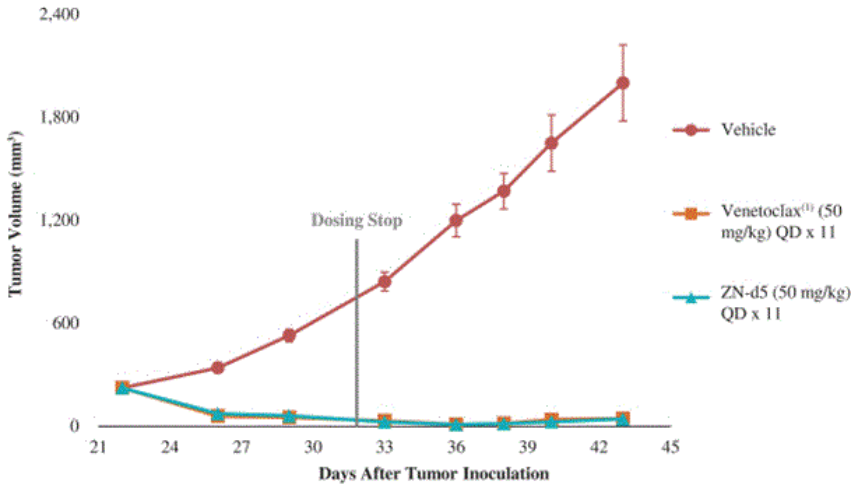
We believe genetic mutations in the BCL-2 gene may be responsible for a developed resistance to venetoclax observed in some CLL patients. In a third-party clinical trial, 16 of 29 patients acquired mutations in members of the BCL-2 family of proteins, 14 of which were a mutation in BCL-2. In nine of those 14 patients, the BCL-2 mutation was detected after 24 months on venetoclax. In an in vitro preclinical study, we assessed the affinity of ZN-d5 alongside venetoclax, to bind to such BCL-2 mutations, as measured in nM. In each assay, ZN-d5 was observed to bind with higher affinity to such BCL-2 mutants as compared to venetoclax.

	IC_{50} (nM) BCL-2 Type			
COMPOUND	**WT**	**G101V**	**F104L**	**D103Y**
Venetoclax(1)	1.3	7.3	8.4	18.3
ZN-d5	1.4	3.7	1.4	5.0

(1) Data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company commercializing the compound.

Anti-Tumor Activity of ZN-d5 in Xenograft Leukemia Model

In a preclinical study, we assessed the anti-tumor activity of ZN-d5, alongside venetoclax. In a RS4;11 xenograft leukemia mouse model, ZN-d5, dosed at 50 mg/kg daily for a period of 11 days, showed potent anti-tumor activity with tumors shrinking upon treatment and yielding durable complete responses after cessation of dosing to the end of the study, as shown in the graphic below. We observed similar results with venetoclax in this model.

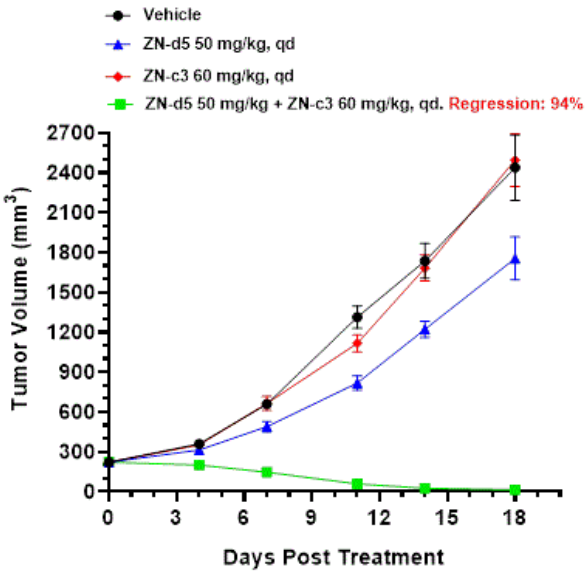


(1) Venetoclax data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company commercializing the compound.

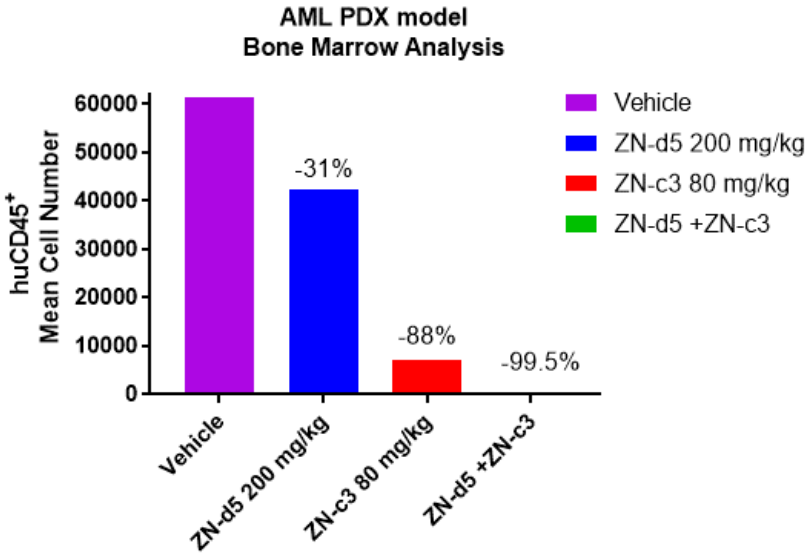
Notes:
QD: Once daily

The Combination of BCL-2 and Wee1 Inhibitors in Several Tumor Models Including AML Model

In a preclinical study, we assessed the anti-tumor activity of a low dose of ZN-d5 alone and in combination with ZN-c3 in the HL-60 xenograft leukemia mouse model. ZN-d5 was dosed at 50 mg/kg QD, p. o., and ZN-c3 was dosed at 60 mg/kg QD, p. o. The combination treatment resulted in better and synergistic anti-tumor effect (94% tumor regression) than each monotherapy treatment.



In a preclinical study, we assessed the anti-tumor activity of ZN-d5 alone and in combination with ZN-c3 in a patient derived model, or PDX, of AML. In this model, human AML cells are injected into mice that had been previously sub-lethally irradiated to allow for the engraftment of the bone marrow by the human cells. ZN-d5 was dosed at 200 mg/kg QD, p. o., and ZN-c3 was dosed at 80 mg/kg QD, p. o. The combination treatment resulted in better anti-tumor effect than each monotherapy treatment as measured by the presence of human $CD45^+$ cells in the mouse bone marrow.



The anti-tumor activity of ZN-d5 combined with ZN-c3 at different doses was tested *in vitro* in samples from patients who had progressed on a venetoclax-based therapy. The combination of ZN-d5 and ZN-c3 was highly active.

Clinical				In vitro (ZN-d5+ZN-c3)	
Patient	Blasts % (before treatment)	Post- Collection Treatment	Blasts % (After Treatment)	ZN-d5/ZN-c3 Treatment (nM)	Blasts % (After Treatment)
3930	93.4	Vidaza/Venetoclax	Residual AML (33% blast) (~2 months post-treatment)	120/500	4.6
3977	62.1	Vidaza/Venetoclax	Residual AML (68% blast) (~2 months post-treatment)	65/100	0
3978	41.1	Gilteritinib/Venetoclax	Residual AML (32% blast) (~1 month post-treatment)	65/500	3.6

Clinical Studies Update

Phase 1 dose escalation study of ZN-d5 in NHL and AML

Our first-in-human Phase 1 dose escalation study of ZN-d5, opened to relapsed or refractory NHL subjects in October 2020 and to relapsed or refractory AML subjects in the third quarter of 2021. As of the database cutoff date of November 3, 2021, 27 subjects had been treated with ZN-d5, including 23 subjects with NHL and 4 with AML.

Preliminary Safety and Clinical Activity Observations

At our R&D Day in December 2021, we reported preliminary interim data from the NHL subjects in this study. As of the November 3, 2021 database cutoff date, ZN-d5 has been well-tolerated, with 74% of the NHL subjects having experienced AEs. Anemia (22%), diarrhea (13%), and nausea and vomiting (9% each) comprise the most commonly experienced AEs. Investigator-reported responses among eleven response-evaluable subjects with diffuse large B-cell lymphoma, according to the Lugano 2014 classification, have included a complete response, a partial response, and two subjects with SD, as of the database cutoff date of November 3, 2021.

Phase 1/2 study of ZN-d5 in AL amyloidosis

In the first quarter of 2022, we will initiate our Phase 1/2 study of ZN-d5 in subjects with relapsed or refractory AL amyloidosis. 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, AL amyloidosis is a difficult and progressive disease that is 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. AL amyloidosis is a rare disease that is often progressive despite multiple lines of therapy, and we believe represents an unmet medical need.

This Phase 1/2 study in amyloidosis consists of a dose-escalation phase to establish the RP2D, and an expansion phase to assess the safety and efficacy of ZN-d5 in this population. The study is expected to enroll up to approximately 140 subjects.

Phase 1/2 study of ZN-d5 and ZN-c3 in AML

In 2022, we plan to initiate a Phase 1/2 combination trial of ZN-d5 with ZN-c3 in AML, based on the mechanism of action for both compounds and strong preclinical proof-of-concept data that suggest the combination may have potent activity in 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 subsequently assessed in several phase 2 expansion cohorts comprising specific AML populations. This study is expected to enroll up to approximately 100 subjects.

ZN-e4, an Inhibitor of EGFR for the Treatment of NSCLC

Overview

We are developing ZN-e4, an irreversible inhibitor of EGFR, a driver of tumorigenesis in lung cancer. We have designed ZN-e4 to be highly selective against mutant EGFR while lacking metabolites that bind potently to the wild-type EGFR, potentially leading to fewer toxicities, including skin rash, compared to drugs that have metabolites that actively bind the wild-type receptor. We believe that eliminating the formation of such a metabolite will allow for a wide therapeutic window. In addition, we believe a more tolerable EGFR inhibitor would, if approved, allow for use in combination with other therapeutics while limiting the toxicity associated with use in combination.

Role of EGFR Inhibition in NSCLC

Lung cancer is the leading cause of cancer death for both men and women, accounting for approximately 18% of all cancer deaths globally in 2020, according to the World Health Organization. There are an estimated 228,000 new cases of lung cancer diagnosed and 143,000 deaths in the United States annually. More than half of the people with lung cancer die within one year of being diagnosed. Non-small cell lung cancer, or NSCLC, accounts for approximately 80-85% of lung cancer cases. EGFR mutations are detected in approximately 10% to 15% and 30% to 40% of Caucasian and Asian patients, respectively, with NSCLC.

EGFR mutations lead to activation of EGFR signaling and oncogenic transformation both in vitro and in vivo. Cancers with EGFR mutations depend on EGFR signaling for growth and survival and are often sensitive to treatment with EGFR inhibitors. Two inhibitors of EGFR were approved in the early 2000s to treat patients with advanced NSCLC based on anti-tumor responses in a subset of patients. These first-generation drugs, erlotinib and gefitinib, were reversible EGFR inhibitors. Although most NSCLC patients with EGFR mutations displayed an initial pronounced response to these first-generation EGFR inhibitors, they acquired resistance to the drugs after approximately nine to 14 months of treatment. The T790M mutation of EGFR was the most common mechanism of such an acquired resistance, having been detected in over 50% of patients treated with EGFR inhibitors.

A second-generation of EGFR inhibitors was developed to address this treatment resistance and to improve upon the efficacy of the first-generation therapies. The second-generation of EGFR inhibitors, including afatinib, marketed as Gilotrif® by Boehringer Ingelheim, and dacomitib, marketed as Vizimpro® by Pfizer, are irreversible inhibitors which covalently bind to EGFR. As such, they are more potent, but are associated with increased toxicity. Further, T790M-mediated acquired resistance occurred at a similar frequency in patients receiving a second-generation therapy as those receiving first generation therapy. Third-generation therapies, such as osimertinib, specifically targeting the T790M mutation have been clinically shown to be a useful strategy in the treatment of NSCLC.

FDA-Approved Third-Generation EGFR Inhibitor, Osimertinib

Osimertinib, which represents the third-generation of EGFR inhibitors, targets EGFR mutations and acquired resistance EGFR mutations such as T790M in order to improve upon the efficacy of previous generations of EGFR inhibitors. In a randomized Phase 3 clinical trial in patients with EGFR-mutated metastatic NSCLC, osimertinib demonstrated a median PFS period of 18.9 months versus 10.2 months for the control arm in which patients received gefitinib or erlotinib. Based on these results, osimertinib was approved by the FDA in November 2015. AstraZeneca reported sales of Tagrisso® of $4.3 billion in 2020, an increase of 36% from 2019 and are expected to grow to $9.5 billion in 2026.

Osimertinib was also designed to have reduced potency against non-mutated, or wild-type, EGFR found in healthy cells, thereby minimizing the toxicities associated with first and second-generation EGFR inhibitors. Despite its observed success in addressing the T790M-mediated acquired resistance and improved efficacy, osimertinib has a similar adverse event profile to first and second-generation EGFR inhibitors. As demonstrated by third-party clinical data, approximately 60% of patients dosed with osimertinib reported rashes compared to 80% of those dosed with gefitinib or erlotinib and a range of 70% to 90% for the second-generation EGFR inhibitor, afatinib. In addition, similar levels of gastrointestinal disorders such as diarrhea were observed in each of the patient populations. Osimertinib also has warnings and precautions regarding interstitial lung disease, QT prolongation, a surrogate marker for the risk of developing tachycardias, cardiomyopathy, keratitis and Stevens-Johnson Syndrome.

We believe one of the major metabolites of osimertinib, AZ5104, which accounts for approximately 9% to 10% of the total drug concentration at clinical doses, may be contributing to these toxicities. In addition, the off-target toxicities are exacerbated by the long half-life of osimertinib.

Our EGFR Solution: ZN-e4

ZN-e4 is our irreversible EGFR inhibitor product candidate which we have designed to potently inhibit mutant EGFR, including the T790M resistance mutation. We have designed ZN-e4 to be highly selective against mutant EGFR and have observed in preclinical studies that the administration of ZN-e4 does not produce a metabolite potent for wild-type EGFR. We have also designed ZN-e4 with improved physical-chemical characteristics, including improved solubility. In a head-to-head preclinical study, ZN-e4 showed greater than 450-fold solubility within 48 hours when compared to osimertinib.

We are conducting a Phase 1/2 clinical trial of ZN-e4 in patients with advanced NSCLC with activating EGFR mutations. Preliminary results from the Phase 1 portion of this trial were presented in December 2021 at our R&D Day.

Preclinical Results

Selectivity Across EGFR Cell Lines

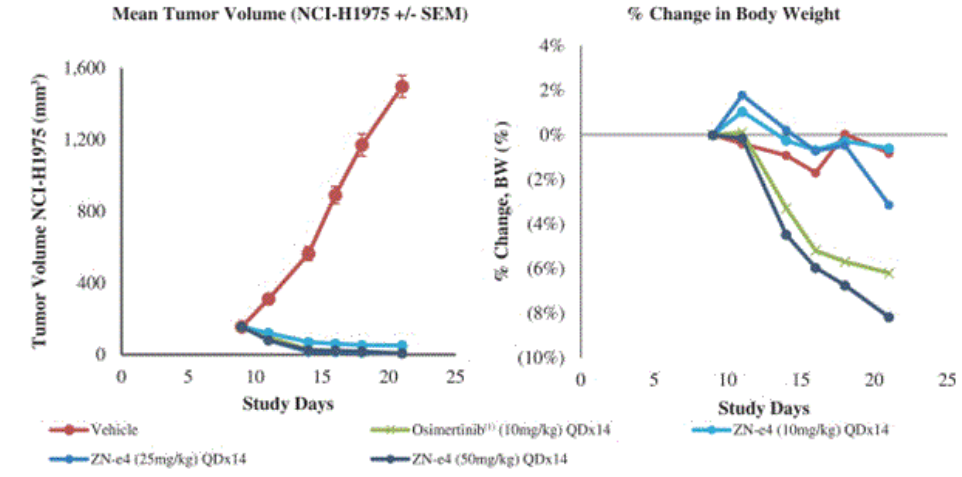
In a preclinical study, we evaluated the potency of ZN-e4 alongside osimertinib against three types of EGFR cell lines –double mutant (DM cell), single mutant (AM cell) and wild-type (WT cell). As shown in the table below, we observed similar potency in the DM and AM cell lines and three times greater selectivity than osimertinib based on the wild-type binding. In addition, we also observed that the administration of ZN-e4 did not produce a metabolite potent for wild type EGFR.

	DOUBLE MUTANT CELL IC_{50} (nM)	SINGLE MUTANT CELL IC_{50} (nM)	WILD-TYPE CELL IC_{50} (nM)
Osimertinib[(1)]: Core Drug	15	29	294
ZN-e4: Core Drug	**20**	**38**	**839**

(1) Osimertinib data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company commercializing the compound.

Anti-tumor Activity, Tolerability and Solubility of ZN-e4

In a preclinical study, we evaluated the anti-tumor activity of ZN-e4 alongside that of osimertinib. In a NCI-H1975 NSCLC tumor model in which there is a double mutation in EGFR, T790M and L858R, oral dosing of ZN-e4 for 14 days at the dose tested, 10 mg/kg, induced complete tumor regression, as did 10 mg/kg osimertinib dosed orally. In addition, ZN-e4 at this dose was well tolerated in these models with no apparent loss in body weight throughout the study. In contrast, the 10 mg/kg dose of osimertinib led to a loss of greater than 8% of total body weight. We observed a similar loss of body weight with ZN-e4 when we increased the dose to 50 mg/kg, roughly five times the dose we found to reduce tumor volumes.



(1) Osimertinib data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company commercializing the compound.

Note:
QD: Once daily

We also assessed the relative solubility of ZN-e4, alongside a proxy chemical compound of osimertinib, using a standard *in vitro* assay. The solubility of ZN-e4 was observed to be 1,614,000 nM, greater than 450 fold the solubility that of osimertinib which was observed at 3,500 nM. In addition, we did not observe confirmed cardiac toxicity as measured by the standard electrophysiological hERG safety assay.

Clinical Results

In January 2022, enrollment in ZN-e4-001 was closed after achieving enrollment in the Phase 1 dose-escalation portion of the study sufficient to determine the recommended phase 2 dose. As of January 18, 2022, we treated a total of 34 subjects with daily doses of ZN-e4 ranging from 20 mg to 480 mg, and five subjects remained on treatment. The majority of discontinuations were for disease progression.

