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, 2025

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: 001-40671

NUVALENT, INC.

(Exact name of registrant as specified in its charter)

Delaware	**81-5112298**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
One Broadway, 14th Floor Cambridge, MA	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (857) 357-7000

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

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

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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	☐	Smaller reporting company	☐
Emerging growth company	☐		

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

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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

Based on the closing price of the registrant's Class A common stock on the last business day of the registrant's most recently completed second fiscal quarter, which was a closing price of $76.30 per share on June 30, 2025, as reported on the Nasdaq Global Select Market, the aggregate market value of its Class A common stock and Class B common stock held by non-affiliates was approximately $3.6 billion.

As of February 19, 2026, the registrant had 73,181,747 shares of Class A common stock, $0.0001 par value per share, outstanding and 5,435,254 shares of Class B common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for its 2026 Annual Meeting of Stockholders, which the registrant intends to file with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2025, are incorporated by reference into Part III of this Annual Report on Form 10-K.

Nuvalent, Inc.
Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K (Annual Report) of Nuvalent, Inc. contains express or implied forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act), that are based on our management's beliefs and assumptions and on information currently available to our management. These statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements contained in this Annual Report include, among other things, statements about:

- the initiation, timing, progress, results, and costs of our zidesamtinib (NVL-520), neladalkib (NVL-655), NVL-330 and discovery programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, alignment with the U.S. Food and Drug Administration (FDA) regarding the design of trials, and when the results of the studies or trials will become available;
- the ability of our preclinical studies and clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results;
- the beneficial characteristics, and the potential safety, efficacy and therapeutic effects of our product candidates;
- the timing, scope and likelihood of regulatory filings and approvals, including timing of Investigational New Drug applications (INDs), New Drug Applications (NDAs), and final FDA approval of our current product candidates or any future product candidates;
- the timing, scope or likelihood of foreign regulatory filings and approvals;
- our ability to identify research priorities and apply a risk-mitigated strategy to efficiently discover and develop product candidates, including by applying learnings from one program to other programs and from one indication to other indications;
- our estimates of the number of patients that we will enroll and our ability to initiate, recruit, and enroll patients in and conduct and successfully complete our clinical trials at the pace that we project;
- our ability to scale-up our manufacturing and processing approaches to appropriately address our anticipated commercial needs, which will require significant resources;
- our ability to maintain and further develop the specific shipping, storage, handling and administration of zidesamtinib, neladalkib and NVL-330 at clinical sites;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- our ability to take advantage of accelerated regulatory pathways for our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our ability to commercialize our product candidates, if approved, including the geographic areas of focus and sales strategy;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business, product candidates, and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and other product candidates we may develop, including the extensions of existing patent terms where available, the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- estimates of our future expenses, revenues, capital requirements, and our needs for additional funding;
- the period over which we estimate our existing cash, cash equivalents and marketable securities will be sufficient to fund our future operating expenses and capital expenditure requirements;
- future agreements with third parties in connection with the development and commercialization of our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our financial performance;
- the rate and degree of market acceptance of our product candidates, if approved;

- regulatory developments in the United States (the U.S.) and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our ability to produce our product candidates with advantages in turnaround times or manufacturing cost;
- our competitive position and the success of competing therapies that are or may become available;
- our need for and ability to attract, retain and hire key scientific, management, sales and marketing and other personnel;
- the impact of laws and regulations;
- developments relating to our competitors and our industry;
- the effect of public health emergencies, natural disasters or geopolitical events, including actual or threatened tariffs or other changes in trade policy, civil or political unrest or military conflicts, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and clinical trials; and
- other risks and uncertainties, including those listed under the section titled "Risk Factors."

In some cases, you can identify forward-looking statements by terminology such as "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target," "aim" or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," and elsewhere in this Annual Report. If one or more of these risks or uncertainties were to occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Annual Report and the documents that we reference in this Annual Report and have filed with the Securities and Exchange Commission (SEC) completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We do not undertake any obligation to publicly update any forward-looking statement except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

This Annual Report also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. All of the market data used in this Annual Report involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Except where the context otherwise requires or where otherwise indicated, the terms "Nuvalent," "we," "us," "our," "our Company," "the Company," and "our business" in this Annual Report refer to Nuvalent, Inc. and its consolidated subsidiary. Solely for convenience, the trademarks and trade names in this Annual Report may be referred to without the symbols ® and ™. Nuvalent and associated logos are trademarks of Nuvalent. Other brands, names and trademarks contained in this Annual Report are the property of their respective owners.

SUMMARY OF RISK FACTORS

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the section titled "Risk Factors" and should be carefully considered, together with other information in this Annual Report and our other filings with the SEC before making investment decisions regarding our common stock.