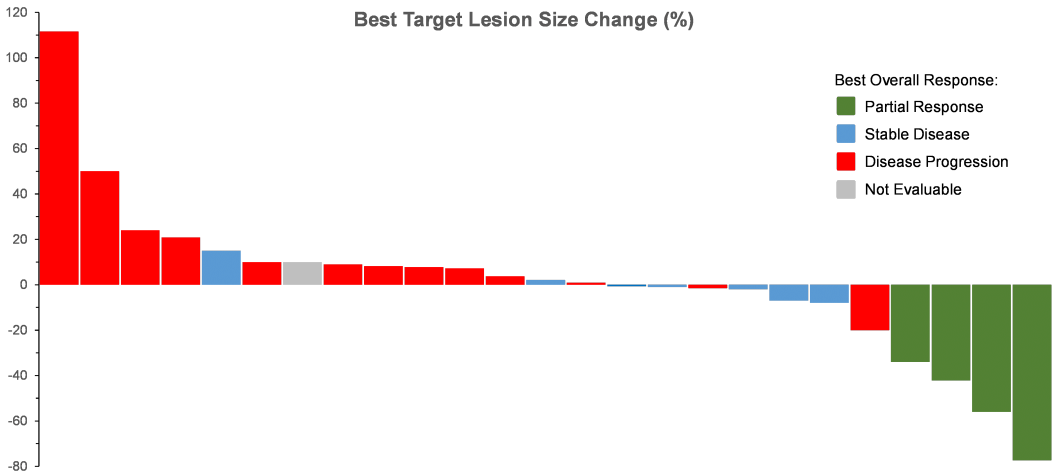
The interim and preliminary data described herein are subject to change as more data on these subjects and additional patients become available and are subject to authorization and verification procedures that could result in material changes in the final data.

Interim Preliminary Safety Results

An updated safety analysis was performed with a database cutoff date of January 18, 2022. ZN-e4 has continued to be generally well tolerated. TEAEs occurred in 29 of 34 subjects (85%), and a total of eleven SAEs have been reported in five subjects. There has been no change in the safety profile of ZN-e4 since the last reported study update.

Interim Preliminary Efficacy Results

28 subjects are included in the efficacy analysis as of the November 1, 2021 database cutoff date. The ORR was 14%, with four subjects demonstrating a PR. In addition, seven subjects had SD. Among subjects previously treated with osimertinib, ORR was 36%. The waterfall plot below presents the best percent change in target lesion size for individual subjects and the response to treatment, as assessed by the investigators according to RECIST criteria, as of the November 1, 2021 cutoff date.



BCL-xL Heterobifunctional Degrader

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.

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 are developing BCL-xL heterobifunctional degraders based on E3 ligases not expressed in platelets, allowing for the avoidance of dose-limiting thrombocytopenia associated with BCL-xL inhibitors.

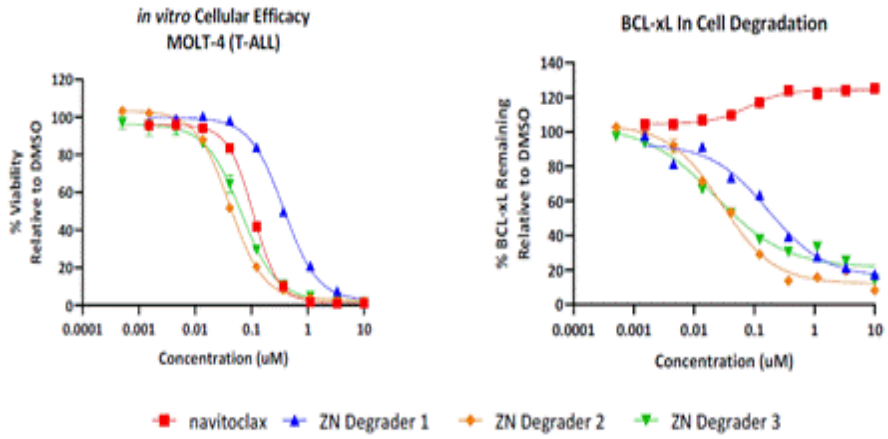
- ***Potency***. In our preclinical studies, the degradation of BCL-xL in tumor cells with our heterobifunctional degraders is associated to a decrease in cell viability.
- ***Tolerability***. Contrary to navitoclax, our BCL-xL heterobifunctional degraders are not significantly affecting the viability of human platelets in *in vitro* studies.

We believe that our Discovery efforts to select a BCL-xL degrader will lead to an attractive candidate for evaluation as monotherapy and in combination with other therapies, such as ZN-d5 and ZN-c3, for the treatment of hematological and solid malignancies.

Preclinical Results

Potency in Acute Lymphocytic Leukemia (ALL) – *in vitro* studies

In an *in vitro* preclinical study, we assessed the potency of our BCL-xL heterobifunctional degraders alongside navitoclax. As shown in the table below, we assessed the effect of each molecule on the viability of the ALL cell line model, MOLT4, by CellTiter Glo, and on the degradation of BCL-xL protein by ELISA. IC_{50} and DC_{50} are reported in nM for MOLT4 viability and BCL-xL degradation, respectively. Ymax and Dmax indicate the maximum percentage of reduction in viability and BCL-xL degradation, respectively. While navitoclax doesn't decrease the levels of BCL-xL protein, our degraders cause a significant reduction of BCL-xL protein associated with a reduction in viability of tumor cells.

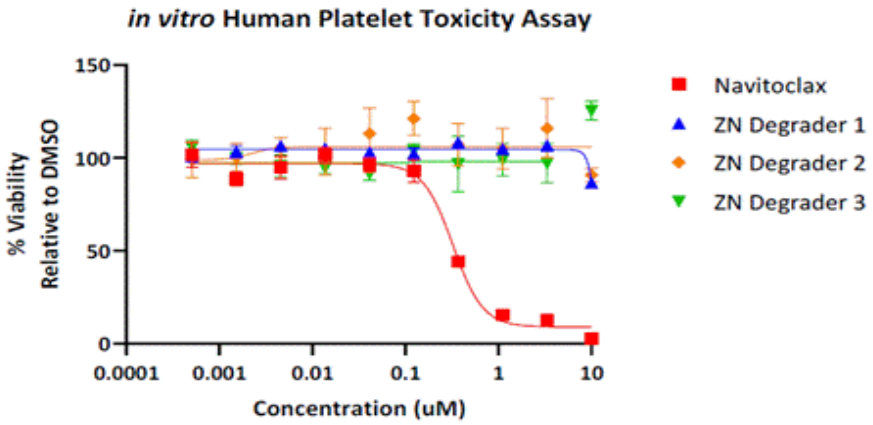


Compound	MOLT-4 Viability		BCL-xL Degradation	
	IC_{50} (nM)	Ymax (%)	DC_{50} (nM)	Dmax (%)
Navitoclax*	98.19	98.21	>10000	0
ZN Degrader 1	404.68	95.79	136.02	72.5
ZN Degrader 2	58.85	97.85	36.99	71.53
ZN Degrader 3	60.98	98.21	31.26	69.96

**Data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company commercializing the compound.*

Assessment of BCL-xL degrader toxicity in platelets in *in vitro* studies

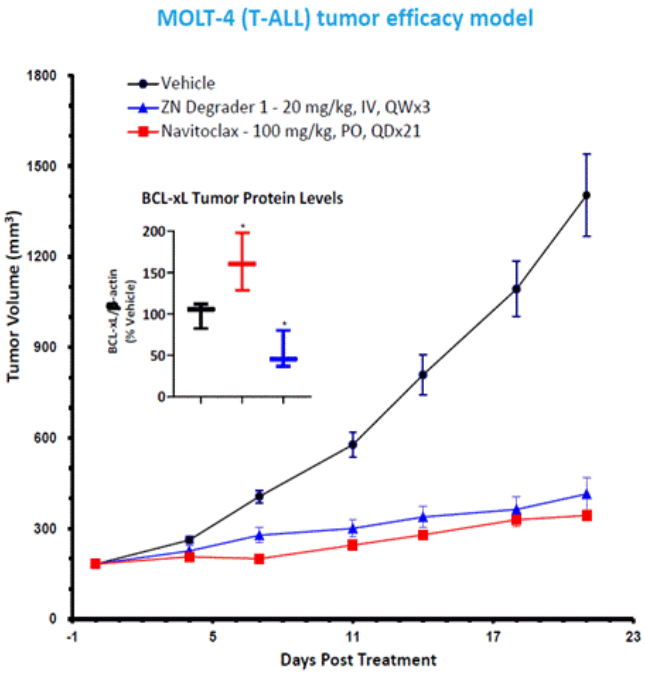
In a preclinical study, we assessed the platelet toxicity of our degraders against navitoclax by assessing their effect on the viability of human platelets using CellTiter Glo. IC_{50} values are reported in nM for platelet viability and Ymax represents the maximum percentage of reduction in viability. While navitoclax has an IC_{50} of 372 nM and kills 95% of platelets, our degraders are sparing the viability of platelets.



**Representative graph from ≥ 2 independent studies*

Anti-Tumor Activity of BCL-xL degrader in a xenograft ALL Model

In an *in vivo* study, we assessed the anti-tumor activity of our BCL-xL degraders, alongside navitoclax. In a MOLT4 xenograft ALL mouse model, our BCL-xL heterobifunctional degrader ZN degrader 1, dosed weekly at 20 mg/kg for 3 weeks, shows comparable efficacy to navitoclax, dosed daily at 100 mg/kg for 3 weeks. BCL-xL protein was assessed by semi-quantitative western blot in the tumors after 3 days of treatment and demonstrates ZN degrader 1 induces a >50% decrease in protein levels, while navitoclax induces an increase in BCL-xL protein.



**Navitoclax data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than the pharmaceutical company commercializing the compound.*

Manufacturing

We currently do not own or operate 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 substances and finished drug products in accordance with current Good Manufacturing Practices, or cGMPs, and all other applicable laws and regulations. We maintain agreements with our manufacturers that include confidentiality and intellectual property provisions to protect our proprietary rights related to our product candidates.

We have engaged CMOs to manufacture and package ZN-c3, ZN-c5, ZN-d5 and ZN-e4 for preclinical and clinical use. Additional CMOs are used to label and distribute ZN-c3, ZN-c5, ZN-d5 and ZN-e4 for clinical use. We obtain our 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 all of these product candidates, it is our goal to identify and contract with at least two manufacturers for active pharmaceutical ingredient and two manufacturers for drug product. More broadly, for each of our product candidates, we intend to identify and qualify additional manufacturers to provide the active pharmaceutical ingredient and fill-and-finish services 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. 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.

If the product candidates for our priority programs are approved for the indications we are currently targeting, they will compete with the drugs discussed below. Furthermore, it is possible that other companies are also engaged in discovery or preclinical development of drug candidates for the same indications. These competitors, if successful in clinical development, may achieve regulatory approval and market adoption in advance of our product candidates, constraining our ability to gain significant market share for such product candidates. In addition, our product candidates, if approved, will complete with multiple approved drugs or drugs that may be approved for future indications for which we develop such product candidate.

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. We also plan to rely on data exclusivity, market exclusivity and patent term extensions 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 effective 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 foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. 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 is 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

Recurium IP Holdings, LLC or Zeno Management, Inc., are currently the listed owner/assignee, or retained the exclusive license to 72 families of patent applications directed to our technology across our pipeline. As of February 4, 2022, our in-licensed portfolio consists of twenty U.S. patents and forty-five foreign patents in 13 jurisdictions, including Australia, China, Europe, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Russian Federation, Singapore, South Korea and Taiwan.

As of February 4, 2022, 22 of the 72 families have a single application pending or issued patent, and 50 of 72 families have multiple applications pending or issued patents. The 72 families include 55 U.S. applications (including pending U.S. provisional patent applications and pending U.S. non-provisional patent applications), 30 PCT applications and more than 300 international applications in approximately 18 countries, including major markets in North America, South America, Europe and Asia, each having a nominal expiration date ranging from 2034 to 2041. The nominal expiration of our patents and patent applications does not account for any applicable patent term adjustments or extensions.

U.S. Patent No. 10,513,509, or the ‘509 Patent, includes claims directed to composition of matter, including ZN-e4, a pharmaceutical composition, a method for inhibiting replication of a malignant growth or a tumor, a method for ameliorating or treating a cancer and a method for inhibiting the activity of EGFR. The ‘509 Patent has an expected expiration date in May 2037. However, we believe the ‘509 Patent may be eligible for a patent term extension under the Hatch-Waxman Act.

U.S. Patent No.11,065,233, or the ‘233 Patent, includes claims directed to composition of matter, including ZN-c5, a pharmaceutical composition and a method of making ZN-c5. U.S. Patent No. 11,065,234, or the ‘234 Patent, includes claims directed to a method for treating breast cancer with ZN-c5. The ‘233 Patent and the ‘234 Patent each have an expected expiration date in March 2037. However, we believe the ‘233 Patent and/or the ‘234 Patent may be eligible for a patent term extension under the Hatch-Waxman Act.

One of the aforementioned pending U.S. and PCT patent applications includes claims directed to ZN-c3 or ZN-d5, and has an expected expiration in 2039. However, there can be no assurance that any of our pending in-licensed 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 our in-licensed issued patents or patents that are issued in the future. The applicable authorities, including the FDA in the United States, may not agree with our assessment of whether such patent term extensions should be granted, and, if granted, they may grant more limited extensions than we request.

Trademarks

As of February 4, 2022, 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. The portfolio has an International Madrid Trademark Application designating Australia, Brazil, Canada, China, Europe, the United Kingdom, Israel, India, Japan, Korea, Mexico, New Zealand, the Russian Federation and Singapore for each of the marks ZENTALIS and the stylized "Z". The portfolio also has pending applications for registration and/or a registration has issued in Argentina, Hong Kong, and Taiwan for each of the marks ZENTALIS and stylized "Z".

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

In December 2014, and as amended and restated effective as of December 2017 and September 2019 and as amended in May 2020, we entered into a license agreement, or the Recurium Agreement, with Recurium IP Holdings, LLC, or Recurium IP, under which we were 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 pain. 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.

Mayo Foundation for Medical Education and Research

In February 2016, and as amended in April 2017 and December 2017, we entered into an option agreement, or the Mayo Agreement, with Mayo Foundation for Medical Education and Research under which we were granted an exclusive option to obtain a nonexclusive worldwide license to know-how and an exclusive worldwide license to related patent rights created by Mayo under the Mayo Agreement. 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.

SciClone Pharmaceuticals International (Cayman) Development Ltd.

In December 2014, and as amended in December 2016 and December 2017, we entered into a collaboration and license agreement, or the SciClone Agreement, with SciClone Pharmaceuticals International (Cayman) Development Ltd., or SciClone, under which we granted an exclusive license certain intellectual property rights in the People's Republic of China (including the territories of Macao and Hong Kong), South Korea, Taiwan and Vietnam, or the SciClone Territory, for SciClone to develop and commercialize a licensed product for the treatment or prevention of oncologic diseases and an exclusive option to obtain a similar license for up to two additional licensed products. 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.

Pfizer Clinical Trial Collaboration and Supply Agreement

In May 2018, we entered into a clinical trial collaboration and supply agreement with Pfizer, Inc. to evaluate the safety, tolerability and efficacy of ZN-c5 in combination with their CDK4/6 inhibitor, palbociclib, in our ongoing Phase 1/2 clinical trial 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" for additional information.

Eli Lilly and Company Clinical Trial Collaboration and Supply Agreement

In July 2020, we entered into a clinical trial collaboration and supply agreement with Eli Lilly and Company, or Lilly, to evaluate the safety, tolerability and efficacy of ZN-c5 in combination with their CDK4/6 inhibitor, abemaciclib, in a Phase 1b open label multi-center clinical trial that we initiated in November 2020. 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.

GlaxoSmithKline Clinical Trial Collaboration and Supply Agreement

In April 2021, we entered into a clinical trial collaboration and supply agreement with GlaxoSmithKline plc, or GSK, pursuant to which we are evaluating the combination of ZN-c3, our oral Wee1 inhibitor product candidate, and niraparib, GSK's poly (ADP-ribose) polymerase (PARP) inhibitor, in patients with advanced epithelial 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 subsidiaries Zeno Alpha, Inc., K-Group Alpha, Inc. Zeno Management, 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-c3, ZN-c5 and ZN-d5, respectively, whether alone or in a licensed product, 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. 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.

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 NDA 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 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 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 GCP requirements to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA 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 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 central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and

pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. 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. 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 Phase 4 clinical trials as a condition of approval of an NDA.

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 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development.

Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

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 adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

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 requesting approval to market the product. The submission of an NDA 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 for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA 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 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 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. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA 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 a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs.

After the FDA evaluates an NDA, 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. 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 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 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 does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a 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. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once 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 require 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 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. For example, 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 on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

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.

Any product candidate submitted to the FDA for approval, including a product candidate with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. An NDA 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 filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

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 may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing 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 post-marketing studies 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.

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 adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical 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 first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, 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.

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.

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 marketing of the product candidates in those countries. 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.

In addition, 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 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 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 of 2% per fiscal year and reduced payments to several types of Medicare providers, which will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, absent additional congressional action. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship

between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. 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.

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. 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, which consists of the 27 EU member states plus Iceland, Liechtenstein and Norway. 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 of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. 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. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. 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.

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, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with

the Quality System Regulation, 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.

Environmental, Social and Governance (ESG)

Social

Zentalis is committed to driving social impact through our therapeutics and operating in a way that is respectful and inclusive of all stakeholders. Below are a few initiatives that demonstrate our commitment to social impact:

- We are committed to the safety and well-being of our employees and our stakeholders. Our employees receive rigorous annual trainings on general safety, on-site lab safety procedures, quality assurance and standard operating procedures (QA SOPs) to help ensure that we are managing risks and operating safely.
- We are committed to being an equal opportunity employer and enhancing diversity and inclusion across our business. Our Code of Business Conduct and Ethics prohibits discrimination of any protected group and our employees participate in regular anti-harassment training, with managers receiving additional manager-specific anti-harassment training.
- We are always working to enrich our diversity and inclusion, or D&I, strategies and performance, and we are proud of the gender diversity we have cultivated throughout the company and our management team. Over 52% of our VPs and above are female and 50% of our C-suite team is female. We intend to continue to develop our D&I practices and improve performance across our workforce.
- We are dedicated to building a talented team and as such offer competitive compensation and comprehensive benefits to attract and retain top talent. 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 (vacation, sick leave, company shutdown during the holiday season), voluntary life-illness-accident insurance, wellness challenges and healthy food options onsite. We also have a variety of company-wide events 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 –a benefit we are proud to offer and that we believe will help to foster our corporate culture and encourage collaboration towards our shared business success.
- In an effort to ensure the safety of our staff and clinical patients during the COVID-19 pandemic, we have closed our corporate offices in New York City temporarily and have been operating our labs in San Diego with limited staff to maintain proper social distancing while keeping our science and discovery work on track.

- During 2021, we continued providing benefits for our employees to accommodate continued working from home during the COVID-19 pandemic including flexible work arrangements, supplementary time off and communications to help ensure employees felt cared for and supported both at home and at work.

Human Capital Management

As of December 31, 2021, Zentalis had 177 full-time employees, all of whom are based in the United States. Our workforce is highly skilled, with 39% of our employees holding an MD, PhD, or PharmD degree. Of these full-time employees, 134 employees are engaged in research and development activities. None of these employees are 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. To attract, maintain and motivate our team of ambitious professionals, we offer competitive compensation and benefits, a collaborative work environment, ongoing skills development initiatives, attractive career advancement opportunities, and a culture that values D&I. At Zentalis, everyone's voice is heard, the work is meaningful, and employees are encouraged to think outside of the box.

Environmental

Zentalis is committed to minimizing the environmental impacts of our business, with the goal of being "green chemists," applying our science in the labs carefully to efficiently use and conserve precious recourses. 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 commitment to environmental impact:

- 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.
- We dispose 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 in all facilities for both regular recyclables and lab waste.

Governance

Zentalis is committed to strong governance systems and policies that ensure fair, transparent and efficient business practices. Here are a few initiatives that demonstrate our commitment to good governance:

- Our board of directors and executive management team have oversight of all the relevant ESG issues that we have outlined in this section.
- Our approaches to cybersecurity and privacy are overseen by our Chief Information Security Officer.
- We have employee trainings, procedures and policies in place to train our employees on data privacy and cybersecurity. Trainings take place at regular intervals during our Company-wide meetings, 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 with regular trainings and provisions related to corporate ethics, bribery and corruption, whistleblower policies, political involvement and other dimensions of corporate ethics.

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 acquisition, 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, we converted to a Delaware corporation pursuant to a statutory conversion and changed our 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, have not completed any clinical trials, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and 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 ZN-c3, ZN-c5, ZN-d5 and ZN-e4. We have not yet demonstrated our ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales 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 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, have not generated any revenue from product sales to date and have financed our operations principally through private financings, our initial public offering, or IPO, and follow-on public offerings of our common stock. We have incurred net losses of $166.1 million and $118.5 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $359.6 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. Four of our product candidates, ZN-c3, ZN-c5, ZN-d5 and ZN-e4, are in clinical trials. Our other programs are in preclinical research. As a result, 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 ZN-c3, ZN-c5, ZN-d5 and ZN-e4 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 the COVID-19 pandemic or other causes;
- 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 ZN-c3, ZN-c5, ZN-d5 and ZN-e4 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;
- 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 patent protection, trade secret protection 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 coverage and adequate 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.

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, ZN-c3, ZN-c5, ZN-d5, ZN-e4 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 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. Other unanticipated costs may also arise. In addition, if we obtain marketing approval for any of our product candidates, including ZN-c3, ZN-c5, ZN-d5 and ZN-e4, 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, 2021, we had cash and cash equivalents and marketable securities of $339.9 million. Based on current business plans, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2021 will be sufficient to fund our operating expenses and capital expenditures requirements into the third quarter of 2023, 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 the COVID-19 pandemic 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, ZN-c3 and/or ZN-c5, 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 ZN-c3 and ZN-c5. ZN-c3 and ZN-c5 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 ZN-c3 or ZN-c5, or any other product candidate, before we receive marketing approval from the FDA and comparable foreign 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 clinical trials of ZN-c3 and ZN-c5;
- the initiation and successful patient enrollment and completion of additional clinical trials of ZN-c3 and ZN-c5 on a timely basis;
- maintaining and establishing relationships with CROs and clinical sites for the clinical development of ZN-c3 and ZN-c5 both in the United States and internationally;
- the frequency and severity of adverse events in the clinical trials;
- the efficacy, safety and tolerability profiles that are satisfactory to the FDA, EMA or any comparable foreign regulatory authority for marketing approval;
- the timely receipt of marketing approvals for ZN-c3 and ZN-c5 from applicable regulatory authorities;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- the maintenance of existing or the establishment of new supply arrangements with third-party drug product suppliers and manufacturers for clinical development of ZN-c3 and ZN-c5;

- 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 ZN-c3 and ZN-c5 if approved, including for supplies of drugs that we are testing in combination with ZN-c3 and ZN-c5;
- obtaining and maintaining patent protection, trade secret protection 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 ZN-c3 and ZN-c5, which would materially harm our business. If we do not receive marketing approvals for ZN-c3 and ZN-c5, we may not be able to continue our operations.

We expect to depend on 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 anticipate seeking third-party collaborators for the research, development and commercialization of some of our product candidates. 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.

Collaborations involving our research programs or any 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 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, 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 valuation 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 GLP and GCP requirements or to secure approval for clinical development plans from the FDA or foreign regulatory authorities.

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.

There is currently no FDA-approved oral SERD, and our development of ZN-c5 may never lead to a marketable product.

We are developing ZN-c5 as an oral SERD. There is currently no FDA-approved oral SERD. We have not received regulatory approval for ZN-c5 and cannot be certain that our approach will lead to the development of an approvable or marketable product, alone or in combination with other therapies. We may not succeed in demonstrating safety and efficacy of ZN-c5 in our ongoing Phase 1/2 clinical trial or in larger-scale clinical trials. Advancing ZN-c5 as an oral SERD creates significant challenges for us, including:

- obtaining marketing approval, as the FDA or other regulatory authorities have never approved an orally available SERD;
- if ZN-c5 is approved, educating medical personnel regarding the potential efficacy and safety benefits, as well as the challenges, of incorporating our ZN-c5 into existing treatment regimens, including in combination with other treatments for breast cancer; and
- establishing the sales and marketing capabilities upon obtaining any marketing approvals to gain market acceptance.

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
- adverse events 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 foreign 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. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and other comparable foreign 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 foreign 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.

Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control. For example, a U.S. federal government shutdown or budget sequestration, such as ones that occurred during 2013, 2018 and 2019, may result in significant reductions to the FDA's budget, employees and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates or obtain regulatory approval for our product candidates.

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

- the FDA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA or other comparable foreign 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 foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a New Drug Application, or 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 foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or other comparable foreign 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; and

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

In addition, the policies of the FDA and other regulatory authorities' with respect to clinical trials may change and additional government regulations may be enacted. For instance, 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. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may also be impacted.

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, or a Risk Evaluation and Mitigation Strategy, or 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 foreign regulatory authorities or otherwise produce positive results.

Before obtaining marketing approval from the FDA or other comparable foreign 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. 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. 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.

In addition, we may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product candidates. While we have or will have agreements governing these third parties' services, 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 foreign 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 institutional review boards, or 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 adverse events 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 foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice, or cGMP, regulations or similar foreign 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, good clinical practices, or GCP, or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner; or
- 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.

In addition, disruptions caused by the COVID-19 pandemic have caused and we expect will 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 foreign 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 foreign 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 foreign 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 foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign 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 foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

If 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.

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

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for their intended uses. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical studies and early-stage clinical trials does not mean that future clinical trials will be successful. We do not know whether ZN-c3, ZN-c5, ZN-d5 and ZN-e4 will perform in current or future clinical trials as ZN-c3, ZN-c5, ZN-d5 and ZN-e4 have performed in preclinical studies, or, with respect to ZN-c3, ZN-c5 and ZN-e4, ongoing clinical trials to date. Product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA, EMA and other comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our product candidates may also be undergoing surgical, radiation and chemotherapy treatments and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our product candidate. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain marketing approval to market our product candidates. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. We cannot be certain that our planned clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could seriously harm our business.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or comparable foreign regulatory authority approval. We cannot guarantee that the FDA or foreign 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. To the extent that the results of the trials are not satisfactory to the

FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidate, which may also limit its commercial potential. Furthermore, the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval, which may lead to the FDA or comparable foreign regulatory authorities delaying, limiting or denying approval of our product candidates.

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 preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline 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 preliminary or 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 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;
- 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 other comparable foreign 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 intend to develop ZN-c3, ZN-c5, ZN-d5, ZN-e4 and potentially other product candidates in combination with other therapies, which exposes us to additional risks.

We intend to develop ZN-c3, ZN-c5, ZN-d5, ZN-e4 and likely other future product candidates in combination with one or more other approved or unapproved therapies to treat cancer or other diseases. For example, we are currently evaluating ZN-c3 in combination with the approved agent niraparib, and ZN-c5 in combination with certain approved agents including palbociclib and abemaciclib.

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 foreign

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 foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

We also may choose to evaluate ZN-c3, ZN-c5, ZN-d5, ZN-e4 or any other future product candidates in combination with one or more cancer therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market and sell ZN-c3, ZN-c5, ZN-d5, ZN-e4 or any product candidate we develop in combination with an unapproved cancer therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved cancer therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

If the FDA or comparable foreign 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.

We intend to initially focus our product candidate development on treatments for various oncology indications. 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 prove 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 foreign 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 foreign 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, the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS determines 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 European Union, or 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 foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for 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.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

We may be unable to obtain U.S. or foreign 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 foreign 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 foreign 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. 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 foreign regulatory authorities policy during the period of drug development, clinical trials and FDA or foreign 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 foreign 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 foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign 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 foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval.

Our current or future product candidates may cause significant adverse events, 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 adverse events 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 foreign 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 adverse events 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 adverse events 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 adverse events 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 adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical 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, EMA and other comparable foreign 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, EMA or other comparable foreign 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 foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop 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 foreign 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 foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we 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 foreign regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event 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 foreign requirements and GCP for any clinical trials that we conduct post-approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations or similar foreign 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 foreign 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 are required by the FDA or similar regulatory authorities to obtain approval (or clearance, or certification) of a companion diagnostic test in connection with approval of any of our product candidates, and we do not obtain or face delays in obtaining approval (or clearance, or certification) of a diagnostic device, we will not be able to commercialize such product candidate and our ability to generate revenue will be materially impaired.

If safe and effective use of any of our product candidates depends on an *in vitro* diagnostic that is not otherwise commercially available, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves our product candidates if at all. 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 all companion diagnostics for cancer therapies. 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 a companion diagnostic for any of our product candidates, whether before or after it obtains marketing approval, we, and/or future collaborators, may encounter difficulties in developing and obtaining approval for such product candidate. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval, 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.

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 new In Vitro Medical Devices Regulation (NO 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 will become applicable in May 2022. However on October 14, 2021, the European Commission proposed a "progressive" roll-out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices. The European Parliament and Council adopted the proposed regulation on December 15, 2021. The IVDR will fully apply on May 26, 2022 but there will be 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 regulation of companion diagnostics in the EU will be subject to further requirements as of May 2022. 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 a CE certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a 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 hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA 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 foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of the Securities and Exchange Commission, or 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. Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation as of September 2021. More recently, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to hinder or prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We may attempt to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated approval pathways or any other form of expedited development or review. If we are unable to obtain such approval, 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 any other 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 post-approval confirmatory studies to verity and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

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 drug 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 any other form of expedited development or review for any of our product candidates, we intend to seek feedback from the FDA or foreign regulatory authorities and will otherwise evaluate our ability to seek and receive accelerated approval or any other 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 any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA or foreign regulatory authorities feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or receive an expedited regulatory designation (e.g., breakthrough therapy designation) for our product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign 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 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 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 of the Biden administration will impact our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 unless additional congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several

providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

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 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. 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 foreign 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 federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, and government price reporting laws, which could expose us to, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings.

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 foreign 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 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 foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by 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 foreign 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 foreign 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 is expected to increase data breach litigation. Further, the California Privacy Rights Act, or CPRA, recently passed in California. The CPRA significantly amends the CCPA and will impose 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 will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia 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 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. 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 must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must 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 launched a public consultation on its draft revised data transfers mechanisms in August 2021. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. 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. The GDPR may increase our responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms to ensure compliance. This may be onerous and if our efforts to comply with GDPR or other applicable EEA laws and regulations are not successful, it could adversely affect our business in Europe.

Further, from January 1, 2021, companies 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. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how the UK data protection laws or regulations will develop in the medium to longer term. On June 28, 2021, the European Commission adopted an adequacy decision in favor of the UK, enabling data transfers from member states in the EU to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission renews or extends that decision.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare laws and regulations will involve on-going substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant 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. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

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

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA and other foreign authorities regulations, provide accurate information to the FDA or foreign regulatory authorities, comply with federal, state and foreign 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 foreign export controls, trade sanctions, and import laws and regulations. Compliance with these legal requirements could limit our ability to compete in foreign 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 foreign officials under the FCPA. Recently the SEC and 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 foreign 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. In response to the spread of COVID-19, we have limited access to our executive offices, with the majority of employees continuing their work outside of our offices, and we have limited the number of staff in any given research and development laboratory. As a result of the COVID-19 pandemic, we have experienced and we expect to continue to experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- continued delays or difficulties in enrolling patients in our clinical trials;
- continued 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 foreign governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- 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 rapidly evolve. The extent to which the pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the 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 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 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 currently do not have and have never had a marketing or sales team. In order to commercialize any product candidates, if approved, 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.

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 executive officers to manage. 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, if we 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.

We have never commercialized a product candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize any products on our own or together with suitable collaborators.

We have never commercialized a product candidate, and we currently have no sales force, marketing or distribution capabilities. To achieve commercial success for the product candidates, which we may license to others, we will rely on the assistance and guidance of those collaborators. For product candidates for which we retain commercialization rights, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party.

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. Developing a sales and marketing organization will be expensive and time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization. If we are unable to build

our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may not generate revenues from them or be able to reach or sustain profitability.

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 transition into operating as a public company, we expect to need additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA, EMA and other comparable foreign regulatory agencies' review process for ZN-c3, ZN-c5, ZN-d5 and ZN-e4 and any other future 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, ZN-c3, ZN-c5, ZN-d5 and ZN-e4 and any other future 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, Ltd., pursuant to intercompany and collaborative service 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 ZN-c3, ZN-c5, ZN-d5 and ZN-e4 and any other future 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 ZN-c3, ZN-c5, ZN-d5 and ZN-e4 and any other future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

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

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants, collaborators and third-party service providers, are vulnerable to damage from computer viruses, cybersecurity threats, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failure. Attacks upon information technology systems are 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.

If such an event were to occur and cause interruptions in our operations or result in the unauthorized acquisition of or access to personally identifiable information or individually identifiable health information (violating certain privacy laws such as HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations promulgated thereunder, or collectively, HIPAA and GDPR), it could result in a material disruption of our drug discovery and development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. Some federal, state and foreign 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 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 foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign 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.

A portion of our manufacturing of our lead product candidates takes place in China through third-party manufacturers. A significant disruption in the operation of those manufacturers, a trade war or political unrest in 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 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 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 in China, 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 Chinese governments, political unrest or unstable economic conditions 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 China. 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 China.

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 facility is located in a region which experiences 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, 2021, we had available federal and state net operating loss, or NOL, carryforwards of approximately $361.1 million and $90.4 million, respectively. $340.2 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 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 NOL carryforwards begin to expire in 2033.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the “Code”) if a corporation undergoes an “ownership change” (generally defined as a cumulative change in our 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 foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements and reimbursement regimes in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign 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 foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign 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.

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 as well as our and our licensors' ability to operate without infringing the proprietary rights of others. 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 abroad 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 not be infringed, 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 foreign 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 foreign 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 foreign 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 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 foreign 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, third-party manufacturers, 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, in September 2019, we entered into an exclusive license agreement with Recurium IP Holdings, LLC, or Recurium IP, to obtain an exclusive license to certain intellectual property rights to develop and commercialize ZN-e5, ZN-c3 and ZN-e4.

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 our rights under our existing license agreement with Recurium with respect to any licensed product, we may be required to pay to Recurium a specified percentage of all revenue 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 licensed-in 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 foreign 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 of third parties, 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 has been discovered through government-funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

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, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO and/or foreign patent offices. Numerous third-party U.S. and foreign 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 Annual Report on Form 10-K, 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, and our licensors 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 counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation, defendant counterclaims alleging invalidity and/or unenforceability 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 foreign 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 may 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 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 foreign 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 foreign 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 may also 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 foreign 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 foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we 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 foreign jurisdictions. The legal systems of many foreign 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 foreign 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 foreign 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 foreign 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 and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign 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 foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations and similar foreign 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 foreign 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. Furthermore, the raw materials for our product candidates are sourced, in some cases, from a single-source supplier. 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. For example, the extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of our products and product candidates will depend on the severity and duration of the spread of the virus, and the actions undertaken to contain COVID-19 or treat its effects.

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 to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors 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 contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;

- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third party 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 contract manufacturing partners for compliance with cGMP regulations or similar foreign 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 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 foreign 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 foreign 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.

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

We have and may in the future seek third-party collaborators for the development and commercialization of one or more of our product candidates. Our likely collaborators for any future collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We may have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. 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 product candidates could pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, 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 that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates 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;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;
- collaborators may not properly obtain, maintain, defend or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;

- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all; and
- if a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our drug development or commercialization program could be delayed, diminished or terminated.

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 rapidly evolve. 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.

Current beneficial owners of 5% or more of our common stock 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, 2021, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially own approximately 70.8% of our outstanding common stock. As a result, these stockholders will be able to significantly influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. 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 have registered 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 and July 2021, we completed underwritten public offerings 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.

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 are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- 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 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 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.

General Risk Factors

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.

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.

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.

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 will be 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 terminates 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

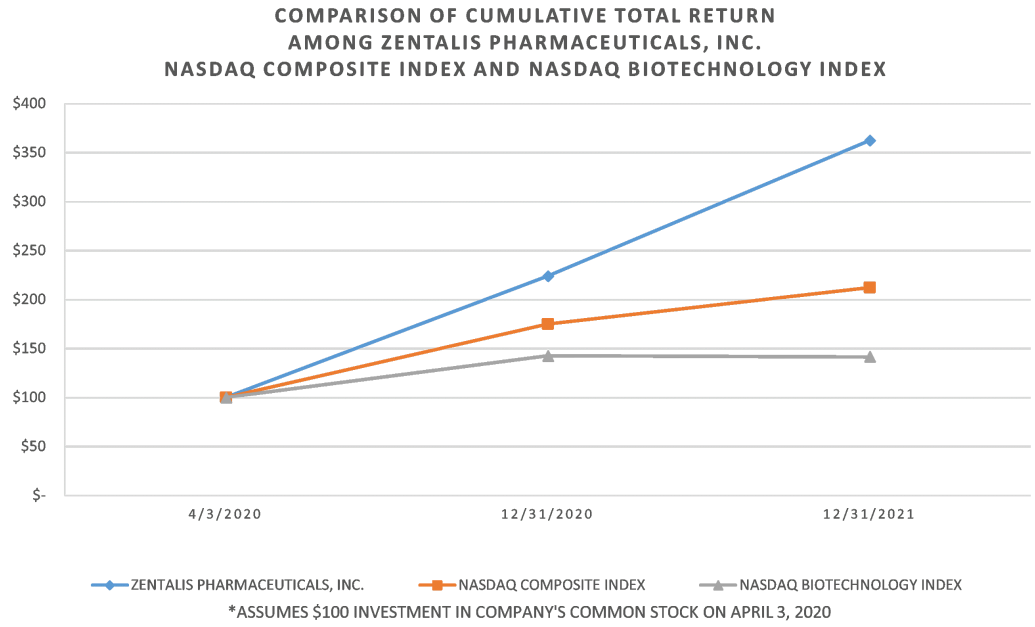
Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

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 initial public offering) through December 31, 2021, 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 are not intended to forecast the future performance of our stock and may not be indicative of our future performance.



Holders

As of February 22, 2022, there were approximately 25 holders of record of our common stock.

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, 2021 that were not registered under the Securities Act.

Use of Proceeds

On April 7, 2020, we completed our initial public offering and issued and sold 10,557,000 shares of our common stock (including 1,377,000 shares of our common stock in connection with the full exercise of the underwriters' option to purchase additional shares) at a price to the public of $18.00 per share for net proceeds of approximately $172.4 million.