- We have a limited operating history, have no products approved for commercial sale and have not generated any revenue, which may make it difficult for investors to evaluate our current business and likelihood of success and viability;
- We have incurred significant net losses in each period since our inception, and we expect to continue to incur significant net losses for the foreseeable future;
- Our future prospects are substantially dependent on zidesamtinib (NVL-520), neladalkib (NVL-655) and NVL-330. If we are unable to advance these product candidates through development, obtain regulatory approval and ultimately commercialize such product candidates, or experience significant delays in doing so, our business will be materially harmed. Even if we obtain regulatory approval for such candidates, there is no assurance that our commercialization efforts will be successful or that we will be able to generate revenues or profits at the levels or on the timing we expect, if at all;
- Our preclinical studies and clinical trials may fail to adequately demonstrate the safety and efficacy of our product candidates, which would prevent or delay development, regulatory approval and commercialization;
- Our discovery and development activities are focused on the development of targeted therapeutics for patients with cancer-associated genomic alterations, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs may never lead to approved or marketable products;
- The outcome of preclinical testing and early clinical trials may not be predictive of the success of later-stage clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA, European Medicines Agency (EMA) or other comparable foreign regulatory authorities and we may not be able to commercialize our product candidates;
- In addition to zidesamtinib, neladalkib and NVL-330, our prospects depend in part upon discovering, developing and commercializing additional product candidates from our discovery programs, which may fail in development or suffer delays that adversely affect their commercial viability;
- Our product candidates may cause significant adverse events, toxicities or other undesirable adverse events when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences;
- Interim, preliminary and topline data from our preclinical studies and clinical trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data;
- If we experience delays or difficulties in the enrollment or maintenance of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented;
- We have never commercialized a product candidate as a company before and currently lack substantially all of the necessary expertise, personnel and resources to successfully commercialize any products on our own or together with suitable collaborators;
- Even if one of our product candidates receives marketing approval, we or others may later discover that the product is less effective or tolerable than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of our collaborators, to market the product;
- We face substantial competition which may result in others discovering, developing or commercializing products before or more successfully than we do;
- 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;
- The market opportunities for any product candidates we develop, if approved, may be limited to certain smaller patient subsets and may be smaller than we estimate them to be;
- We may be unable to obtain U.S. or foreign regulatory approval and, as a result, may be unable to commercialize our product candidates;
- Even if our product candidates receive regulatory approval, they will be subject to significant post-marketing regulatory requirements and oversight;

- Where appropriate, we plan to pursue approval from the FDA, EMA or comparable foreign regulatory authorities through the use of accelerated registration pathways. 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, EMA or comparable regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA, EMA or such other regulatory authorities may seek to withdraw accelerated approval;
- If our product candidates are licensed for marketing and receive federal healthcare reimbursement, any relationships we may have with healthcare providers will be subject to applicable healthcare fraud and abuse laws and regulations, which could expose us to criminal and civil penalties and exclusion from participation in government healthcare programs;
- If we are unable to establish adequate sales, marketing and distribution capabilities or enter into agreements with third parties to sell, market or distribute our product candidates, we may not be able to successfully commercialize our product candidates that obtain regulatory approval;
- If we are unable to obtain, maintain and enforce patent protection for our technology and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected;
- We may become involved in lawsuits to protect or enforce our patent or other intellectual property rights, which could be expensive, time-consuming and unsuccessful;
- Third parties may allege that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on our business;
- If we are unable to protect the confidentiality of our trade secrets and other proprietary information, our business and competitive position would be adversely affected;
- If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business may be adversely affected;
- We rely on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies;
- If we decide to establish collaborations, but are not able to establish those collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans;
- Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance;
- Our principal stockholders own a significant percentage of our stock and can exert significant control over matters subject to stockholder approval. Two of our directors are affiliated with one of our principal stockholders; and
- We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company focused on creating precisely targeted therapies for patients with cancer. We leverage our team's deep expertise in chemistry and structure-based drug design to develop innovative small molecules that are designed with the aim to overcome the limitations of existing therapies for clinically proven kinase targets.

Limitations faced by currently available kinase inhibitors can include (i) kinase resistance, or the emergence of new mutations in the kinase target that can enable resistance to existing therapies, (ii) kinase selectivity, or the potential for existing therapies to inhibit other structurally similar kinase targets and lead to off-target adverse events, and (iii) limited brain penetrance, or the ability for the therapy to treat disease that has spread or metastasized to the brain. By prioritizing target selectivity, we believe our drug candidates have the potential to overcome resistance, avoid dose-limiting off-target adverse events, address brain metastases, and drive more durable responses. This may result in the potential to drive deeper, more durable responses with minimal adverse events, and we believe these potential benefits may support opportunities for clinical utility earlier in the treatment paradigm.

Zidesamtinib (NVL-520)

Our first lead product candidate, zidesamtinib (NVL-520), is being developed for patients with ROS proto-oncogene 1 (ROS1)-positive non-small cell lung cancer (NSCLC). Zidesamtinib is a novel ROS1-selective inhibitor designed with the aim to address the clinical challenges of emergent treatment resistance, central nervous system (CNS)-related adverse events, and brain metastases that may limit the use of currently available ROS1 tyrosine kinase inhibitors (TKIs). Zidesamtinib has received FDA Breakthrough Therapy designation for the treatment of patients with locally advanced or metastatic (advanced) ROS1-positive NSCLC who have previously been treated with two or more prior ROS1 TKIs, and orphan drug designation for ROS1-positive NSCLC.

Our ARROS-1 clinical trial is a first-in-human global Phase 1/2, multicenter, open-label, dose-escalation and expansion study evaluating zidesamtinib as an oral monotherapy in patients with advanced ROS1-positive NSCLC and other solid tumors. Dosing was initiated in the Phase 1 portion of the ARROS-1 clinical trial in January 2022. From January 2022 to August 2023, the Phase 1 portion of the ARROS-1 trial enrolled 104 patients (99 NSCLC, 5 other solid tumors).

In September 2023, we announced the initiation of the Phase 2 portion of the ARROS-1 clinical trial, following alignment with the FDA on a recommended Phase 2 dose (RP2D) of 100 mg once daily (QD). The Phase 2 portion of the ARROS-1 clinical trial is designed to evaluate the safety and activity of zidesamtinib in patients with advanced ROS1-positive NSCLC and other solid tumors, examining several specific cohorts of patients based on the prior anti-cancer therapies that such patients have received. The Phase 2 cohorts have been designed to support potential registration in TKI-naïve and/or TKI pre-treated ROS1-positive NSCLC patients.

Between September 2023 and June 16, 2025, 435 patients were enrolled in the Phase 2 portion of the ARROS-1 clinical trial. In June 2025, we announced positive pivotal data for zidesamtinib in TKI pre-treated patients with advanced ROS1-positive NSCLC from the global ARROS-1 Phase 1/2 clinical trial, and in September 2025, we presented the pivotal dataset at the International Association for the Study of Lung Cancer 2025 World Conference on Lung Cancer. The primary efficacy analysis population for this pivotal dataset consisted of 117 TKI pre-treated patients with advanced ROS1-positive NSCLC with measurable disease who received zidesamtinib at the RP2D by May 31, 2024, with duration of response (DOR) follow-up of at least 6 months available for nearly all responders.

In June 2025, we also shared preliminary data from the Phase 2 TKI-naïve cohort in the ARROS-1 clinical trial, in which enrollment is ongoing. Encouraging preliminary data were available for 35 TKI-naïve patients with advanced ROS1-positive NSCLC treated with zidesamtinib at RP2D as of August 31, 2024. As of June 16, 2025, a total of 104 patients had been enrolled in the ongoing TKI-naïve cohort of the ARROS-1 trial.

In November 2025, the FDA accepted for filing our NDA for zidesamtinib for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who received at least 1 prior ROS1 TKI. The application has been assigned a Prescription Drug User Fee Act (PDUFA) target action date of September 18, 2026. Additionally, we plan to submit data from the ongoing TKI-naïve cohort in the Phase 2 portion of the ARROS-1 clinical trial to the FDA to support a potential label expansion of zidesamtinib in TKI-naïve patients with advanced ROS1-positive NSCLC in the second half of 2026.

Neladalkib (NVL-655)

Our second lead product candidate, neladalkib (NVL-655), is being developed for patients with anaplastic lymphoma kinase (ALK)-positive NSCLC. Neladalkib is a brain-penetrant ALK-selective inhibitor designed with the aim to address the clinical challenges of emergent treatment resistance, CNS-related adverse events, and brain metastases that may limit the use of first-generation (1G; crizotinib), second-generation (2G; ceritinib, alectinib, or brigatinib), and third-generation (3G; lorlatinib) ALK inhibitors. Neladalkib has received FDA Breakthrough Therapy designation for the treatment of patients with locally advanced or metastatic ALK-positive NSCLC who have been previously treated with two or more ALK TKIs, and orphan drug designation for ALK-positive NSCLC.

Our ALKOVE-1 clinical trial is a first-in-human global Phase 1/2, multicenter, open-label, dose-escalation and expansion study evaluating neladalkib as an oral monotherapy in patients with advanced ALK-positive NSCLC and other solid tumors. Dosing was initiated in the Phase 1 portion of the ALKOVE-1 clinical trial in June 2022. From June 2022 to February 2024, the Phase 1 portion of the ALKOVE-1 clinical trial enrolled 133 patients (131 NSCLC, 2 other solid tumors).

In February 2024, we announced the initiation of the Phase 2 portion of the ALKOVE-1 clinical trial, following alignment with the FDA on a RP2D of 150 mg QD. The Phase 2 portion of the ALKOVE-1 clinical trial is designed to evaluate the safety and activity of neladalkib in several expansion cohorts of patients defined based on the number and type of prior anti-cancer therapies they have received. The Phase 2 cohorts are designed with registrational intent for TKI pre-treated patients with ALK-positive NSCLC and to enable preliminary evaluation for patients with ALK-positive NSCLC who are TKI-naïve.

In July 2025, we announced the initiation of the ALKAZAR Phase 3 clinical trial with registrational intent for TKI-naïve patients with advanced ALK-positive NSCLC. The ALKAZAR clinical trial is a global, randomized, controlled trial designed to evaluate neladalkib versus the current standard of care. Patients are randomized 1:1 to receive neladalkib monotherapy or ALECENSA (alectinib) monotherapy, reflecting input from collaborating physician-scientists and alignment with global regulatory agencies. The ALKAZAR clinical trial is designed to enroll approximately 450 patients with TKI-naïve ALK-positive NSCLC. The primary endpoint is progression free survival (PFS) based on Blinded Independent Central Review (BICR). Secondary endpoints include overall survival, PFS based on investigator's assessment, time to intracranial response, and BICR assessment of intracranial objective response rate (IC-ORR), intracranial duration of response (IC-DOR), objective response rate (ORR), DOR, time to intracranial progression, and safety.

At the European Society for Medical Oncology Congress (ESMO) in October 2025, we presented preliminary data for neladalkib in patients with advanced ALK-positive solid tumors outside of NSCLC from the ongoing ALKOVE-1 clinical trial. Neladalkib demonstrated encouraging preliminary activity across a diverse set of ALK TKI-naïve and previously treated advanced ALK-positive solid tumors, and was considered generally safe and well-tolerated with a preliminary overall safety profile consistent with its ALK-selective, tropomyosin receptor kinase (TRK)-sparing design, and with previously reported data.

In November 2025, we announced positive topline data for neladalkib in TKI pre-treated patients with advanced ALK-positive NSCLC from the global ALKOVE-1 Phase 1/2 clinical trial. In this topline dataset, data were pooled across Phase 1 and 2 and reported for the primary endpoint of objective response rate (ORR, RECIST 1.1) by BICR. Key secondary endpoints include DOR, IC-ORR, and safety.

As of the data cut-off date of August 29, 2025, 781 patients with ALK-positive solid tumors had received neladalkib at any starting dose across the Phase 1 and Phase 2 portions of the ALKOVE-1 clinical trial. Of these, 656 patients with advanced ALK-positive NSCLC were treated with neladalkib at the RP2D.