Upon receipt, the net proceeds from our IPO were held in cash, cash equivalents and marketable securities. As of December 31, 2021, we had used all of the net proceeds from our IPO. There was no material change in the planned use of such proceeds from that described in the final prospectus, dated April 2, 2020, filed with the SEC pursuant to Rule 424(b) relating to our registration statement on Form S-1 (Registration No. 333-236959), as amended, filed in connection with our IPO.

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, 2021 and 2020, including a year-to-year comparison between 2021 and 2020, is presented below. For a discussion regarding our financial condition and results of operations for the year ended December 31, 2019, including a year-to-year comparison between 2020 and 2019, 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, 2020 filed on March 25, 2021.

Overview

We are a clinical-stage biopharmaceutical company focused on discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancers. We use our highly efficient drug discovery engine, which we refer to as our "Integrated Discovery Engine", to identify targets and develop small molecule new chemical entities, or NCEs, with properties that we believe could result in potentially differentiated product profiles. Our discovery engine combines our extensive experience and capabilities across cancer biology and medicinal chemistry. 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.

Clinical Program Overview

We are developing a broad pipeline of product candidates with an initial focus on validated oncology targets with the potential to address large patient populations. We currently have two lead product candidates - ZN-c3, an inhibitor of Wee1, a protein tyrosine kinase, and ZN-c5, an oral selective estrogen receptor degrader, or SERD. Our other clinical product candidates include ZN-d5, a selective inhibitor of B-cell lymphoma 2, or BCL-2, and ZN-e4, an irreversible inhibitor of mutant epidermal growth factor receptor, or EGFR.

ZN-c3 (Wee1 Inhibitor)

ZN-c3 is currently being evaluated in multiple ongoing clinical trials, including a Phase 2 monotherapy clinical trial for the treatment of women with recurrent or persistent uterine serous carcinoma, or USC. The study was initiated following an end-of-Phase 1 meeting with the U.S. Food and Drug Administration, or FDA, which concurred in principle with the proposal that ZN-c3 has the potential for an accelerated approval pathway based on the proposed global study design. The FDA granted Fast Track designation in November 2021 to ZN-c3 for the treatment of recurrent or persistent uterine serous carcinoma in adult women.

In addition, ZN-c3 in combination with chemotherapy has received orphan drug designation and rare pediatric disease designation from the FDA for osteosarcoma. We initiated a Phase 1/2 clinical trial of ZN-c3 in combination with chemotherapy in pediatric and adult patients with osteosarcoma during the third quarter of 2021. We expect to report initial results from this trial in the second half of 2022. If ZN-c3 were to obtain approval for the designated indication, we believe it may be eligible for a rare pediatric disease priority voucher upon approval.

ZN-c3 is also being evaluated in an ongoing Phase 1/2 clinical trial for the treatment of advanced solid tumors as a monotherapy and in an ongoing Phase 1b clinical trial in combination with chemotherapy in patients with advanced ovarian cancer.

In the fourth quarter of 2021, we initiated a Phase 2 monotherapy trial for a tumor agnostic, predictive biomarker, subject to FDA feedback. This Phase 2 tumor agnostic trial planned with registrational intent would investigate ZN-c3 in patients with solid tumors that express the identified predictive biomarker. We also initiated a Phase 1/2 clinical trial evaluating ZN-c3 in combination with GlaxoSmithKline's PARP inhibitor niraparib (ZEJULA®), as part of a clinical research collaboration in ovarian cancer. We also announced the plans to initiate a Phase 1/2 combination trial of ZN-d5 + ZN-c3 in AML and a Phase 1b combination trial of ZN-c5 + ZN-c3 in CDK4/6i resistant breast cancer in 2022.

We have agreed to support two planned additional investigator-initiated trials that we expect to initiate in 2022: a trial with the Ivy Brain Center in glioblastoma multiforme and a trial in combination with immunotherapy with Dana Farber in triple negative breast cancer.

ZN-c5 (Oral SERD)

In the ongoing Phase 1/2 clinical trial evaluating ZN-c5 in combination with Pfizer's CDK4/6 palbociclib, and the Phase 1b clinical trial evaluating ZN-c5 in combination with Lilly's CDK4/6 abemaciclib, the safety and tolerability data suggested ZN-c5 has the potential to be a promising candidate for further evaluation in combinations. We continue to enroll patients in the two separate combination trials and expect to report initial results in the first half of 2022 from these trials. In the fourth quarter of 2021, we announced plans to initiate a Phase 1b combination of ZN-c5 + ZN-c3 in CDK4/6i resistant breast cancer in 2022.

ZN-d5 (BCL-2 Inhibitor)

The ongoing Phase 1 monotherapy dose escalation trial for ZN-d5 is enrolling patients with relapsed/refractory Non-Hodgkin's Lymphoma and additionally began enrolling patients with acute myeloid leukemia in the third quarter of 2021. We reported initial results from this Phase 1 trial in the fourth quarter of 2021. We also announced plans to initiate a Phase 1 clinical trial in amyloidosis and a Phase 1/2 combination trial of ZN-d5 + ZN-c3 in AML.

ZN-e4 (EGFR Inhibitor)

We reported initial results from the Phase 1/2 dose escalation trial for ZN-e4 in patients with advanced non-small cell lung cancer (NSCLC) in both osimertirab-naive and experienced patients in the fourth quarter of 2021.

Zentera Therapeutics

Our China joint venture, Zentera, is also advancing corresponding clinical trials in China for ZN-c3, ZN-c5 and ZN-d5. See "License Agreements and Strategic Collaborations—Zentera Therapeutics" below and Notes 3 and 15 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

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 and obtain regulatory approval for 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 $166.1 million for the year ended December 31, 2021. We had an accumulated deficit of $359.6 million as of December 31, 2021. We had cash, cash equivalents and marketable securities of $339.9 million as of December 31, 2021. We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2023.

Corporate Conversion

In connection with our IPO, we converted from a Delaware limited liability company into a Delaware corporation pursuant to a statutory conversion, and changed our name from Zentalis Pharmaceuticals, LLC to Zentalis Pharmaceuticals, Inc. We refer to all transactions related to our conversion to a corporation as the Corporate Conversion. As a result of the Corporate Conversion, all holders of units of Zentalis Pharmaceuticals, LLC became holders of shares of common stock of Zentalis Pharmaceuticals, Inc.

In connection with the Corporate Conversion, our outstanding Series A convertible preferred units, Series B convertible preferred units, Series C convertible preferred units, Class A common units and Class B common units, or Units, converted into an aggregate of 25,288,854 shares of our common stock (including 1,160,277 shares of restricted common stock) based on the IPO price of $18.00 per share of common stock.

Impact of COVID-19 Pandemic

We continue to monitor how the COVID-19 pandemic is affecting our employees, business, preclinical studies and clinical trials. In response to the spread of COVID-19, we have closed our executive offices with our administrative employees continuing their work outside of our offices and limited the number of staff in any given research and development laboratory to maintain proper social distancing while keeping our science and discovery work on track. 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. Limited operations at our laboratory facilities have also 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 significant 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, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, the continued impact on financial markets and the global economy, and the effectiveness of the global response to contain and treat the disease. 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.

License Agreements and Strategic Collaborations

Recurium IP Holdings, LLC

In December 2014, and as amended and restated effective as of December 2017 and September 2019 and as amended in May 2020, we entered into a license agreement, or the Recurium Agreement, with Recurium IP Holdings, LLC, or Recurium IP, under which we were 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 pain. In connection with the May 2020 amendment, we clarified certain aspects of the sublicensing payment provisions. We have the right to sublicense our rights under the Recurium Agreement, subject to certain conditions. We are required to use commercially reasonable efforts to develop and commercialize at least one product that comprises or contains a licensed compound and to execute certain development activities.

Under the terms of the Recurium Agreement, we are obligated to make development and regulatory milestone payments, pay royalties for net sales and make sublicensing payments with respect to certain licensed products directed to one of ten specific biological targets, including ZN-c3, ZN-c5 and ZN-e4. We are obligated to make development and regulatory milestone payments for such licensed products of up to $44.5 million. In addition, we are obligated to make milestone payments up to $150,000 for certain licensed products used in animals. We are also obligated to pay royalties on sales of such licensed products at a mid- to high-single digit percentage. In addition, if we choose to sublicense or assign to any third parties our rights under the Recurium Agreement with respect to such licensed products, we must pay to Recurium IP 20% of sublicensing income received in connection with such transaction.

Mayo Foundation for Medical Education and Research

In February 2016, and as amended in April 2017 and December 2017, we entered into an option agreement, or the Mayo Agreement, with Mayo Foundation for Medical Education and Research under which we were granted an exclusive option to obtain a nonexclusive worldwide license to know-how and an exclusive worldwide license to related patent rights created by Mayo under the Mayo Agreement. The Mayo Agreement provided that it will expire on the date of the last to expire of the Mayo patent rights or, if no Mayo patent rights arise, on February 11, 2021. No Mayo patent rights were created under the Mayo Agreement; therefore the agreement expired on February 11, 2021. In consideration for the grant of know-how we provided grants of common stock on the first anniversary and Class A common units on the second and third anniversaries following entry into the Mayo Agreement. As of December 31, 2021, we have granted equity securities which amount to 15,435 shares of common stock under the Mayo Agreement.

SciClone Pharmaceuticals International (Cayman) Development Ltd.

In December 2014, and as amended in December 2016 and December 2017, we entered into a collaboration and license agreement, or the SciClone Agreement, with SciClone Pharmaceuticals International (Cayman) Development Ltd., or SciClone, under which we granted an exclusive license certain intellectual property rights in the People’s Republic of China (including the territories of Macao and Hong Kong), South Korea, Taiwan and Vietnam, or the SciClone Territory, for SciClone to develop and commercialize a licensed product for the treatment or prevention of oncologic diseases and an exclusive option to obtain a similar license for up to two additional licensed products. Under the SciClone Agreement, SciClone is responsible for clinical development activities required in order to obtain regulatory approval in the SciClone Territory. SciClone paid to us a one-time

upfront payment of $1.0 million upon entering into the SciClone Agreement, and $4.0 million in aggregate milestone payments. No additional development or commercial milestones or reimbursement for research and development expenses are payable under the SciClone Agreement, as amended. We are entitled to receive a mid-single digit royalty on net sales of licensed products in the SciClone Territory, which royalty is subject to certain reductions in the event that SciClone is unable to achieve certain gross margins or if generic products are sold or if technology covering a licensed product is licensed from a third party. We have also agreed to pay SciClone tiered royalties pursuant to the terms of the SciClone Agreement, the applicable rate of which are determined based on whether a compound is developed to a successful dual IND submission and the costs incurred by SciClone for the development of such product candidate. Following the December 2016 amendment to the SciClone Agreement, SciClone retains the exclusive license to develop and commercialize our EGFR inhibitor product candidate, ZN-e4, in the SciClone Territory, and the exclusive option to obtain an exclusive license to develop up to two specified compounds under the SciClone Agreement for which we submit an IND by providing notice and paying $5.0 million to us. SciClone's and our royalty obligations will expire on a licensed product-by-licensed product and country-by-country basis on the later of fifteen years from the date of first commercial sale or when there is no longer a valid patent claim covering such licensed product in such country.

Pfizer Clinical Trial Collaboration and Supply Agreement

In May 2018, we entered into a clinical trial collaboration and supply agreement with Pfizer, Inc. to evaluate the safety, tolerability and efficacy of ZN-c5 in combination with their CDK4/6 inhibitor, palbociclib, in our ongoing Phase 1/2 clinical trial of ZN-c5. Pursuant to this agreement, we will be 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 Pfizer that meets quarterly. Pfizer will supply palbociclib for use in the trial, at no cost to us.

Eli Lilly and Company Clinical Trial Collaboration and Supply Agreement

In July 2020, we entered into a clinical trial collaboration and supply agreement with Eli Lilly and Company, or Lilly, to evaluate the safety, tolerability and efficacy of ZN-c5 in combination with their CDK4/6 inhibitor, abemaciclib, in a Phase 1b open label multi-center clinical trial that we initiated in November 2020. Pursuant to this agreement, we will be responsible for the conduct and cost of the relevant studies. Lilly is obligated to supply abemaciclib for use in the trial, at no cost to us. We are required to provide to Lilly clinical data and other reports at major decision points during the trial and no later than 60 days following completion of the planned Phase 1b clinical trial.

This agreement does not grant any right of first negotiation to participate in future clinical trials, and each of the parties retains all rights and ability to evaluate their respective compounds in any clinical studies, either as monotherapy or in combination with any other product or compound, in any therapeutic area.

The agreement with Lilly will expire upon completion of all obligations of the parties thereunder or upon termination by either party. We and Lilly 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. Lilly also has the right to terminate this agreement if it notifies us in writing that it reasonably and in good faith believes that abemaciclib 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.

GlaxoSmithKline Clinical Trial Collaboration and Supply Agreement

In April 2021, we entered into a clinical trial collaboration and supply agreement with GlaxoSmithKline plc, or GSK, in which we will evaluate the combination of ZN-c3, our oral Wee1 inhibitor product candidate, and niraparib, GSK's poly (ADP-ribose) polymerase (PARP) inhibitor, in patients with advanced epithelial ovarian cancer. We are currently conducting clinical studies with ZN-c3 both as a monotherapy and in combination with certain standard of care therapies.

Pursuant to this agreement, we will be 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 will supply 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 each of the parties retains all rights and ability to evaluate their respective compounds in any 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 subsidiaries Zeno Alpha, Inc., K-Group Alpha, Inc. Zeno Management, 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-c3, ZN-c5 and ZN-d5, respectively, whether alone or in a licensed product, or 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". 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, 2021, we hold a 40.3% equity interest in Zentera. Anthony Y. Sun, M.D., our President and Chief Executive Officer, serves as Chief Executive Officer and a member of the board of directors of Zentera, and Kevin D. Bunker, Ph.D., our Chief Operating 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 under the Recurium Agreement, to develop and commercialize the Collaboration Products in the Zentera Field and 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 and 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 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. 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 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.

Zentera filed four Clinical Trial Applications, or CTAs (China equivalent of IND), and four have been approved in China to date for ZN-c3, ZN-c5, ZN-d5 and ZN-c3 in combination. Zentera has begun enrolling four clinical trials for ZN-c3, ZN-c5 and ZN-d5.

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 contract research organizations, or CROs, and other third parties that conduct research, preclinical activities and clinical trials on our behalf as well as contract manufacturing organizations, or 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 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 track external development costs by product candidate or development program, but we do not allocate personnel costs, 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,	
	2021	2020
	(in thousands)	
ZN-c3	$ 42,191	$ 13,910
ZN-c5	24,851	24,013
ZN-d5	16,035	7,947
ZN-e4	1,414	2,554
Unallocated research and development expenses	91,110	36,477
Total research and development expenses	$ 175,601	$ 84,901

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

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 increased research and development activities relating to ZN-c3, ZN-c5, ZN-d5, ZN-e4, and any other product candidate we may develop. We also expect to incur increased expenses associated with being a public 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 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, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020, together with the changes in those items in dollars:

	Year Ended December 31,		
	2021	2020	Increase (Decrease)
	(in thousands)		
Operating Expenses			
Research and development	$ 175,601	$ 84,901	$ 90,700
General and administrative	40,941	33,886	7,055
Total operating expenses	216,542	118,787	97,755
Loss from operations	(216,542)	(118,787)	(97,755)
Investment and other income, net	401	683	(282)
Gain on deconsolidation of Zentera	51,582	—	51,582
Net loss before income taxes	(164,559)	(118,104)	(46,455)
Income tax expense (benefit)	(297)	444	(741)
Loss on equity method investment	1,831	—	1,831
Net loss	(166,093)	(118,548)	(47,545)
Net loss attributable to noncontrolling interests	(7,368)	(707)	(6,661)
Net loss attributable to Zentalis	$ (158,725)	$ (117,841)	$ (40,884)

Revenue

We did not generate any revenue for the years ended December 31, 2021 and 2020.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2021 were $175.6 million, compared to $84.9 million for the year ended December 31, 2020. The increase of $90.7 million was primarily due to increases in external research and development expenses related to our lead product candidates, as we advanced our clinical pipeline in 2021. In addition, in 2021, we conducted additional preclinical studies, incurred additional manufacturing costs, and incurred increased costs for study and lab materials. Increases of $23.6 million, $22.9 million and $15.0 million were seen in clinical trial spend, personnel expenditures, and chemistry, manufacturing and controls costs, respectively. Lab equipment and supplies also increased by $1.8 million. Additionally, during the year ended December 31, 2021 we incurred $10.0 million in milestone payments, $7.0 million in increased collaboration costs and recorded an $8.8 million impairment charge on Kalyra's IPR&D. Increases of $6.4 million and $0.3 million were the result of additional overhead allocation to research and development as well as a decrease in grant revenue, respectively. These amounts were partially offset by $5.3 million in reimbursements from Zentera.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2021 were $40.9 million, compared to $33.9 million during the year ended December 31, 2020. The increase of $7.1 million was primarily attributable to an increase of $8.7 million in employee-related costs, of which $4.5 million was driven by non-cash stock-based compensation from incentive grants issued during the period and increased headcount to support our growth. Other increases include $2.4 million in rent and depreciation, $2.0 million in office supplies, equipment and software, and $0.7 million in insurance costs. These amounts were partially offset by a reduction of $6.4 million in allocable overhead and $0.3 million in external consultant expense.

Investment and Other Income, Net

Investment and other income was $0.4 million for the year ended December 31, 2021, compared to $0.7 million for the year ended December 31, 2020. The decrease of $0.3 million was primarily the result of a loss on foreign currency from our Australian subsidiary.

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 2020.

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 COVID-19 pandemic. The COVID-19 pandemic could adversely affect the economies and financial markets of the global economy, resulting in an economic downturn that could also 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, 2021, we raised a total of $701 million in gross proceeds from the sale of shares of our common stock and Series A, B and C convertible preferred units. As of December 31, 2021, we had $59.7 million in cash and cash equivalents, $280.2 million in marketable securities, and an accumulated deficit of $359.6 million. We had no indebtedness as of December 31, 2021.

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. From May 3, 2021 to December 31, 2021, we sold 125,643 shares of common stock under the 2021 Sales Agreement at a volume weighted-average price of $79.59 per share, raising aggregate gross proceeds of $10.0 million, before fees and expenses of $0.3 million.

July 2021 Follow-On Offering

In July 2021, we completed a follow-on offering of our common stock in which we issued and sold 3,565,000 shares of our common stock (including 465,000 shares of common stock in connection with the full exercise of the underwriters’ option to purchase additional shares) at a public offering price of $48.50 per share, resulting in aggregate gross proceeds of $172.9 million, before deducting underwriting discounts and commissions and offering expenses of $10.7 million.

Cash Flows

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

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Net cash used in operating activities	$ (154,093)	$ (86,825)
Net cash used in investing activities	(18,115)	(284,832)
Net cash provided by financing activities	178,521	360,439
Net increase/(decrease) in cash, cash equivalents and restricted cash	$ 6,313	$ (11,218)

Operating Activities

We have incurred losses since inception. 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, as well as changes in operating assets and liabilities of $16.6 million, partially offset by non-cash adjustments of $4.6 million.