The primary analysis population consisted of 253 TKI pre-treated patients with advanced ALK-positive NSCLC with measurable disease by BICR who received neladalkib at the RP2D by September 30, 2024, with DOR follow-up of at least 6 months available for nearly all responders.

The primary analysis population was distinct from the ALK TKI pre-treated populations that have been reported for the currently available ALK TKIs:

- Patients received a median of 3 prior lines of therapy (range, 1 – 11) and 51% had received prior chemotherapy.
- 78% of patients had received 2 or more prior ALK TKIs ± prior chemotherapy, of which 91% had received prior lorlatinib. No approved therapies have demonstrated activity after lorlatinib.
- 19% of patients had a secondary ALK G1202R resistance mutation, and 17% had a compound ALK resistance mutation, which are key drivers of disease progression.
- 40% of patients had active CNS disease by BICR at baseline.

Of the overall TKI pre-treated population, 25% (63/253) of patients were lorlatinib-naïve. Within this subpopulation:

- 25% received prior chemotherapy.
- 100% had received ≥ 1 prior 2G ALK TKI ± prior chemotherapy, of which 70% received prior alectinib only. No patients received crizotinib as their only ALK TKI.
- 19% of patients had a secondary ALK G1202R mutation.
- 35% had active CNS disease by BICR at baseline.

Activity was observed across subsets of TKI pre-treated patients, and DOR was assessed as the probability of patients remaining in response for at least 6, 12, and 18 months by Kaplan-Meier estimate (Table 1).

Table 1.	Any prior ALK TKI ± chemotherapy[a]	TKI Pre-treated, Lorlatinib-naïve[b]
n	253	63
ORR, % (n/N) (95% CI)	31% (79/253)[c,d] (26, 37)	46% (29/63)[e] (33, 59)
% DOR ≥ 6 months[f] (95% CI)	76% (64, 84)	89% (69, 96)
% DOR ≥ 12 months[f] (95% CI)	64% (51, 75)	80% (58, 91)
% DOR ≥ 18 months[f] (95% CI)	53% (34, 68)	60% (19, 85)
G1202R mutation[g]		
n	47	12
ORR, % (n/N) (95% CI)	68% (32/47)[h,i] (53, 81)	83% (10/12) (52, 98)
% DOR ≥ 6 months[f] (95% CI)	84% (65, 93)	90% (47, 99)
% DOR ≥ 12 months[f] (95% CI)	80% (61, 91)	77% (34, 94)
% DOR ≥ 18 months[f] (95% CI)	70% (42, 86)	77% (34, 94)
Measurable CNS lesions		
n	92[j]	24[k]
IC-ORR, % (n/N) (95% CI)	32% (29/92)[l,m] (22, 42)	63% (15/24)[l] (41, 81)
IC-CR, % (n/N)	13% (12/92)[n]	21% (5/24)[n]
% IC-DOR ≥ 6 months[f] (95% CI)	81% (59, 91)	92% (57, 99)
% IC-DOR ≥ 12 months[f] (95% CI)	71% (48, 85)	92% (57, 99)
% IC-DOR ≥ 18 months[f] (95% CI)	71% (48, 85)	92% (57, 99)

[a] Median DOR (mDOR) not reached with median follow-up of 11.3 months.

[b] mDOR not reached.

[c] Includes 2 unconfirmed partial responses (uPRs).

[d] Includes responses in patients previously treated with lorlatinib (ORR = 26% (50/190 including 2 uPRs) with mDOR = 17.6 months (95% CI: 6.9, not estimable (NE))).

[e] For patients receiving only 1 prior 2G ALK TKI (alectinib (n = 44) or brigatinib (n = 2)) ± chemotherapy, ORR was 48% (22/46) with mDOR not reached, and DOR ≥ 12 and 18 months of 74% (95% CI: 48, 88).

[f] Estimated for responders by Kaplan-Meier analysis.

[g] ALK G1202R mutation identified in local or central testing of blood or tissue. Patients may have had other mutations in addition to ALK G1202R.

[h] Includes responses in patients with compound ALK mutations (≥ 2 ALK mutations, cis allelic configuration not determined in all cases) after ≥ 2 prior ALK TKIs (ORR = 58% (25/43, including 1 uPR) with DOR ≥ 12 months of 69% (95% CI: 45, 84)) and in patients with ALK resistance mutations other than G1202R, including C1156Y, I1171N, I1171T, F1174C, F1174L, V1180L, L1196M, L1198F, D1203N, E1210K, and G1269A.

[i] Includes 1 uPR.

[j] For intracranial (IC) responders, the emerging IC-mDOR was 21.6 months (95% CI: 10.1, NE) and continues to mature.

[k] For IC-responders, the emerging IC-mDOR was 21.6 months (95% CI: 21.6, NE) and continues to mature.

[l] Includes 2 IC-uPRs.

[m] IC responses were also observed in lorlatinib-experienced patients with measurable CNS lesions at baseline (IC-ORR = 21%, 14/68) with IC-mDOR not reached, IC-DOR ≥ 6 months of 71% (95% CI: 41, 88), and IC-DOR ≥ 12 and 18 months of 55% (95% CI: 26, 77).

[n] Includes 1 intracranial unconfirmed complete response (IC-uCR) with prior confirmed IC-PR.