Net cash used in operating activities for the year ended December 31, 2020 was $86.8 million, consisting primarily of our net loss of $118.5 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 $7.8 million and non-cash adjustments of $23.9 million.

Investing Activities

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

Net cash used in investing activities for the year ended December 31, 2020 of $284.8 million was attributable to the net investment of excess cash of $284.1 million and the purchases of property and equipment of $0.8 million.

Financing Activities

Net cash provided by financing activities for 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.

Net cash provided by financing activities in the year ended December 31, 2020 of $360.4 million primarily relates to net proceeds from the completion of our initial public offering of $172.5 million, net proceeds from our August 2020 follow-on offering of $155.9 million, net proceeds from the issuance of our Series C convertible preferred units of $14.2 million, and contributions from noncontrolling interest owners of $18.4 million.

Funding Requirements

Our operating expenses have increased substantially in 2021 and 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 ZN-c3, ZN-c5, ZN-d5 and ZN-e4 for the treatment of oncology indications;
- pursue the preclinical and clinical development of other current and future research programs and 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 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, 2021, we have $1.5 million and $44.5 million in current and long-term lease liabilities, respectively. We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2023. 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 ZN-c3, ZN-c5, ZN-d5 and ZN-e4;
- the progress, costs and results of additional research and preclinical studies in other research programs we initiate in the future;
- the costs and timing of process development and manufacturing scale-up activities associated with our product candidates and other programs 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 the pandemic continues to evolve globally. We have considered and will continue to consider the availability of relief provided by such legislative actions as the Families First Act and the CARES Act, and have opted to pursue certain, but not all measures including the deferral of employer payroll taxes, but not including Payroll Protection Plan loans. 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, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements and marketing and distribution arrangements.

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 requires 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.

Goodwill

Methodology	*Judgment and Uncertainties*	*Effect if Actual Results Differ From Assumptions*
Our goodwill 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 net tangible assets and intangible assets acquired. 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 value, we record an impairment loss based on the difference.	We use available market information and valuation methodologies using estimates to determine the fair values of the goodwill. We base our estimates on the best information available at the time and available market information may vary. If we over estimate the fair value of the goodwill, our actual impairment charge may differ from our estimates.

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 contract research organizations, (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, 2021 or 2020.

Share-Based Payments

Methodology	*Judgment and Uncertainties*	*Effect if Actual Results Differ From Assumptions*
The Company maintains a Stock Incentive Plan, which provides for share-based payment awards, including stock options, employee stock purchase plan, restricted stock and performance awards. 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, 2021, would have affected pre-tax earnings by approximately $3.6 million in 2021.

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 2021 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. We held cash and cash equivalents of $59.7 million and $55.0 million as of December 31, 2021 and 2020, 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, 2021.

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 Rule 13a-15(f). Under the supervision and with the participation of our management, including our CEO and our CFO, 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 CEO and CFO have concluded that our internal control over financial reporting was effective as of December 31, 2021.

The effectiveness of our internal control over financial reporting at December 31, 2021 has also been audited by Ernst & Young LLP, our independent registered public accounting firm, as stated in their report included in this Annual Report on Form 10-K on page F-1.

Changes in Internal Control over Financial Reporting

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

Item 9B. Other Information.

None.

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

Not applicable.

Part III

Item 10. Directors, Executive Officers and Corporate Governance.

Director Biographical Information

Biographical information concerning each of our directors is set forth below:

Name	Age	Position(s)
Anthony Y. Sun, M.D	49	President, Chief Executive Officer and Executive Chairman
David M. Johnson	56	Lead Director
Kimberly Blackwell, M.D.	52	Director
Cam S. Gallagher	52	Director
Enoch Kariuki, Pharm.D.	40	Director
Karan S. Takhar	30	Director

Anthony Y. Sun, M.D., has served as our President and Chief Executive Officer and a member of our Board of Directors since December 2014. From 2002 to 2015, Dr. Sun served in a variety of positions, including at Perseus-Soros BioPharmaceutical Fund and, most recently, as partner at Aisling Capital, a private equity firm dedicated to investing in life sciences companies. Dr. Sun currently serves on the board of directors of Immusoft Corporation, a preclinical gene therapy company, Eyenovia, Inc., a public ophthalmic biopharmaceutical company, and Alloy Therapeutics, Inc., a drug discovery platform company. Dr. Sun received a B.S. in Electrical Engineering from Cornell University, an M.D. from Temple University School of Medicine and an M.B.A from The Wharton School at the University of Pennsylvania. Dr. Sun trained in internal medicine at the Hospital of the University of Pennsylvania and was board certified in Internal Medicine. We believe Dr. Sun's extensive experience in the life sciences industry as an M.D., investor and executive and his deep understanding of our business, operations and strategy qualify him to serve on our Board of Directors.

David M. Johnson has served as a member of our Board of Directors since January 2020 and as our Lead Director since April 2020. Mr. Johnson has over 25 years of experience in biopharmaceutical oncology drug development and has made significant contributions to drugs ultimately garnering NDA/sNDA approval. He currently serves as the Chief Executive Officer of SolveTx, a venture backed start-up focused on developing next-generation mAb based oncology therapeutics, a position he has held since December 2021, as Board Chairman of Aura Biosciences, a clinical-stage biotechnology company developing virus-like drug conjugates, and as a board member of Palleon Pharmaceuticals, a biopharma company focused on novel immuno-oncology therapeutics. Mr. Johnson serves as Chairman of Lengo Therapeutics, a developer of precision medicines targeting driver mutations in oncology. Lengo was acquired by Blue Print Medicine during the fourth quarter of 2021. Prior to SolveTx, Mr. Johnson served as CEO of VelosBio, a clinical stage, oncology biopharmaceutical company until its acquisition by Merck in 2020. Prior to VelosBio, Mr. Johnson served as Chief Executive Officer of Acerta Pharma from 2014 to 2016 until the execution of a strategic transaction with AstraZeneca. Mr. Johnson's early career experience spanned from preclinical development to all phases of clinical development through product launch. He is a co-author on numerous publications and holds a bachelor's degree from Indiana University. We believe Mr. Johnson's extensive and diverse expertise in the life sciences industry, as an experienced executive of clinical stage companies, qualifies him to serve on our Board of Directors.

Kimberly Blackwell, M.D., has served as a member of our Board of Directors since July 2020. Dr. Blackwell currently serves as the Chief Medical Officer of Tempus Labs, a technology company advancing precision medicine through the practical application of artificial intelligence in healthcare, a position she has held since March 2020. From 2018 to 2020, Dr. Blackwell served as the Vice President of Early Stage Oncology and Immuno-oncology at Eli Lilly, where she led clinical teams advancing early phase therapeutics. From 2000 to 2018, Dr. Blackwell was a professor at Duke University where she oversaw the women's cancer program. Dr. Blackwell received an M.D. from Mayo Clinic Medical School and a B.S. 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 of Directors.

Cam S. Gallagher has served as a member of our Board of Directors since December 2014. Mr. Gallagher currently serves as the Chief Business Officer at Immusoft Corporation, a preclinical gene therapy company, a position he has held since April 2018, and as Board Chairman of Ocuphire, a clinical stage ophthalmology company. He was previously a board member of VelosBio, a clinical stage, oncology biopharmaceutical company, until its acquisition by Merck in December 2020. From 2016 to 2019, Mr. Gallagher served as the Head of Corporate Development and as a board member at Oncternal Therapeutics, Inc., a clinical stage, oncology biopharmaceutical company and, from 2014 to 2016, he served as a board member and the Chief Business Officer at Retrosense Therapeutics, LLC, a gene therapy company, until its acquisition by Allergan. From September 2012 to August 2014, Mr. Gallagher served on the board of directors of Sorrento Therapeutics, Inc., a clinical stage biopharmaceutical company developing therapies to treat malignant cancers. 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 of Directors.

Enoch Kariuki, Pharm. D., has served as a member of our Board of Directors since February 2021. Dr. Kariuki currently serves as a member of the board of directors and audit chair at Imago Biosciences, Inc. Most recently, Dr. Kariuki served as Chief Executive Officer of Lengo Therapeutics, until its acquisition by Blueprint Medicines during the fourth quarter of 2021. Previously, Dr. Kariuki served as Chief Financial Officer of VelosBio, a clinical stage, oncology biopharmaceutical company, from July 2020 until its acquisition by Merck in December 2020. From June 2018 to February 2020, Dr. Kariuki served as SVP, Corporate Development at Synthorx, Inc., a publicly-traded clinical stage biotechnology company, which was acquired by Sanofi and, from 2014 to April 2018, Dr. Kariuki served as VP at H.I.G. Capital, a private equity and alternative assets investment firm. Dr. Kariuki received an M.B.A. from the Tuck School of Business at Dartmouth College and a Pharm.D. from Texas Southern University. We believe Dr. Kariuki's experience as a senior financial executive, with both large and small commercial and clinical stage companies, in the life sciences industry qualifies him to serve on our Board of Directors.

Karan S. Takhar has served as a member of our Board of Directors since December 2017. Since 2013, Mr. Takhar has served in a variety of positions, most recently as Managing Director and head of Life Sciences investing at Matrix Capital Management Company, L.P., an investment fund focused on technology and life sciences. Mr. Takhar currently serves on the board of numerous private companies, including Aura Biosciences, Inc., Encoded Therapeutics Inc., ElevateBio LLC, Palleon Pharmaceuticals and Kalyra Pharmaceuticals, Inc. 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 of Directors.

Information about our Executive Officers

Biographical information concerning each of our executive officers is set forth below:

Name	Age	Position(s)
Anthony Y. Sun, M.D.	49	President, Chief Executive Officer and Executive Chairman
Melissa B. Epperly	44	Chief Financial Officer and Treasurer
Kevin D. Bunker, Ph.D.	49	Chief Operating Officer
Alexis M. Pinto, J.D.	55	Chief Legal Officer and Secretary
Dimitris Voliotis, M.D.	58	Senior Vice President, Clinical Development

Information concerning Anthony Y. Sun, M.D., our President and Chief Executive Officer, may be found above in the section entitled "Director Biographical Information."

Melissa B. 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, a clinical-stage gene therapy cancer company, where she led the company's financial operations. Prior to joining PsiOxus, Ms. Epperly served as Chief Financial Officer and head of Business Development at R-Pharm US, 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, 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. She received an M.B.A. from Harvard Business School and a B.A. in Biochemistry and Economics from the University of Virginia.

Kevin Bunker, Ph.D., has served as our Chief Operating Officer since 2015. Dr. Bunker serves as Chief Scientific/Operations Officer of Kalyra Pharmaceuticals, Inc., or 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. From 2006 to 2011, prior to founding Kalyra, Dr.

Bunker was part of the medicinal chemistry department at Pfizer, including as a Senior Scientist, where he made meaningful contributions to Pfizer'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. He also held a post-doctorate position as a research associate at The Scripps Research Institute under the direction of Professor Dale Boger.

Alexis M. Pinto, J.D., has served as our Chief Legal Officer since August 2020 and as Secretary since March 2021. Prior to joining Zentalis, Ms. Pinto served as Corporate Vice President and Corporate Secretary at Celgene Corporation, a global pharmaceutical company focusing on therapies to treat cancer and inflammatory diseases. During her tenure with Celgene, from 2015 to 2020, she led the company's legal operations in support of business development and strategy, executive compensation and securities, in addition to her role as Corporate Secretary. From 1997 to 2015, Ms. Pinto served in various roles at Merck & Co., Inc. During her tenure with Merck, Ms. Pinto held positions of increasing responsibility and scope in the areas of business development, mergers and acquisitions, labor and employment, licensing and vaccines. Prior to moving into the life sciences industry, Ms. Pinto was at Paul, Hastings, Janofsky & Walker LLP. She received her J.D. from the University of Virginia School of Law and her B.A. from the University of Virginia.

Dimitris Voliotis, M.D., has served as our Senior Vice President of Clinical Development since March 2020. Prior to joining Zentalis, Dr. Voliotis was Chief Development Officer at CureVac AG, a biopharmaceutical company that develops therapies based on messenger RNA, a position he held beginning in January 2019. At CureVac AG, Dr. Voliotis oversaw preclinical and clinical development activities for prophylactic vaccines, rare diseases/molecular therapies and oncology. From January 2016 to January 2019, Dr. Voliotis served as Senior Vice President and Head of Global Clinical Development in the Oncology Business Group at Eisai Inc., a pharmaceutical company focused on therapeutic areas of oncology and neurology. From 2014 to 2106, Dr. Voliotis served as Vice President, Therapeutic Area Head and Head of Global Clinical Research Oncology at Eisai Inc.. Prior to joining Eisai, Dr. Voliotis served in various leadership positions at Bayer Healthcare from 2001 to 2014, including most recently as Vice President and Head of Global Development Specialty Medicine/Oncology. Dr. Voliotis received his M.D. and his doctorate degree from the University of Cologne Medical School and is board certified in Medical Oncology & Hematology and Internal Medicine.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of our code of business conduct and ethics is available under the Corporate Governance section of our investor relations website at ir.zentalis.com. In addition, we intend to post on our website all disclosures that are required by law or the Nasdaq rules concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider our website to be a part of this Annual Report on Form 10-K.

Other

The remaining information required by this item will be included under the headings "Election of Directors," "Corporate Governance," and "Delinquent Section 16(a) Reports" (if applicable) in our definitive proxy statement for our 2022 Annual Meeting of Stockholders, and such required information is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this item will be included under the headings "Compensation Discussion and Analysis" and "Compensation Committee Interlocks and Insider Participation" (if applicable) in our definitive proxy statement for our 2022 Annual Meeting of Stockholders, and such information 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 under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance Under Equity Compensation Plans" in our definitive proxy statement for our 2022 Annual Meeting of Stockholders, and such required information is incorporated herein by reference.

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

The information required by this item will be included under the headings "Certain Relationships and Related Person Transactions," "Corporate Governance" and "Director Independence" in our definitive proxy statement for our 2022 Annual Meeting of Stockholders, and such information is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this item will be included under the heading "Principal Accountant Fees and Services" in our definitive proxy statement for our 2022 Annual Meeting of Stockholders, and such information is 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-35 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.

		Incorporated by Reference				
Exhibit Number	**Description**	**Form**	**File No.**	**Exhibit**	**Filing Date**	**Filed/Furnished Herewith**
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	
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	

Exhibit Number	Description	Incorporated by Reference				Filed/Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
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#	Form of Indemnification Agreement for Directors and Officers	S-1/A	333-236959	10.6	03/30/2020	
10.7	Lease Agreement, dated April 12, 2019, between Zeno Management, Inc. and G&S Realty 1, LLC	S-1	333-236959	10.7	03/06/2020	
10.8	Sublease Agreement, dated September 16, 2019, between Zeno Management, Inc. and Lundbeck La Jolla Research Center, Inc.	S-1	333-236959	10.8	03/06/2020	
10.9.1	Lease Agreement, dated November 12, 2015, between the Registrant and BMR-Road to the Cure, LP	S-1	333-236959	10.9	03/06/2020	
10.9.2	First Amendment to Lease Agreement, dated December 6, 2018, between the Registrant and BMR-Road to the Cure, LP	S-1	333-236959	10.1	03/06/2020	
10.10.1	Lease Agreement, dated January 14, 2020, between Zeno Management, Inc. and ARE-SD Region NO. 44, LLC	S-1	333-236959	10.11	03/06/2020	
10.10.2	Agreement for Termination of Lease and Voluntary Surrender of Premises, dated July 14, 2020, by and between Zeno Management, Inc. and ARE-SD-Region NO. 44, LLC	S-1/A	333-240115	10.23	07/28/2020	
10.11.1	Lease, effective September 30, 2020, between Zentalis Pharmaceuticals, Inc. and TPSC IX, LLC	8-K	001-39263	10.1	10/02/2020	
10.11.2	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	11/20/2021	
10.12	Lease, effective March 24, 2021, between Zentalis Pharmaceuticals, Inc. and ESRT 1359 BROADWAY, L.L.C.	10-K	001-39263	10.12	3/25/2021	
10.13#	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	

Exhibit Number	Description	Incorporated by Reference				Filed/Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
10.14#	Amended and Restated Employment Agreement, effective as of October 1, 2020, between Zeno Management, Inc. and Kevin Bunker, Ph.D.	8-K	001-39263	10.3	10/02/2020	
10.15#	Amended and Restated Employment Agreement, effective as of October 1, 2020, between Zeno Management Inc. and Melissa Epperly	8-K	001-39263	10.4	10/02/2020	
10.16#	Employment Agreement, effective as of July 20, 2020, between Zeno Management, Inc. and Alexis Pinto	10-Q	001-39263	10.7	11/09/2020	
10.17#	Employment Agreement, dated March 25, 2020, by and between Zeno Management, Inc. and Dimitris Voliotis, M.D.	S-1/A	333-236959	10.2	03/30/2020	
10.18#	Employment Agreement, effective as of October 1, 2020, between Zeno Management, Inc. and Cam Gallagher	10-Q	001-39263	10.6	11/09/2020	
10.19.1†	Second Amended and Restated License Agreement, dated September 6, 2019, between the Registrant and Recurium IP Holdings, LLC	S-1	333-236959	10.2	03/06/2020	
10.19.2†	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	
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					*
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: February 24, 2022

By: /s/ Anthony Y. Sun, M.D
Anthony Y. Sun, M.D.
Chief Executive Officer, President and Chairman

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/ Anthony Y. Sun, M.D. **Anthony Y. Sun, M.D.**	Chief Executive Officer, President and Executive Chairman *(principal executive officer)*	February 24, 2022
/s/ Melissa B. Epperly **Melissa B. Epperly**	Chief Financial Officer *(principal financial and accounting officer)*	February 24, 2022
/s/ David M. Johnson **David M. Johnson**	Lead Director	February 24, 2022
/s/ Kimberly Blackwell, M.D. **Kimberly Blackwell, M.D.**	Director	February 24, 2022
/s/ Cam S. Gallagher **Cam S. Gallagher**	Director	February 24, 2022
/s/ Enoch Kariuki **Enoch Kariuki**	Director	February 24, 2022
/s/ Karan S. Takhar **Karan S. Takhar**	Director	February 24, 2022

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, 2021 and 2020, 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, 2021, 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, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, 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, 2021, 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 February 24, 2022 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 Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters 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 matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Accrued clinical trial expenses

Description of the Matter

During 2021, the Company incurred $175.6 million for research and development expenses and as of December 31, 2021, the Company accrued $18.5 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.

Accounting for Zentera Therapeutics deconsolidation

Description of the Matter	As discussed in Note 3 to the consolidated financial statements, in July 2021, the Company's investee, Zentera Therapeutics (Cayman), Ltd., ("Zentera"), completed a Series B financing in which the Company did not participate. Until this date, the Company was deemed to be the primary beneficiary of Zentera, which is a variable interest entity, and consolidated Zentera accordingly. Upon the completion of the Series B financing, the Company concluded that it ceased to be the primary beneficiary in Zentera as equity ownership was reduced and changes were made to the corporate governance of Zentera. The Company concluded that it no longer was the primary beneficiary of Zentera, which resulted in the deconsolidation of Zentera effective July 13, 2021. The Company recorded its retained equity investment in Zentera at fair value under the equity method of accounting and recorded a gain of $51.6 million in the consolidated statement of operations as a result of the deconsolidation. Auditing management's conclusion that it ceased to be the primary beneficiary of Zentera and management's valuation of the resulting equity method investment in Zentera were complex and required significant auditor judgment. In particular, there was judgment involved in determining whether the Company continued to be the primary beneficiary of Zentera based on the contractual arrangements and corporate governance of Zentera. Additionally, the fair value measurement of the resulting equity method investment required specialized valuation knowledge.
How We Addressed the Matter in Our Audit	In assessing the appropriateness of the accounting for the deconsolidation of Zentera, our substantive audit procedures included, among others, reviewing management's analysis of whether the Company had the power to direct the activities that most significantly affected Zentera's economic performance. We reviewed management's analysis and compared certain information to underlying corporate governance documents, where we obtained an understanding of the composition and governance of the entity. To test the valuation of the resulting equity method investment in Zentera, we performed audit procedures that included, but were not limited to, assessing the methodologies used by the Company and testing the significant assumptions as well as the completeness and accuracy of the underlying data used by the Company in its analysis. We involved our valuation specialists to assist in evaluating the significant assumptions as well as the model utilized to derive the concluded fair value.

/s/ Ernst & Young LLP

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

San Diego, California
February 24, 2022

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

	December 31,	
	2021	2020
ASSETS		
Current assets		
Cash and cash equivalents	$ 59,714	$ 54,951
Marketable securities, available for sale	280,173	283,554
Accounts receivable from government grants, net	4	417
Prepaid expenses and other current assets	10,636	6,182
Restricted cash	243	—
Total current assets	350,770	345,104
Property and equipment, net	8,148	1,099
Operating lease right-of-use assets	44,691	2,520
Prepaid expenses and other assets	7,040	2,976
Goodwill	3,736	3,736
In-process research and development	—	8,800
Investment in Zentera Therapeutics	37,495	—
Restricted cash	2,627	1,320
Total assets	$ 454,507	$ 365,555
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 11,590	$ 8,661
Accrued expenses	32,354	19,940
Total current liabilities	43,944	28,601
Deferred tax liability	1,622	2,480
Long-term lease liability	44,459	1,097
Total liabilities	90,025	32,178
Commitments and contingencies (see Note 11)		
EQUITY		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, no shares issued and outstanding at December 31, 2021 and 2020	—	—
Common stock, $0.001 par value; 250,000,000 shares authorized; 45,490,764 and 41,040,286 shares issued and outstanding at December 31, 2021 and 2020, respectively	45	41
Additional paid-in capital	723,593	509,339
Accumulated other comprehensive income (loss)	(125)	36
Accumulated deficit	(359,559)	(200,834)
Total stockholders' equity	363,954	308,582
Noncontrolling interests	528	24,795
Total equity	364,482	333,377
Total liabilities and stockholders' equity	$ 454,507	$ 365,555

See accompanying notes to consolidated financial statements.

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

	Year ended December 31,		
	2021	2020	2019
Operating Expenses			
Research and development	$ 175,601	$ 84,901	38,386
General and administrative	40,941	33,886	8,459
Total operating expenses	216,542	118,787	46,845
Loss from operations	(216,542)	(118,787)	(46,845)
Other Income (Expense)			
Investment and other income, net	401	683	482
Gain on deconsolidation of Zentera	51,582	—	—
Net loss before income taxes	(164,559)	(118,104)	(46,363)
Income tax expense (benefit)	(297)	444	15
Loss on equity method investment	1,831	—	—
Net loss	(166,093)	(118,548)	(46,378)
Net loss attributable to noncontrolling interests	(7,368)	(707)	(715)
Net loss attributable to Zentalis	$ (158,725)	$ (117,841)	(45,663)
Net loss per common share outstanding, basic and diluted	$ (3.72)	$ (4.19)	$ —
Net loss per Class A common unit outstanding, basic and diluted	$ —	$ —	$ (8.16)
Common shares/units used in computing net loss per share/Class A common unit, basic and diluted	42,688	28,113	5,597

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,		
	2021	2020	2019
Net loss	$ (166,093)	$ (118,548)	$ (46,378)
Other comprehensive income (loss):			
Unrealized gain (loss) on marketable securities, net	(161)	36	—
Total comprehensive loss	(166,254)	(118,512)	(46,378)
Comprehensive loss attributable to noncontrolling interests	(7,368)	(707)	(715)
Comprehensive loss attributable to Zentalis	$ (158,886)	$ (117,805)	$ (45,663)

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, 2019														
	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, 2018	—	$ —	5,103	$59,830	5,594	$ 672	1,612	$1,598	—	$ —	$ —	$ —	$ (37,330)	$ 7,536	$ 32,306
Issuance of Series C convertible preferred units at $17.50 per unit net of issuance costs	4,847	81,876	—	—	—	—	—	—	—	—	—	—		—	—
Reclassification of convertible preferred units for contingent liquidation features not within the Company's control	5,103	59,830	(5,103)	(59,830)	—	—	—	—	—	—	—	—	—	—	(59,830)
Issuance of profit interest awards, net	—	—	—	—	—	—	1,059	—	—	—	—	—	—	—	—
Share-based compensation expenses	—	—	—	—	7	37	—	580	—	—	—	—	—	—	617
Net loss attributable to noncontrolling interest	—	—	—	—	—	—	—	—	—	—	—	—	—	(715)	(715)
Net loss attributable to Zentalis	—	—	—	—	—	—	—	—	—	—	—	—	(45,663)	—	(45,663)
Balance at December 31, 2019	9,950	$141,706	—	$ —	5,601	$ 709	2,671	$2,178	—	$ —	$ —	$ —	$ (82,993)	$ 6,821	$(73,285)

	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

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,		
	2021	**2020**	**2019**
Operating activities:			
Net loss	$ (166,093)	$ (118,548)	$ (46,378)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	544	160	111
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	35,737	23,146	617
Loss on disposal of equipment	15	—	—
Amortization of premiums on marketable securities, net	908	556	—
Loss on equity method investment	1,831	—	—
Deferred income taxes	—	17	—
Changes in operating assets and liabilities:			
Accounts receivable	413	(277)	777
Prepaid expenses and other assets	881	(5,519)	(1,508)
Accounts payable and accrued liabilities	13,916	14,307	7,123
Operating lease right-of-use assets and liabilities, net	1,347	(667)	115
Net cash used in operating activities	(154,093)	(86,825)	(39,143)
Investing activities:			
Purchases of marketable securities	(363,508)	(400,984)	—
Proceeds from maturities of marketable securities	365,820	116,910	—
Deconsolidation of Zentera cash	(14,320)	—	—
Purchases of property and equipment	(6,107)	(758)	(352)
Net cash used in investing activities	(18,115)	(284,832)	(352)
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	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	171,973	155,305	—
Proceeds from the issuance of Series C convertible preferred units, net	—	14,228	81,876
Deferred financing costs	—	—	(46)
Net cash provided by financing activities	178,521	360,439	81,830
Net increase/(decrease) in cash, cash equivalents and restricted cash	6,313	(11,218)	42,335
Cash, cash equivalents and restricted cash at beginning of year	56,271	67,489	25,154
Cash, cash equivalents and restricted cash at end of year	$ 62,584	$ 56,271	$ 67,489
Supplemental disclosure of cash flow information:			
Income taxes paid	$ 20	$ 18	$ 15
Supplemental disclosure of non-cash investing and financing activities:			
Right-of-use assets obtained in exchange for operating lease liabilities	$ 44,613	$ 300	$ 1,412
Accrued capital expenditures	$ 1,510	$ —	$ —
Costs incurred in connection with initial public offering included in accounts payable and accrued expenses	$ —	$ —	$ 795

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,		
	2021	2020	2019
Cash and cash equivalents	$ 59,714	$ 54,951	$ 67,246
Restricted cash, current	243	—	—
Restricted cash, non-current	2,627	1,320	243
Total cash, cash equivalents and restricted cash reported in the Consolidated Statement of Cash Flows	$ 62,584	$ 56,271	$ 67,489

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 pharmaceutical company focused on discovering and developing clinically differentiated, novel small molecule therapeutics targeting fundamental biological pathways of cancer. 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.

The Company was formed and incorporated in the state of Delaware as Zeno Pharmaceuticals, Inc. on December 23, 2014. Effective November 21, 2017, Zeno Pharma, LLC was formed by the shareholders of Zeno Pharmaceuticals, Inc. On December 21, 2017, Zeno Pharmaceuticals, Inc. became a wholly owned subsidiary of Zeno Pharma, LLC. In connection with this restructuring, the rights and preferences of the Preferred Stock of Zeno Pharmaceuticals, Inc. were exchanged for preferred units with similar rights and preferences of Zeno Pharma, LLC. As part of the restructuring, the employees, consultants and board members of Zeno Pharmaceuticals, Inc. exchanged their equity grants in Zeno Pharmaceuticals, Inc. stock for Class B common units in Zeno Pharma, LLC. Additionally, existing common stockholders of Zeno Pharmaceuticals, Inc. exchanged their common stock for Class A common units in Zeno Pharma, LLC. All exchanges were made on a one-for-one basis. The restructuring was accounted for as a common control transaction. In December 2019, the Company was renamed to Zentalis Pharmaceuticals, LLC.

Immediately prior to the effectiveness of the registration statement pertaining to the Company's initial public offering ("IPO") on April 2, 2020, the Company converted from a Delaware limited liability company into a Delaware corporation, and changed its name to Zentalis Pharmaceuticals, Inc. Pursuant to the statutory corporate conversion, all of the outstanding units of Zentalis Pharmaceuticals, LLC converted into shares of common stock of Zentalis Pharmaceuticals, Inc. based upon the value of Zentalis Pharmaceuticals, Inc. at the time of the IPO with a value implied by the price of the shares of common stock sold in the IPO. Based on the IPO price of $18.00 per share, the outstanding converted units converted into 25,288,854 shares of common stock (including 1,160,277 shares of restricted common stock).

On April 7, 2020, the Company completed the IPO in which the Company issued and sold 10,557,000 shares of common stock (including 1,377,000 shares of common stock in connection with the full exercise of the underwriters' option to purchase additional shares) at a public offering price of $18.00 per share. The Company's aggregate gross proceeds from the sale of shares in the IPO, including the sale of shares pursuant to the full exercise of the underwriters' option to purchase additional shares, was $190.0 million before fees and expenses of $17.6 million.

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 entity ("VIE"), for which we are 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 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, 2021 and 2020, 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, 2021 and 2020, restricted cash of $2.9 million and $1.3 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, accounts receivable, 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, account receivable, 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, 2021, 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, 2021 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 and common shares issuable upon the exercise of stock options.

Adoption and Pending Adoption of Recent Accounting Pronouncements

The following table provides a brief description of recently issued accounting standards, those adopted in the current period and those not yet adopted:

Standard	Description	Effective Date	Effect on the Financial Statements or Other Significant Matters
In January 2020, the FASB issued ASU 2020-01, Investments — Equity Securities (Topic 321).	This standard clarifies the interaction between accounting standards related to equity securities (ASC 321), equity method investments (ASC 323), and certain derivatives (ASC 815)	January 1, 2021	As of January 1, 2021, we did not hold equity securities, equity method investments or derivatives. The impact of this new accounting guidance in 2021 did not have a material impact to our consolidated financial statements at the time of adoption. As of July 2021, we hold an equity method investment which is accounted for under ASC 323. The investment is recorded on the consolidated statement of financial position at fair value as of the date of deconsolidation. The Company's subsequent share of earnings or losses of the investment entity are reported on the consolidated statement of operations through investment and other income, net with a corresponding increase or decrease to the equity investment.

3. Significant Transactions

Zentera Therapeutics

In May 2020, we became a majority common shareholder of Zentera Therapeutics, Ltd., 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 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 $37.5 million is recorded on our balance sheet at December 31, 2021. A deferred tax liability of $8.0 million representing the tax impact of the unrealized gain on deconsolidation is recorded on our balance sheet at December 31, 2021. 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 $7.1 million as of December 31, 2021. 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., Zeno Management 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-c3, ZN-c5 and ZN-d5, respectively, 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 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 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 period subsequent to deconsolidation to December 31, 2021, the amounts incurred under this arrangement totaled $5.3 million 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 Series B Preferred Stock representing a 25% equity interest in Kalyra Pharmaceuticals, Inc. 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 variable interest entity, 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 the change of control, Zentalis 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, 2021 and 2020 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,	
	2021	2020
Noncontrolling interest at beginning of period	$ 24,795	$ 6,821
Net loss attributable to noncontrolling interest	(7,368)	(450)
Contributions from noncontrolling interest holders of Zentera	—	18,424
Deconsolidation of Zentera	(16,899)	—
Noncontrolling interest at end of period	$ 528	$ 24,795

5. Fair Value Measurement

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

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Commercial paper	$ 199,321	$ 11	$ (55)	$ 199,277
Corporate debt securities	10,085	—	(7)	10,078
US government agencies	20,032	1	—	20,033
US Treasury securities	50,860	—	(75)	50,785
	$ 280,298	$ 12	$ (137)	$ 280,173

As of December 31, 2021, twenty-nine of our available-for-sale debt securities with a fair market value of $174.6 million were in a gross unrealized loss position of one hundred thirty-seven thousand dollars. 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, 2021, 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, 2021
	Estimated Fair Value
Due within one year	$ 258,948
After one but within five years	21,225
	$ 280,173

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, 2021			December 31, 2020		
	Level 1	Level 2	Total estimated fair value	Level 1	Level 2	Total estimated fair value
Cash equivalents:						
Money market funds	$ 43,653	$ —	$ 43,653	$ 24,016	$ —	$ 24,016
Corporate debt securities	—	—	—	—	4,999	4,999
Total cash equivalents:	43,653	—	43,653	24,016	4,999	29,015
Available-for-sale marketable securities:						
Commercial paper	—	199,277	199,277	—	147,388	147,388
Corporate debt securities	—	10,078	10,078	—	23,571	23,571
US government agencies	—	20,033	20,033	—	81,486	81,486
US Treasury securities	50,785	—	50,785	31,109	—	31,109
Total available-for-sale marketable securities:	50,785	229,388	280,173	31,109	252,445	283,554
Total assets measured at fair value	$ 94,438	$ 229,388	$ 323,826	$ 55,125	$ 257,444	$ 312,569

There were no transfers between Level 1 and Level 2 of the fair value hierarchy during the year ended December 31, 2021. We had no instruments that were classified within Level 3 as of December 31, 2021 or 2020.

6. Prepaid Expenses and Other Assets

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

	December 31,	
	2021	2020
Prepaid insurance	$ 990	$ 1,021
Prepaid software licenses and maintenance	403	563
Foreign R&D credit refund	1,808	692
Prepaid research and development expenses	11,204	5,963
Interest receivable	258	478
Zentera receivable	2,373	—
Other prepaid expenses	640	441
Total prepaid expenses and other current assets	17,676	9,158
Less long-term portion	7,040	2,976
Total prepaid expenses and other assets, current	$ 10,636	$ 6,182

7. Property and Equipment, net

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

	December 31,	
	2021	2020
Lab equipment	$ 2,057	$ 424
Leasehold improvements	4,515	49
Office equipment and furniture	2,123	405
Computer equipment	211	124
Construction in process	34	347
Subtotal	8,940	1,349
Accumulated depreciation and amortization	(792)	(250)
Property and equipment, net	$ 8,148	$ 1,099

Depreciation and amortization expense was approximately $0.5 million and $0.2 million for the years ended December 31, 2021 and 2020, respectively.

8. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,	
	2021	2020
Accrued research and development expenses	$ 18,531	$ 11,947
Accrued employee expenses	9,250	5,649
Accrued general and administrative expenses	1,480	996
Lease liability	1,453	902
Income taxes payable	971	410
Other	669	36
Total accrued expenses	$ 32,354	$ 19,940

9. Convertible Preferred Units

Series A Convertible Preferred Units

In September 2015, Zeno Pharmaceuticals, Inc. entered into a Series A Preferred Stock Purchase Agreement (the "Series A Preferred Agreement"). Under the terms of the Series A Preferred Agreement, Zeno Pharmaceuticals, Inc. issued 1,293,104 shares of Series A convertible preferred stock at $11.60 per share for gross proceeds of $15.0 million. The net proceeds of this financing were $14.9 million after issuance costs of $0.1 million. In February and March 2016, Zeno Pharmaceuticals, Inc. issued an aggregate of 286,205 additional shares of Series A convertible preferred stock at $11.60 per share for additional gross proceeds of $3.3 million. The issuance costs of this additional financing were approximately thirty-nine thousand dollars. All Series A convertible preferred stock issued and outstanding by Zeno Pharmaceuticals, Inc. was converted into Series A convertible preferred units of Zentalis Pharmaceuticals, LLC in conjunction with the corporate restructuring and merger (see Note 10).

Series B Convertible Preferred Units

In December 2017, Zentalis Pharmaceuticals, LLC entered into a Series B Preferred Unit Purchase Agreement (the "Series B Preferred Agreement"). Under the terms of the Series B Preferred Agreement, Zentalis Pharmaceuticals, LLC issued 2,735,320 Series B preferred units at $12.43 per unit for gross proceeds of $34.0 million. The net proceeds of this financing were $32.1 million after issuance costs of $1.9 million. In January and August 2018, Zentalis Pharmaceuticals, LLC issued an aggregate of 788,419 additional shares of Series B preferred units at $12.43 per unit for additional gross proceeds of $9.8 million. The net proceeds of this additional financing were $9.5 million after issuance costs of $0.3 million.

Series C Convertible Preferred Units

In September 2019, Zentalis Pharmaceuticals, LLC entered into a Series C Preferred Unit Purchase Agreement (the "Series C Preferred Agreement"). Under the terms of the Series C Preferred Agreement, Zentalis Pharmaceuticals, LLC issued 4,847,106 units of Series C convertible preferred units at $17.50 per unit for gross proceeds of $84.8 million. The net proceeds of this financing were $81.9 million after issuance costs of $2.9 million. In February 2020, Zentalis Pharmaceuticals, LLC issued 867,194 additional units of Series C preferred units under the Series C Preferred Agreement. The units were issued for $17.50 per unit for gross proceeds of $15.2 million. The net proceeds of this financing were $14.2 million after issuance costs of $1.0 million.

There were no authorized, issued, and outstanding shares of convertible preferred units at December 31, 2021 and 2020.

During 2019, we reclassified the convertible preferred units from members' equity to temporary equity because, in conjunction with the Series C convertible preferred units issuance, all units were now deemed to contain contingent liquidation features that are not solely within our control. During the year ended December 31, 2020, we did not adjust the carrying values of the convertible preferred units to the deemed redemption values of such units since a liquidation event was not probable.

Dividends

Dividends are payable if and when declared by the Board of Directors. No dividends have been declared through December 31, 2021.