In November 2025, we also shared preliminary data from the Phase 2 exploratory cohort for TKI-naïve patients with advanced ALK-positive NSCLC from the ALKOVE-1 study. Encouraging preliminary data were available for 44 TKI-naïve patients with advanced

ALK-positive NSCLC and measurable disease by BICR. These patients were treated with neladalkib at RP2D in an exploratory cohort of ALKOVE-1, with data cut-off of August 29, 2025. Patients may have received up to one prior line of chemotherapy.

In the TKI-naïve ALK-positive NSCLC population, the preliminary ORR was 86% (38/44; 2 uPRs) and a CR rate of 9% (4/44; 1 uCR with prior confirmed PR) was observed. DOR ranged from 1.7+ to 14.8+ months with DOR ≥ 6 and 12 months of 91% (95% CI: 70, 98) and only two progression events among responders. In 9 patients with measurable intracranial lesions, the IC-ORR was 78% (7/9) and the intracranial CR rate was 44% (4/9; 1 IC-uCR with prior confirmed IC-PR). The IC-DOR ranged from 3.1+ to 7.0+ months with no CNS progression among responders.

Neladalkib demonstrated a generally well-tolerated safety profile consistent with its ALK-selective, TRK-sparing design. In the 656 patients with advanced ALK-positive NSCLC treated at RP2D as of the data cut-off date, the median duration of exposure was 6.0 months (range, 0.1, 28.4). The most frequent treatment-emergent adverse events (TEAEs) occurring in ≥ 15% of patients were alanine aminotransferase increased (47%), aspartate aminotransferase increased (44%), constipation (28%), dysgeusia (23%), peripheral edema (18%) and cough and nausea (16% each). The most common TEAE of transaminase elevations were generally observed to be asymptomatic lab abnormalities that were low-grade, transient, and reversible with dose interruptions or reductions. Preliminary data suggest increased incidence in less heavily pre-treated patients. Enhanced monitoring for transaminase elevations and prompt dose interventions have been implemented in the protocol for the ALKAZAR Phase 3 randomized, controlled clinical trial. Across the 656 patients treated in ALKOVE-1 at RP2D, dose reductions due to TEAEs occurred in 17% of patients and 5% of patients discontinued treatment due to TEAEs.

We have completed our pre-NDA meeting with the FDA and plan to move forward with an NDA submission of the data for TKI pre-treated patients with advanced ALK-positive NSCLC from our ALKOVE-1 study of neladalkib in the first half of 2026. We plan to present detailed study results at a future medical meeting.

NVL-330

Our third product candidate, NVL-330, is a brain-penetrant human epidermal growth factor receptor 2 (HER2)-selective inhibitor designed with the aim to address the combined medical needs of treating tumors driven by HER2 mutations and alterations, including HER2 exon 20 insertion mutations (HER2ex20), treating brain metastases, and avoiding treatment-limiting adverse events including due to off-target inhibition of wild-type epidermal growth factor receptor (EGFR). Preclinical data have shown that NVL-330 inhibited a broad range of HER2 oncogenic alterations, including HER2ex20, in cell-based assays, was brain penetrant and was selective for HER2 oncogenic alterations over the structurally related wild-type EGFR. Additionally, new preclinical data were presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in October 2025, further supporting NVL-330's potentially differentiated brain-penetrant profile. Compared to several currently available and investigational HER2 TKIs in the same preclinical assays, NVL-330 demonstrated a favorable efflux ratio and brain partitioning, metrics that are potentially positive predictors of brain exposure in humans. In preclinical models of intracranial activity, NVL-330 induced deep intracranial regression in mice. In the same models, the approved therapies Enhertu (T-DXd) and Hernexeos (zongertinib) did not induce intracranial regression at their clinically relevant doses. Additionally, NVL-330 induced intracranial tumor regression in mice that had progressed in the CNS on zongertinib.

We are currently enrolling patients in the HEROEX-1 clinical trial, a global Phase 1a/1b, multicenter, open-label, dose-escalation and expansion trial evaluating NVL-330 in pre-treated patients with advanced HER2-altered NSCLC, including those with HER2ex20 mutations. In July 2024, we announced that the first patient was dosed with NVL-330 in the HEROEX-1 trial. The HEROEX-1 trial is evaluating the overall safety and tolerability of NVL-330. Additional objectives include determination of the RP2D, characterization of the pharmacokinetic profile, and preliminary evaluation of anti-tumor activity.

Discovery Programs

We have prioritized a number of additional small molecule research programs following an assessment of medical need. Research for these programs is ongoing, and we plan to disclose a new development candidate by year-end 2026.

Our approach

Our approach is built on four core principles:

- ***Patient-driven focus.*** We prioritize therapeutic targets where patient needs and limitations of existing therapies can be identified and characterized in partnership with physician-scientists. Leveraging our team's deep expertise and experience in drug discovery, we translate those medical insights into detailed target product profiles with well-defined selection criteria to ensure that our product candidates are purpose-built to address specific and current medical needs.
- ***Deep expertise in chemistry and structure-based drug design to achieve precise selectivity ("Threading the needle").*** We prioritize exquisite target selectivity in the design of our molecules to precisely meet the selection criteria we have pre-defined in our target product profiles. Leveraging our team's deep expertise in chemistry and structure-based drug design, we 'thread the needle' to navigate competing molecular challenges and develop innovative small molecules that have the potential to overcome resistance, minimize adverse events, optimize CNS activity, and drive more durable responses.