Conversion

Each Series A preferred unit, Series B preferred unit and Series C preferred unit was convertible at the option of the holder thereof, at any time after the issuance of such unit, into Class A common units at a conversion price equal to the original purchase price (subject to anti-dilution adjustments, discussed below) which was $11.60, $12.43 and $17.50 per unit, respectively. The convertible preferred units automatically converted at the then applicable conversion rate upon the closing of a firm commitment underwritten public offering of shares of a successor corporations' common stock, at a public offering price per share of equal to or greater than the Series C original purchase price (as adjusted for any stock splits, stock dividends, combinations or other similar recapitalization) resulting in aggregate gross cash proceeds of at least $75.0 million (a "Qualified IPO"). Additionally, the convertible preferred unit would have automatically converted into common stock, at the then applicable conversion rate, upon written consent of a majority of the then outstanding Series A, Series B and Series C convertible preferred units (voting as a separate class on an as converted to Common Unit basis). In conjunction with our IPO on April 2, 2020, which constituted a Qualified IPO, all convertible preferred units were converted into common stock.

Anti-dilution protection

The holders of the convertible preferred units had proportional anti-dilution protection for unit splits, unit dividends and similar recapitalizations. Subject to certain exclusions, anti-dilution price protection for additional sales of securities by us for consideration per unit less than the applicable conversion price per unit of any series of convertible preferred stock, was on a broad-based weighted average basis.

Protective rights

The holders of the convertible preferred units had certain protective rights, including, without limitation, regarding the authorization, alteration, redemption, or sale of Class B common units; commencement of a liquidation or deemed liquidation event; entrance into a joint venture or partnership; any incurrence of indebtedness; certain transactions that exceed a certain dollar threshold; changes to our governing documents; or the declaration of any dividends. Such actions were required to be approved by a majority of the then outstanding Series A, Series B and Series C convertible preferred unit holders (voting as a single class and on an as-converted basis), as specified in the amended and restated LLC agreement. An increase or decrease in the authorized number of Directors constituting the Board or the creation of a membership interest or equity security senior to or pari passu with Series C convertible preferred units was required to be approved by a majority of the then outstanding Series C convertible preferred Units (voting as a separate class on an as converted basis).

Redemption

The Series A, Series B and Series C convertible preferred units were not redeemable except in the event of certain effected deemed liquidation events. As of immediately prior to our IPO on April 2, 2020 we had classified convertible preferred units as temporary equity in accordance with authoritative guidance for the classification and measurement of potentially redeemable securities whose redemption is based upon certain change in control events outside of our control, including liquidation, sale or transfer of control of the Company. We did not adjust the carrying value of the convertible preferred units to the deemed redemption values of such units since a liquidation event was not probable.

Liquidation preference

In the event of the dissolution, liquidation, merger or winding up of the Company, the holders of Series C convertible preferred units were entitled to receive, on a pro rata basis in respect of each such Series C convertible preferred unit, a preference amount of $17.50 per Series C convertible unit (as adjusted for any unit splits, dividends, combinations, recapitalizations or the like).

Subsequent to the payment of the Series C convertible preferred unit preferences, Series A and Series B convertible preferred units were entitled to receive, on a pro rata basis in respect of each convertible preferred unit in proportion to the relative preference amount of each preferred unit, a preference amount of $11.60 and $12.43 per unit of Series A and Series B convertible preferred units (as adjusted for any units splits, dividend, combinations, recapitalizations of the like), respectively.

Subsequent to the payment of the Series C, Series A and Series B convertible preferred unit preferences, Series A, Series B and Series C convertible preferred units were entitled to receive, on an as converted to common unit pro rata basis, an amount equal to distributions made to Class A common units prior to all unit classes sharing in distributions on a pro rata basis. Thereafter, Series A, Series B and Series C convertible preferred units and Series A and Series B common units were entitled to receive the remaining assets of the Company available for distribution to its unit holders pro rata based on the number of common units held by each holder, treating for these purposes as if all units had been converted to common.

Voting Rights

The holders of all units other than Class B common units that were unvested were to vote together as a single class. Each holder of Series A, Series B and Series C convertible preferred units were entitled to the number of votes calculated on an as converted to Class A common unit basis.

10. Equity and Share-based Compensation

In November 2017, Zentalis Pharmaceuticals, LLC was formed in the state of Delaware. In conjunction with a corporate restructuring, Zeno Pharmaceuticals, Inc., a Delaware corporation formed in 2014, was acquired by the Company pursuant to a merger agreement and became a wholly owned subsidiary of the Company. Per the terms of the merger agreement, each share of Zeno Pharmaceuticals, Inc. common stock issued and outstanding immediately prior to the effective time of the merger was

converted into the right to receive one Class A common unit and each share of Zeno Pharmaceuticals, Inc. Series A preferred stock issued and outstanding immediately prior to the effective date of the merger converted into the right to receive one Series A preferred unit. As of the effective time of the merger agreement, all outstanding options to purchase shares of Zeno Pharmaceuticals, Inc. common stock were cancelled and replaced with profit interest awards in the LLC.

In connection with the December 2017 corporate restructuring, we amended and restated the LLC agreement, and as amended, the capital units of the Company consisted of 1,638,000 authorized Series A preferred units, 3,621,000 authorized Series B preferred units, 15,000,000 authorized Class A common units and 872,620 authorized Class B common units.

Class A Common Units

In conjunction with the corporate restructuring in December 2017, 5,187,554 shares of common stock issued and outstanding and 406,831 shares of common stock subject to future vesting provisions of Zeno Pharmaceuticals, Inc. were converted into an equal number of Class A common units of Zentalis Pharmaceuticals, LLC. During the years ended December 31, 2021 and 2020, zero Class A common units were issued. As of December 31, 2021 and 2020, zero Class A common units were subject to future vesting conditions.

Class B Common Units

In conjunction with the corporate restructuring in December 2017, 703,000 options exercisable into Zeno Pharmaceuticals, Inc. common stock were converted into an equal number of Class B common units of Zentalis Pharmaceuticals, LLC. In September 2019, the number of authorized Class B common units was increased to 3,458,522.

IPO and Follow-on Offerings

On April 2, 2020 and immediately prior to the effectiveness of the Company's IPO, Zentalis Pharmaceuticals, LLC converted from a Delaware limited liability company into a Delaware corporation pursuant to a statutory conversion, and changed its name to Zentalis Pharmaceuticals, Inc. In order to consummate the corporate conversion, a certificate of conversion was filed with the Secretary of State of the State of Delaware. All of the outstanding units of Zentalis Pharmaceuticals, LLC converted into shares of common stock of Zentalis Pharmaceuticals, Inc. based upon the value of Zentalis Pharmaceuticals, Inc. at the time of the IPO with a value implied by the price of the shares of common stock sold in the IPO. No cash or fractional shares of common stock were issued in connection with the corporate conversion. Based on the IPO price of $18.00 per share of common stock, all of the outstanding units converted into an aggregate of 25,288,854 shares of common stock (including 1,160,277 shares of restricted common stock).

In connection with the completion of the IPO, the board and stockholders approved the certificate of incorporation to provide for 250,000,000 authorized shares of common stock with a par value of $0.001 per share and 10,000,000 authorized shares of preferred stock with a par value of $0.001 per share.

On April 7, 2020, the Company completed the IPO in which the Company issued and sold 10,557,000 shares of common stock (including 1,377,000 shares of common stock in connection with the full exercise of the underwriters' option to purchase additional shares) at a price of $18.00 per share. The Company's aggregate gross proceeds from the sale of shares in the IPO, including the sale of shares pursuant to the full exercise of the underwriters' option to purchase additional shares, was $190.0 million before fees and expenses of $17.6 million.

On August 3, 2020, the Company completed a follow-on offering in which the Company issued and sold 4,743,750 shares of common stock (including 618,750 shares of common stock in connection with the full exercise of the underwriters' option to purchase additional shares) at a public offering price of $35.00 per share. The Company's aggregate gross proceeds from the sale of shares in the follow-on offering, including the sale of shares pursuant to the exercise of the underwriters' option to purchase additional shares, was $166.0 million before fees and expenses of $10.8 million.

On July 1, 2021, the Company completed a follow-on offering in which the Company issued and sold 3,565,000 shares of common stock (including 465,000 shares of common stock in connection with the full exercise of the underwriters' option to purchase additional shares) at a public offering price of $48.50 per share. The Company's aggregate gross proceeds from the sale of shares in the follow-on offering, including the sale of shares pursuant to the full exercise of the underwriters' option to purchase additional shares, was $172.9 million before fees and expenses of $10.7 million.

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) 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 the Company's common stock. From May 3, 2021 to December 31, 2021 the Company sold 125,643 shares of common stock under the Sales Agreement at a volume weighted-average price of $79.59 per share, raising aggregate gross proceeds of $10.0 million before fees and expenses of $0.3 million.

Share-based Compensation

In the Company’s 2017 Profit Interest Plan ("the Plan") as approved and adopted by the Board of Directors on December 21, 2017, the Company was authorized to issue up to 3,458,522 shares of Class B common units ("profit interest award units"), subject to restrictions as described in the Plan.

In April 2020, the Plan was terminated and the Company’s board of directors adopted, and the Company’s stockholders approved the 2020 Incentive Award Plan ("the 2020 Plan"), which became effective upon the corporate conversion.

The number of common shares available for issuance under the 2020 Plan is 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. At December 31, 2021, 4,517,677 shares were subject to outstanding awards and 1,971,266 shares were available for future grants of share-based awards.

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.

During 2021, we issued an aggregate of 232,684 shares of common stock in connection with the exercises of stock options for cash in the aggregate amount of approximately $7.2 million. We did not issue any shares of common stock in connection with grants of RSA's. We issued 516,831 shares of common stock, upon vesting of RSU's. The RSU holders surrendered 17,080 RSU's to pay for minimum withholding taxes totaling approximately $1.1 million.

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

	Year ended December 31,		
	2021	2020	2019
Research and development expense	$ 20,858	$ 7,296	$ 339
General and administrative expense	14,879	15,850	278
Total share-based compensation expense	$ 35,737	$ 23,146	$ 617

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

	Year ended December 31,		
	2021	2020	2019
Profits interest award units	$ —	$ 329	$ 617
Stock options	20,773	6,925	—
RSAs and RSUs	14,643	15,892	—
Employee Stock Purchase Plan	321	—	—
	$ 35,737	$ 23,146	$ 617

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 and zero for the same period in 2020 and 2019, respectively.

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, 2021	
	Unrecognized Expense	Remaining Weighted-Average Recognition Period (Years)
Stock options	$ 71,753	3.0
RSAs	1,244	1.6
RSUs	6,157	2.3

Profits Interest Award Units: The following table provides a summary of the profits interest units award activity under the Plan. The amounts include profits interest units granted to both employees and non-employees:

	Number of Units	Weighted Average Fair Value
Outstanding at Outstanding at December 31, 2018	1,612,311	$ 1.56
Granted	1,095,545	$ 2.73
Forfeited	(37,188)	$ 1.62
Outstanding at Outstanding at December 31, 2019	2,670,668	$ 2.04
Granted	70,000	$ 3.06
Cancelled upon conversion	(2,740,668)	$ 2.07
Outstanding at December 31, 2020	—	$ —

The fair value of the profits interest award units was estimated using an option pricing model with the following assumptions:

	Year ended December 31,	
	2020	2019
Members' equity value (in thousands)	$271,207	$197,041 - $271,207
Threshold amounts (in thousands)	$309,824	$143,800 - $309,824
Risk-free rate	1.5%	1.5%
Volatility	75.0%	75.0%
Time to liquidity (in years)	1.1	1.1 - 1.8
Lack of marketability discount	26.5%	18.8% - 26.4%
Grant date fair value	$3.06	$1.88 - $3.06

The Black-Scholes-Merton option pricing model ("Black-Scholes model) was used to estimate the fair value of each profit interest award units on the date of grant. The members' equity value was based on a recent enterprise valuation analysis performed. The threshold amounts were determined by the Board of Directors at the time of grant. The expected life of the profits interest award units granted during the period presented was determined based on an expected liquidation event under the plan. We applied the risk-free interest rate based on the U.S. Treasury yield in effect at the time of the grant consistent with the life of the award. The expected volatility was based on a peer group in the industry in which the Company does business consistent with the expected time to liquidity. The dividend yield was set at zero as the underlying security does not and is not expected to pay a dividend. The Finnerty model and the Asian Protective Put Model methods were used to estimate the discount for lack of marketability inherent to the awards.

Stock Options: The following table summarizes option activity for the year ended December 31, 2021. The amounts include incentive units 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, 2020	3,121,221	$ 25.45		
Granted	1,527,300	$ 50.95		
Exercised	(232,684)	$ 30.73		
Cancelled	(172,355)	$ 34.49		
Outstanding at December 31, 2021	4,243,482	$ 33.97	8.7	$212,566
Vested and expected to vest at December 31, 2021	4,243,482	$ 33.97	8.7	$212,566
Exercisable at December 31, 2021	1,141,421	$ 24.84	8.4	$67,600

The weighted average grant date fair value of stock options granted during the years ended December 31, 2021 and 2020 was $33.27 and $16.79, respectively. The total intrinsic value of options exercised during the year ended December 31, 2021 and 2020 was approximately $8.8 million and zero, respectively.

The exercise price of stock options granted is equal to the closing price of the 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, 2021 was determined with the following assumptions:

	Year ended December 31,	
	2021	2020
Expected volatility	73.2% - 76.6%	76.4% - 78.7%
Average expected term (in years)	5.2 - 6.1	1.0 - 6.0
Risk-free interest rate	0.5% - 1.3%	0.1% - 0.5%
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 provides a summary of the RSA activity. The amounts include incentive units granted to both employees and non-employees:

	Number of Shares	Weighted Average Grant Date Fair Value
Outstanding at Outstanding at December 31, 2020	742,411	$ 3.03
Vested	(376,117)	$ 4.39
Forfeited	(4,462)	$ 3.80
Outstanding at December 31, 2021	361,832	$ 3.47

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 RSA's vested during the years ended December 31, 2021 and 2020 was approximately $1.7 million and $1.1 million, respectively. The fair value of RSA's vested during the years ended December 31, 2021 and 2020, was approximately $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 provides a summary of the restricted stock unit ("RSU") activity under the 2020 Plan. The amounts include incentive units granted to both employees and non-employees:

	Number of Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2020	674,757	$ 23.75
Granted	158,750	$ 39.82
Vested	(533,911)	$ 23.75
Forfeited	(25,401)	$ 23.75
Outstanding at December 31, 2021	274,195	$ 33.06

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 RSU's vested during the years ended December 31, 2021 and 2020 was approximately $12.7 million and $10.1 million, respectively. The fair value of RSUs vested during the years ended December 31, 2021 and 2020 was approximately $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 employee stock purchase plan are as follows:

	Year ended December 31,	
	2021	2020
ESPP		
Volatility	48.2 %	—
Expected term (years)	0.5	—
Risk free rate	0.1 %	—
Expected dividend yield	— %	—

Under the terms of the 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.

11. 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 settlements. 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.

Operating Leases

We entered into a non-cancellable operating lease agreement in January 2016 to lease 11,121 square feet of laboratory and office space in San Diego. In December 2018, we entered into an amendment to the lease to extend the term of the agreement through June 2022. The lease is subject to further extension or earlier termination and subject to approximately 3.0% annual increases throughout the term of the lease. We also pay a pro rata share of operating costs, including utilities, maintenance, insurance costs and real property taxes. As part of the amendment, we received incentives in the form of a base rate abatement period. This lease was terminated in January 2022, effective February 2022.

In April 2019, we entered into a lease for approximately 4,800 square feet of office space in New York, New York. The lease commenced in May 2019 and continues through June 30, 2023. The lease is subject to approximately 3.0% annual increases throughout the term of the lease. We received lease incentives under the agreement, including tenant allowances and a free rent period. We also pay for various operating costs, including utilities and real property taxes. The agreement does not contain a renewal option but does contain an early termination provision. This lease was terminated in April 2021, effective December 2021.

In August 2019, we entered into a sublease for approximately 2,333 square feet of office space adjacent to the existing laboratory and office space in San Diego, California. The lease commenced in October 2019 and continues through February 2022. The lease is subject to approximately 3.0% annual increases throughout the term of the lease. We also pay for various operating costs, including utilities and real property taxes. The agreement does not contain a renewal option or an early termination provision. This lease was terminated in January 2022, effective February 2022.

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 $2.6 million and $1.1 million for the years ended December 31, 2021 and 2020, respectively. We paid approximately $1.3 million and $1.0 million of lease payments, respectively, during the years ended December 31, 2021 and 2020.

The following table presents the weighted average remaining lease term and weighted average discount rates related to our operating leases as of December 31, 2021:

Weighted average remaining lease term (in years)	10.7
Weighted average discount rate	9.0%

Approximate annual future minimum operating lease payments as of December 31, 2021 are as follows (in thousands):

Year	Amount
2022	$ 3,277
2023	6,352
2024	6,498
2025	6,973
2026	7,291
Thereafter	45,622
Total minimum lease payments:	76,013
Less: imputed interest	30,101
Total operating lease liabilities	45,912
Less: current portion	1,453
Lease liability, net of current portion	$ 44,459

12. 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, 2021, 2020 and 2019 is as follows (in thousands):

	Year ended December 31,		
	2021	2020	2019
U.S. net loss before income taxes	$ (171,053)	$ (112,827)	$ (46,363)
Foreign net income (loss) before income taxes	4,663	(5,277)	—
Net loss before income taxes and loss on equity method investment	$ (166,390)	$ (118,104)	$ (46,363)

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,		
	2021	2020	2019
Current tax provision:			
Federal	$ —	$ —	$ —
State	11	16	$ 15
Foreign	550	410	$ —
Total current tax provision	561	426	$ 15
Deferred tax provision:			
Federal	(120)	—	—
State	(736)	—	—
Foreign	(2)	18	—
Total deferred tax provision	(858)	18	—
Total provision for income taxes:	$ (297)	$ 444	$ 15

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,					
	2021		2020		2019	
Expected tax at 21%	$ (34,941)	21.0 %	$ (24,802)	21.0 %	$ (9,730)	21.0 %
State income tax, net of federal tax	(931)	0.6 %	273	(0.3)%	(3,167)	6.8 %
Limited liability company loss	—	— %	—	— %	4	— %
Non-deductible expenses	—	— %	—	— %	164	(0.3)%
Research credits	(6,938)	4.2 %	(4,025)	3.4 %	(1,424)	3.1 %
Share-based compensation	(3,307)	2.0 %	(1,718)	1.5 %	—	— %
Other	939	(0.6)%	146	(0.1)%	(2)	— %
Section 162(m) limitations	3,982	(2.4)%	2,956	(2.5)%	—	— %
Change in valuation allowance	40,899	(24.6)%	27,614	(23.4)%	14,170	(30.6)%
Provision for income taxes	$ (297)	0.2 %	$ 444	(0.4)%	$ 15	0.0 %

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,	
	2021	2020
Deferred tax assets		
Net operating loss	$ 82,117	$ 45,730
Compensation	1,553	892
Share-based compensation	4,123	1,691
ASC 842 lease liability	9,740	425
Intangibles	2,004	—
Accrued liabilities	675	632
Research credits	14,466	7,528
Total gross deferred tax assets	114,678	56,898
Valuation allowance	(97,160)	(56,261)
Net deferred tax assets	17,518	637
Deferred tax liabilities		
Depreciable assets	(1,699)	(145)
ASC 842 right of use asset	(9,481)	(502)
In-process research and development	—	(2,463)
Equity method investment	(7,954)	—
Other	(6)	(7)
Deferred tax liabilities	(19,140)	(3,117)
Net deferred tax liabilities	$ (1,622)	$ (2,480)

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 $97.2 million and $56.3 million was required as of December 31, 2021 and 2020, 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, 2021.