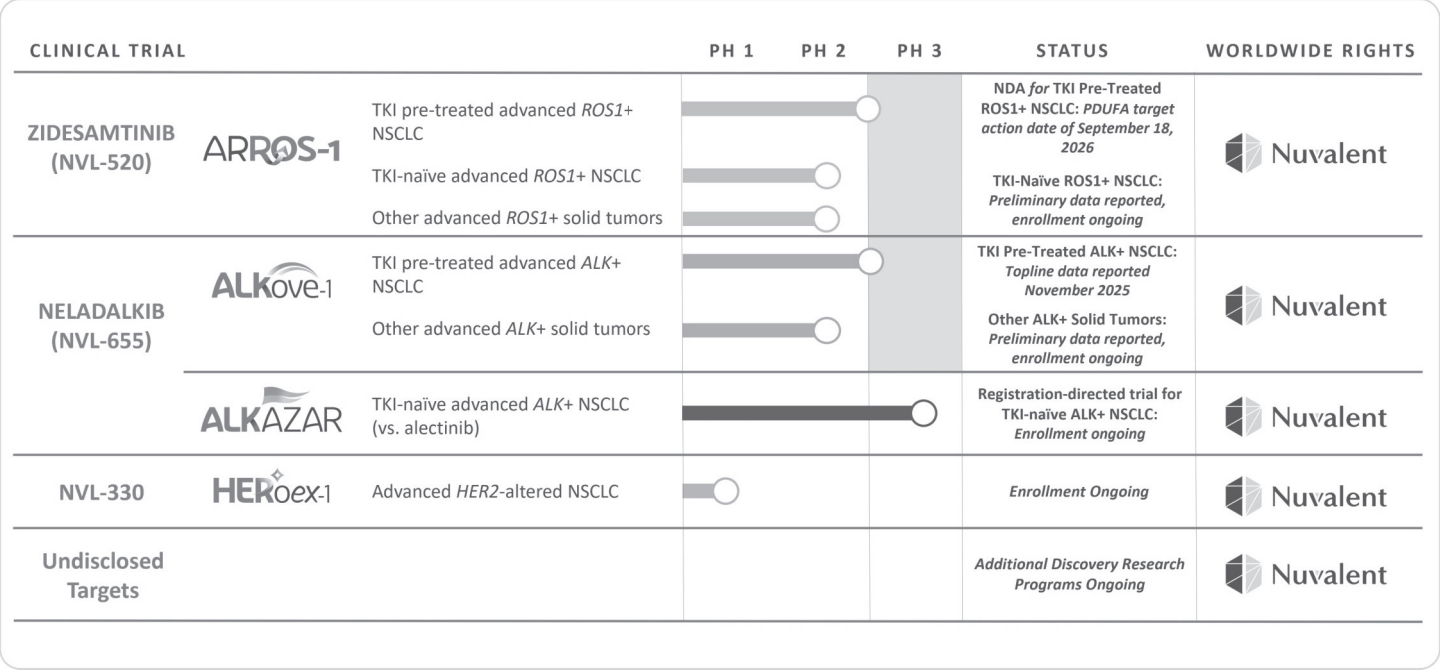
- ***Efficient drug discovery and development.*** We prioritize programs that may leverage our pipeline discovery and development efforts and experience, with a specific focus on clinically proven kinase targets, with the goal of bringing our therapies to patients as soon as possible. Building on existing discovery tools and processes for the investigation of clinically proven kinase targets, we further leverage our team's deep experience in the advancement of oncology product candidates from nomination through product launch, including potential opportunities for accelerated regulatory pathways, to achieve an efficient approach to drug discovery and development.
- ***Commercialization of our product candidates, if approved, in key geographies.*** We retain full development and worldwide commercialization rights to our pipeline of precisely targeted therapies. We are building a fully integrated, commercial-stage biotechnology company capable of not only discovering and developing, but delivering new medicines for patients living with cancer.

With the continued increase in the adoption of kinase inhibitors as the standard of care across a broadening set of indications, we believe that opportunities to apply our established approach of efficient drug discovery and development will continue to grow.

Our programs

We are currently advancing two parallel lead programs in addition to multiple early-stage development and discovery programs, as summarized in Figure 1 below. We hold worldwide development and commercialization rights to our product candidates.

Figure 1. Our pipeline of kinase inhibitor product candidates



Zidesamtinib (NVL-520, ROS1-Selective inhibitor)

ROS1 rearrangements occur in up to approximately 3% of metastatic NSCLCs. At the time of diagnosis, up to 40% of these patients present with accompanying brain metastases. Beyond NSCLC, ROS1 rearrangements have also been reported across a wide range of solid tumors as well as lymphoma.

There are four FDA-approved TKIs for the treatment of patients with ROS1-positive NSCLC: Xalkori (crizotinib), Rozlytrek (entrectinib), Augtyro (repotrectinib), and Ibtrozi (taletrectinib). Additional treatment options for patients who are TKI pre-treated include the TKI lorlatinib, recommended for use according to the National Comprehensive Cancer Network (NCCN) guidelines, chemotherapy with or without immunotherapy, or experimental therapies in clinical trials. The current standard of care for TKI-naïve patients with ROS1-positive NSCLC is crizotinib. There is no clear standard of care for TKI pre-treated patients with ROS1-positive NSCLC.

Zidesamtinib is a brain-penetrant ROS1-selective inhibitor designed with the aim to remain active in tumors that have developed resistance to currently available ROS1 inhibitors, including tumors with the prevalent G2032R resistance mutation and those with the S1986Y/F, F2004C, F2004V, L2026M, D2033N, or G2101A resistance mutations. We believe we have optimized zidesamtinib for brain penetrance and ROS1 selectivity to potentially improve treatment options for patients with brain metastases and avoid CNS adverse events related to off-target inhibition of the structurally related TRK family.

We are currently investigating zidesamtinib in the Phase 2 portion of our ARROS-1 clinical trial, a first-in-human global Phase 1/2, multicenter, open-label, dose-escalation and expansion study evaluating zidesamtinib as an oral monotherapy in patients with advanced ROS1-positive NSCLC and other solid tumors. The Phase 1 dose-escalation portion of the ARROS-1 clinical trial was conducted in patients with advanced ROS1-positive NSCLC or other solid tumors who had received at least one prior ROS1 TKI or any prior therapy, respectively, and evaluated the safety, tolerability and RP2D of zidesamtinib, among other objectives. Upon determination of the RP2D (100 mg QD), the trial transitioned into the ongoing Phase 2 portion designed to evaluate zidesamtinib in patients with advanced ROS1-positive NSCLC and other solid tumors and to support potential registration of zidesamtinib in TKI-naïve and/or TKI pre-treated ROS1-positive NSCLC patients.

In November 2025, the FDA accepted for filing our NDA for zidesamtinib for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who received at least 1 prior ROS1 TKI. The application has been assigned a PDUFA target action date of September 18, 2026. Additionally, we plan to submit data from the ongoing TKI-naïve cohort in the Phase 2 portion of the ARROS-1 trial to the FDA to support a potential label expansion of zidesamtinib in TKI-naïve patients with advanced ROS1-positive NSCLC in the second half of 2026.

Neladalkib (NVL-655, ALK-Selective inhibitor)

ALK rearrangements occur in approximately 5% of metastatic NSCLCs. At the time of initial diagnosis, up to 40% of these patients present with accompanying brain metastases. Beyond NSCLC, ALK fusions have also been reported in various other solid tumors as well as lymphoma.

There are six FDA-approved TKIs for the treatment of patients with ALK-positive NSCLC: Xalkori (crizotinib), Zykadia (ceritinib), Alecensa (alectinib), Alunbrig (brigatinib), Lorbrena (lorlatinib), and Ensacove (ensartinib). Additional treatment options for patients who are TKI pre-treated include chemotherapy with or without immunotherapy, or experimental therapies in clinical trials. The current standard of care for TKI-naïve patients with ALK-positive NSCLC is alectinib, which had an estimated $1.9 billion in reported global 2025 net sales. Following treatment with alectinib, the current second-line TKI standard of care is lorlatinib with an estimated $1.0 billion in reported global 2025 net sales across all indications. There is no clear third-line TKI standard of care for patients with ALK-positive NSCLC.

Neladalkib is a brain-penetrant ALK-selective inhibitor designed with the aim to remain active in tumors that have developed resistance to first-, second-, and third-generation ALK inhibitors, including tumors with the G1202R resistance mutation or compound resistance mutations, including G1202R/L1196M, G1202R/G1269A, or G1202R/L1198F. We believe we have optimized neladalkib for brain penetrance and ALK selectivity to potentially improve treatment options for patients with brain metastases and avoid CNS adverse events related to off-target inhibition of the structurally related TRK family.

We are currently investigating neladalkib in the Phase 2 portion of our ALKOVE-1 clinical trial, a first-in-human global Phase 1/2, multicenter, open-label, dose-escalation and expansion study evaluating neladalkib as an oral monotherapy in patients with advanced ALK-positive NSCLC and other solid tumors. The Phase 1 dose-escalation portion of the ALKOVE-1 clinical trial was conducted in patients with advanced ALK-positive NSCLC or other solid tumors who had received at least one prior ALK TKI or at least one prior systemic anticancer therapy, respectively, and evaluated the safety, tolerability and RP2D of neladalkib, among other objectives. Upon determination of the RP2D (150 mg QD), the trial transitioned into the ongoing Phase 2 portion designed to evaluate neladalkib in patients with advanced ALK-positive NSCLC and other solid tumors, to support potential registration of neladalkib for TKI pre-treated patients with ALK-positive NSCLC, and to enable preliminary evaluation for patients with ALK-positive NSCLC who are TKI-naïve.

We have completed our pre-NDA meeting with the FDA and plan to move forward with an NDA submission of the data for TKI pre-treated patients with advanced ALK-positive NSCLC from our ALKOVE-1 study of neladalkib in the first half of 2026. We plan to present detailed study results at a future medical meeting.

We are also investigating neladalkib in the ALKAZAR Phase 3 clinical trial with registrational intent for TKI-naïve patients. The ALKAZAR clinical trial is a global, randomized, controlled trial evaluating neladalkib versus the current standard of care, alectinib, for the treatment of patients with TKI-naïve ALK-positive NSCLC.

NVL-330 (HER2-Selective inhibitor)

Mutations and alterations in HER2 are oncogenic and are found in approximately 3% of cancers, including up to 4% of advanced NSCLC patients. Within NSCLC, 90% of HER2 mutations occur through HER2ex20. HER2 mutations have also been identified in multiple cancers, including breast, esophageal, endometrial, bladder, colorectal, skin, ovarian, head and neck, and cervical. Brain metastases are present at diagnosis in an estimated 19% of HER2 mutant-positive NSCLC patients, and more patients will develop them during treatment.

There are two HER2 inhibitors approved by the FDA for the treatment of HER2-altered NSCLC: Hernexeos (zongertinib) and Hyrnuo (sevabertinib). Additionally, Enhertu (T-DXd), an antibody-drug conjugate, has been approved by the FDA for the treatment of HER2 mutant NSCLC.

NVL-330 is a brain-penetrant HER2-selective inhibitor which we believe we have optimized for selectivity versus the structurally related wild-type EGFR that is associated with dose-limiting side effects including skin rash and gastrointestinal toxicity. We are currently investigating NVL-330 in our HEROEX-1 clinical trial, a first-in-human global Phase 1a/1b, multicenter, open-label, dose-escalation and expansion trial evaluating NVL-330 as an oral monotherapy in pre-treated patients with advanced HER2-altered NSCLC, including those with HER2ex20 mutations.