At December 31, 2021, we have federal and state net operating loss ("NOL") carryforwards of approximately $361.1 million and $90.4 million, respectively. The federal NOL carryforwards generated prior to January 1, 2018 begin to expire in 2033. The federal NOL carryforwards generated after 2017 of $340.2 million can be carried forward indefinitely and be available to offset up to 80% of future taxable income each year. The state NOL carryforwards begin to expire in 2033.

At December 31, 2021, we have federal and state research tax credit carryforwards, net of reserves, of approximately $10.5 million and $3.9 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 Section 382 of the Code, as well as similar state provisions, has occurred. Utilization of our net operating loss 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 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,		
	2021	2020	2019
Gross unrecognized tax benefits at the beginning of the year	$ 1,932	$ 1,124	$ 741
Increase related to current year tax positions	969	661	383
Increase related to prior year tax positions	—	197	—
Decrease related to prior year tax positions	(66)	(50)	—
Gross unrecognized tax benefits at end of the year	$ 2,835	$ 1,932	$ 1,124

Included in the balance of unrecognized tax benefits at December 31, 2021 is $2.6 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, 2021 , 2020 and 2019 .

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.

In response to the COVID-19 pandemic, the Coronavirus Aid, Relief and Economic Security Act (CARES Act) was signed into law in the U.S. in March 2020. The CARES Act adjusted a number of provisions of the tax code, including the eligibility of certain deductions and the treatment of net operating losses and tax credits. The enactment of the CARES Act did not result in any material adjustments to the Company's income tax provision for the year ended December 31, 2021, or to its deferred tax assets as of December 31, 2021.

California Assembly Bill 85 (AB 85), which intends to close a gap in the budget created by the COVID-19 pandemic, was signed into law by Governor Gavin Newsom on June 29, 2020. It was passed by both houses of the California state legislature on June 15, 2020. AB 85 disallows utilization of California NOL carryforwards for any taxable year beginning on or after January 1, 2020, and before January 1, 2023 for any Corporation with a net business or modified adjusted gross income of more than $1.0 million for the taxable year. The bill also limits business credit utilization to offset a maximum of $5.0 million of California tax, including the California Research Credit. California Senate Bill 113 (SB 113) was signed into law by Governor Newsom on February 9, 2022, which restores the research and development credits net operating loss deductions for tax years beginning after December 31, 2021. We do not expect any material impacts related to this tax law change.

13. Net Loss Per Common Share/Class A Common Unit

Basic and diluted net loss per common share/Class A common unit were calculated as follows (in thousands except per share amounts):

	Year ended December 31,		
	2021	2020	2019
Numerator:			
Net loss attributable to Zentalis	$ (158,725)	$ (117,841)	$ (45,663)
Denominator:			
Weighted average number of common shares/Class A common units outstanding, basic and diluted	42,688	28,113	5,597
Net loss per common share	$ (3.72)	$ (4.19)	$ —
Net loss per Class A common unit			$ (8.16)

Our potential and dilutive securities, which include outstanding stock options, unvested RSAs, unvested RSUs and preferred units, have been excluded from the computation of diluted net loss per common share/Class A common unit as the effect would be anti-dilutive. We considered the impact of presenting a separate earnings per unit calculation for Class B

common units. However, as earnings and losses are only allocable to Class B common units after the applicable threshold had been met, and such thresholds had not been met for earnings per unit purposes, no losses were allocated to Class B common units.

The following common stock/Class A common unit equivalents have been excluded from the calculations of diluted net loss per common share/Class A common unit because their inclusion would be antidilutive (in thousands).

	Year ended December 31,		
	2021	2020	2019
Preferred units, as if converted to Class A common units	—	—	9,950
Incentive units - Class B common units	—	—	2,671
Outstanding stock options	4,243	3,121	—
Unvested RSAs	361	742	—
Unvested RSUs	274	675	—
	4,878	4,538	12,621

14. 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 $991.5 thousand in matching contributions for the year ended December 31, 2021.

15. Related Party Disclosures

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.

Prior to the investment, we entered into a license agreement and a master services agreement with Kalyra. The license agreement was signed and commenced on December 31, 2014 for the exclusive rights to develop and commercialize products derived from Kalyra's technology in the initial area of oncology. The license agreement and all rights were subsequently sold from Kalyra to Recurium IP Holdings, LLC ("Recurium IP"), an entity with common ownership to Kalyra prior to the Zentalis investment. Under the agreement, we have agreed to make payments to Recurium IP based on specific milestones. In addition, the Company shall pay mid- to high-single digit percentage royalties on net product sales to Recurium IP and sublicense fees on any consideration paid to us by a sublicensor. All payments are based on Recurium Equity, LLC's, an affiliated company of Recurium IP, equity ownership stake in us as of December 2020. The license agreement will terminate upon the later of the last expiration of the patent rights or 15 years from the date of commencement. For the years ended December 31, 2021 and 2020, we paid $10.0 million and zero, respectively, in milestone payments to Recurium IP.

The Master Services Agreement ("MSA") was entered into in January 2015 and 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, 2021 and 2020, we incurred an immaterial amount of expense with Kalyra that was eliminated in consolidation for research and development services provided. As of December 31, 2021 and 2020, 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, 2021 and 2020, we provided an immaterial amount of research and development services to Kalyra that was eliminated in consolidation. As of December 31, 2021 and 2020, an immaterial amount was due from Kalyra and eliminated in consolidation.

On June 1, 2020, we entered into an equipment purchase and sale agreement with Kalyra to purchase $0.4 million of equipment and related intangible assets to be used in our operations. As of December 31, 2021 and 2020, there was no balance due to Kalyra for this transaction.

Tempus

Kimberly Blackwell, M.D., is a member of the Company's board of directors and is also the Chief Medical Officer of Tempus Labs, Inc. ("Tempus"). The Company entered into a Master Services Agreement with Tempus in December 2020 to provide data licensing and research services. $1.0 million and zero fees were incurred for services performed by Tempus for the years ended December 31, 2021 and 2020, respectively.

Zentera

Anthony Y. Sun, M.D., our President and Chief Executive Officer, serves as Chief Executive Officer and a member of the board of directors of Zentera, and Kevin D. Bunker, Ph.D., our Chief Operating Officer, serves as a member of the board of directors of Zentera. Accordingly, the Company identifies Zentera as a related party.

In May 2020, we entered into the Zentera Sublicenses, pursuant to which we collaborate with Zentera on the development and commercialization of ZN-c3, ZN-c5 and ZN-d5, 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 period subsequent to deconsolidation through December 31, 2021, the amounts incurred under this arrangement totaled $5.3 million and are presented as contra-research and development expense in the consolidated statement of operations.

16. Selected Quarterly Financial Data (Unaudited)

Selected quarterly financial data is as follows:

	Three months ended			
	3/31/2021	6/30/2021	9/30/2021	12/31/2021
Operating Expenses				
Research and development	$ 38,394	$ 44,770	$ 53,998	$ 38,439
General and administrative	$ 11,953	$ 10,362	$ 8,872	$ 9,754
Total operating expenses	50,347	55,132	62,870	48,193
Operating loss	(50,347)	(55,132)	(62,870)	(48,193)
Other Income (Expense)				
Investment and other income (expense), net	$ 99	$ 115	$ 99	$ 88
Gain on deconsolidation of Zentera	$ —	$ —	$ 51,582	$ —
Net loss before income taxes	(50,248)	(55,017)	(11,189)	(48,105)
Income tax expense	$ 196	$ 45	$ (697)	$ 159
Loss on equity method investment	$ —	$ —	$ —	$ 1,831
Net loss	(50,444)	(55,062)	(10,492)	(50,095)
Net loss attributable to noncontrolling interests	(543)	(488)	(6,301)	(36)
Net loss attributable to Zentalis	$ (49,901)	$ (54,574)	$ (4,191)	$ (50,059)
Net loss per common share outstanding, basic and diluted	$ (1.24)	$ (1.34)	$ (0.09)	$ (1.11)
Common shares used in computing net loss per share, basic and diluted	40,359	40,738	44,609	44,976

	Three months ended			
	3/31/2020	6/30/2020	9/30/2020	12/31/2020
Operating Expenses				
Research and development	$ 13,258	$ 17,452	$ 24,670	$ 29,521
General and administrative	$ 3,141	$ 9,924	$ 10,097	$ 10,724
Total operating expenses	16,399	27,376	34,767	40,245
Operating loss	(16,399)	(27,376)	(34,767)	(40,245)
Other Income (Expense)				
Investment and other income (expense), net	$ 164	$ 84	$ 120	$ 315
Net loss before income taxes	(16,235)	(27,292)	(34,647)	(39,930)
Income tax expense	$ —	$ —	$ 18	$ 426
Net loss	(16,235)	(27,292)	(34,665)	(40,356)
Net loss attributable to noncontrolling interests	(109)	(435)	(110)	(53)
Net loss attributable to Zentalis	$ (16,126)	$ (26,857)	$ (34,555)	$ (40,303)
Net loss per common share outstanding, basic and diluted		$ (0.78)	$ (0.91)	$ (1.01)
Net loss per Class A common unit outstanding, basic and diluted	$ (2.88)			
Common shares/units used in computing net loss per share/Class A common unit, basic and diluted	5,601	34,353	37,959	39,936

ZENTALIS PHARMACEUTICALS, INC.

NON-EMPLOYEE DIRECTOR COMPENSATION PROGRAM

Amended February 22, 2022

Non-employee members of the board of directors (the "***Board***") of Zentalis Pharmaceuticals, Inc. (the "***Company***") shall receive cash and equity compensation as set forth in this Non-Employee Director Compensation Program (this "***Program***"). This Program has been adopted under the Company's 2020 Incentive Award Plan (the "***Equity Plan***") and shall be effective as of February 22, 2022 (the "***Effective Date***"). The cash and equity compensation described in this Program shall be paid or be made, as applicable, automatically and without further action of the Board, to each member of the Board who is not an employee of the Company or any parent or subsidiary of the Company (each, a "***Non-Employee Director***") who is entitled to receive such cash or equity compensation, unless such Non-Employee Director declines the receipt of such cash or equity compensation by written notice to the Company. This Program shall remain in effect until it is revised or rescinded by further action of the Board. This Program may be amended, modified or terminated by the Board at any time in its sole discretion. The terms and conditions of this Program shall supersede any prior cash and/or equity compensation arrangements for service as a member of the Board between the Company and any of its Non-Employee Directors. No Non-Employee Director shall have any rights hereunder, except with respect to equity awards granted pursuant to the Program. Capitalized terms not otherwise defined herein shall have the meanings ascribed in the Equity Plan.

1. Cash Compensation.

(a) Annual Retainers. Each Non-Employee Director shall receive an annual retainer of $45,000 for service on the Board.

(b) Additional Annual Retainers. In addition, each Non-Employee Director shall receive the following additional annual retainers, as applicable:

(i) Chairperson of the Board/Lead Independent Director. A Non-Employee Director serving as Chairperson of the Board or Lead Independent Director shall receive an additional annual retainer of $30,000 for such service.

(ii) Audit Committee. A Non-Employee Director serving as Chairperson of the Audit Committee shall receive an additional annual retainer of $20,000 for such service. A Non-Employee Director serving as a member of the Audit Committee (other than the Chairperson) shall receive an additional annual retainer of $10,000 for such service.

(iii) Compensation Committee. A Non-Employee Director serving as Chairperson of the Compensation Committee shall receive an additional annual retainer of $15,000 for such service. A Non-Employee Director serving as a member of the Compensation Committee (other than the Chairperson) shall receive an additional annual retainer of $7,500 for such service.

(iv) Nominating and Corporate Governance Committee. A Non-Employee Director serving as Chairperson of the Nominating and Corporate Governance Committee shall receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member of the Nominating and Corporate Governance Committee (other than the Chairperson) shall receive an additional annual retainer of $5,000 for such service.

(c) Payment of Retainers. The annual retainers described in Sections 1(a) and 1(b) shall be earned on a quarterly basis based on a calendar quarter and shall be paid by the Company in arrears not later than the fifteenth day following the end of each calendar quarter. In the event a Non-Employee Director does not serve as a Non-Employee Director, or in the applicable positions described in Section 1(b), for an entire calendar quarter, the retainer paid to such Non-Employee Director shall be prorated for the portion of such calendar quarter actually served as a Non-Employee Director, or in such position, as applicable.

2. Equity Compensation. Non-Employee Directors shall be granted the equity awards described below. The awards described below shall be granted under and shall be subject to the terms and provisions of the Equity Plan, or any other applicable Company equity incentive plan then-maintained by the Company, and shall be granted subject to the execution and delivery of award agreements, including attached exhibits, in substantially the forms previously approved by the Board. All applicable terms of the Equity Plan apply to this Program as if fully set forth herein, and all grants of equity awards hereby are subject in all respects to the terms of the Equity Plan and the applicable award agreement.

(a) Initial Awards. Each Non-Employee Director who is initially elected or appointed to the Board after the Effective Date shall receive an award of restricted stock units under the Equity Plan, or any other applicable Company equity incentive plan then-maintained by the Company, covering that number of shares of the Company's common stock as is determined by dividing (i) $1,000,000, by (ii) the average closing price per share of the Company's common stock for the thirty (30) calendar days preceding the date of grant. The awards described in this Section 2(a) shall be referred to as "***Initial Awards***." No Non-Employee Director shall be granted more than one Initial Award.

(b) Subsequent Awards. A Non-Employee Director who (i) is serving on the Board as of the date of any annual meeting of the Company's stockholders after the Effective Date and has been serving as a Non-Employee Director for at least six months as of the date of such meeting, and (ii) will continue to serve as a Non-Employee Director immediately following such meeting, shall be automatically granted an award of restricted stock units under the Equity Plan, or any other applicable Company equity incentive plan then-maintained by the Company, covering that number of shares of the Company's common stock as is determined by dividing (i) $500,000 (or, with respect to the Non-Employee Director serving as Chairperson of the Board or Lead Independent Director, $570,000), by (ii) the average closing price per share of the Company's common stock for the thirty (30) calendar days preceding the grant date. The awards described in this Section 2(b) shall be referred to as "***Subsequent Awards***." For the avoidance of doubt, a Non-Employee Director elected for the first time to the Board at an annual meeting of the Company's stockholders shall only receive an Initial Award in connection with such election, and shall not receive any Subsequent Award on the date of such meeting as well.

(c) Termination of Employment of Employee Directors. Members of the Board who are employees of the Company or any parent or subsidiary of the Company who subsequently terminate their employment with the Company and any parent or subsidiary of the Company and remain on the Board will not receive an Initial Award pursuant to Section 2(a) above, but to the extent that they are otherwise entitled, will receive, after termination from employment with the Company and any parent or subsidiary of the Company, Subsequent Awards as described in Section 2(b) above.

(d) Vesting of Awards Granted to Non-Employee Directors. Each Initial Award shall vest and become exercisable in substantially equal annual installments over the three (3) years following the date of grant, subject to the Non-Employee Director continuing in service on the Board through each such vesting date. Each Subsequent Award shall vest and/or become exercisable on the first to occur of (A) the first anniversary of the date of grant or (B) the next occurring annual meeting of the Company's stockholders, subject to the Non-Employee Director continuing in service on the Board through such vesting date. Unless the Board otherwise determines, no portion of an Initial Award or Subsequent Award which is unvested at the time of a Non-Employee Director's termination of service on the Board shall become vested thereafter. Unless otherwise expressly provided in an award agreement or other written agreement between the Company and a Non-Employee Director, upon a Change in Control (as defined in the Equity Plan), all outstanding equity awards granted under the Equity Plan, and any other equity incentive plan maintained by the Company, that are held by a Non-Employee Director shall become fully vested, irrespective of any other provisions of the Plan or any award agreement.

3. Compensation Limits. Notwithstanding anything to the contrary in this Program, commencing with the first calendar year following the Effective Date, all compensation payable under this Program will be subject to any limits on the maximum amount of Non-Employee Director compensation set forth in the Equity Plan, as in effect from time to time (which limits shall not apply to the compensation for any Non-Employee Director of the Company who serves in any capacity in addition

to that of a Non-Employee Director for which he or she receives additional compensation or any compensation paid to any non-employee director during the calendar year in which the Effective Date occurs).

4. Reimbursements. The Company shall reimburse each Non-Employee Director for all reasonable, documented, out-of-pocket travel and other business expenses incurred by such Non-Employee Director in the performance of his or her duties to the Company in accordance with the Company's applicable expense reimbursement policies and procedures as in effect from time to time.

* * * * *

Exhibit 21.1

Subsidiaries of Zentalis Pharmaceuticals, Inc.

Legal Name of Subsidiary	Jurisdiction of Organization
Zeno Management, Inc.	Delaware
Zeno Pharmaceuticals, Inc.	Delaware
Zeno Alpha, Inc.	Delaware
Zeno Beta, Inc.	Delaware
Zeno Gamma, Inc.	Delaware
K-Group Alpha, Inc.	Delaware
K-Group Beta, Inc.	Delaware
Zentalis Pharmaceuticals Australia Pty Ltd.	Australia
Zentalis Eta, Inc.	Delaware

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 Nos. 333-255737 and 333-255769) of Zentalis Pharmaceuticals, Inc.,
(2) Registration Statement (Form S-8 No. 333-237593) pertaining to the Zentalis Pharmaceuticals, Inc. 2020 Incentive Award Plan, and
(3) Registration Statement (Form S-8 No. 333-254506) pertaining to the Zentalis Pharmaceuticals, Inc. 2020 Employee Stock Purchase Plan;

of our reports dated February 24, 2022, with respect to the consolidated financial statements of Zentalis Pharmaceuticals, Inc. (Successor to Zentalis Pharmaceuticals, LLC) and the effectiveness of internal control over financial reporting of Zentalis Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Zentalis Pharmaceuticals, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

San Diego, California
February 24, 2022

Exhibit 31.1

CERTIFICATION

I, Anthony Y. Sun, M.D. certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: February 24, 2022

By: /s/ Anthony Y. Sun, M.D.
Anthony Y. Sun, M.D.
Chief Executive Officer, President and Chairman
(principal executive officer)

Exhibit 31.2

CERTIFICATION

I, Melissa B. Epperly, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: February 24, 2022

By: /s/ Melissa B. Epperly
Melissa B. Epperly
Chief Financial Officer
(*principal financial officer*)

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Zentalis Pharmaceuticals, Inc. (the "Company") for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

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

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

Date: February 24, 2022

By: /s/ Anthony Y. Sun, M.D.
Anthony Y. Sun, M.D.
Chief Executive Officer, President and Chairman
(principal executive officer)

Exhibit 32.2

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

In connection with the Annual Report on Form 10-K of Zentalis Pharmaceuticals, Inc. (the "Company") for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

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

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

Date: February 24, 2022

By: /s/ Melissa B. Epperly
Melissa B. Epperly
Chief Financial Officer
(*principal financial officer*)