Discovery programs

We continue to evaluate new program areas with a focus on addressing the limitations of existing therapies for other clinically proven kinase targets in oncology. As treatment landscapes evolve, we also continue to work with our physician-scientist partners to anticipate emerging patient needs in established areas of development and leverage our existing expertise in the area with the aim to efficiently discover and develop new product candidates with the potential to comprehensively address those emerging challenges. We believe that opportunities to apply our established model of efficient drug discovery and development continue to expand, and align with the increasing adoption of kinase inhibitors as standard of care across a broadening set of indications. We plan to disclose a new development candidate by year-end 2026.

OnTarget 2026 operating plan

OnTarget 2026 delineates our three-year operating plan towards bringing new, potential best-in-class medicines to patients with cancer and is summarized in Figure 2 below. As part of this plan announced in January 2024, we completed the below milestones in 2024 and 2025:

- **2024: Execute on Global Registrational Strategies**
  - ✓ Progress the Phase 2 portion of the ARROS-1 trial of zidesamtinib in patients with advanced ROS1-positive NSCLC with registrational intent;
  - ✓ Initiate the Phase 2 portion of the ALKOVE-1 trial of neladalkib in patients with advanced ALK-positive NSCLC with registrational intent;
  - ✓ Launch our front-line development strategy for our ALK program;
  - ✓ Present interim data from the ongoing ARROS-1 and ALKOVE-1 clinical trials at medical meetings; and
  - ✓ Initiate a Phase 1 trial for our HER2 program.
- **2025: First Pivotal Data**
  - ✓ Report pivotal data for TKI pre-treated patients with advanced ROS1-positive NSCLC from our ARROS-1 Phase 1/2 trial of zidesamtinib in the first half of 2025;
  - ✓ Complete a rolling NDA submission for zidesamtinib for TKI pre-treated patients with advanced ROS1-positive NSCLC in the third quarter of 2025;
  - ✓ Report pivotal data for TKI pre-treated patients with advanced ALK-positive NSCLC from our ALKOVE-1 Phase 1/2 trial of neladalkib by year-end 2025;
  - ✓ Initiate the ALKAZAR Phase 3 randomized, controlled trial of neladalkib for TKI-naïve patients with ALK-positive NSCLC early in the second half of 2025; and
  - ✓ Progress the HEROEX-1 Phase 1a/1b trial of NVL-330 for patients with advanced HER2-altered NSCLC.

In January 2026, we outlined anticipated milestones for 2026, leading to our first potential U.S. commercial launch:

- **2026: First Approved Product**
  - Commercial launch in the U.S. of zidesamtinib for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who received at least 1 prior ROS1 TKI, pending FDA review;
  - Submit data to the FDA for potential label expansion of zidesamtinib in TKI-naïve patients with advanced ROS1-positive NSCLC in the second half of 2026;
  - Submit an NDA for neladalkib in TKI pre-treated patients with advanced ALK-positive NSCLC in the first half of 2026;
  - Progress the ongoing ALKAZAR Phase 3 randomized, controlled trial of neladalkib for TKI-naïve patients with ALK-positive NSCLC;
  - Progress the ongoing HEROEX-1 Phase 1a/1b trial of NVL-330 for patients with advanced HER2-altered NSCLC; and
  - Disclose a new development candidate by year-end 2026.

Figure 2. OnTarget 2026 Operating Plan: The Path to Patient Impact

Our team

We have assembled a management team of biopharmaceutical industry veterans with extensive experience in developing novel oncology therapies from research through commercialization.

Our seasoned leadership team has broad experience at both large global organizations, including C.H. Boehringer Sohn AG & Ko. KG, Pfizer, Sanofi S.A., EMD Serono, GlaxoSmithKline plc, and BeiGene, Ltd., as well as established biotech companies, including Infinity, Agios Pharmaceuticals Inc., Blueprint Medicines Corporation, and ARIAD Pharmaceuticals, Inc. Together, our leadership team has contributed directly to the regulatory approval of 12 therapies, including five kinase inhibitors, nine oncology therapeutics, and 10 small molecules: CLOLAR/Evoltra (clofarabine), FABRAZYME (agalsidase beta), COPIKTRA (duvelisib), BRUKINSA (zanubrutinib), MOZOBIL (plerixafor injection), BAVENCIO (avelumab), TIBSOVO (ivosidenib tablets), TIVICAY (dolutegravir), ICLUSIG (ponatinib), GAVRETO (pralsetinib), ALUNBRIG (brigatinib) and PYRUKYND (mitapivat).

Our values

Our three core values are:

- ***Patient Impact***. We care deeply about what we are building to change the future for patients.
- ***Empowerment***. We are all responsible for delivering on our mission to develop new medicines for patients: listen, speak up, and engage.
- ***Collaboration***. We know that we are better together and thrive when we challenge each other to find a better way for patients.

Our strategy

Our goal is to be a leading biopharmaceutical company that translates our deep expertise in structure-based drug design to discover, develop, and deliver novel, selective therapeutics that enable durable responses for patients with cancer. The key elements of our strategy include:

- ***Obtain regulatory approval for zidesamtinib, our first lead product candidate and a differentiated ROS1-selective inhibitor, for TKI pre-treated patients with ROS1-positive NSCLC and advance toward potential label expansion in TKI-naïve patients with ROS1-positive NSCLC.*** The FDA has accepted for filing our NDA for zidesamtinib for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who received at least 1 prior ROS1 TKI, and assigned a PDUFA target action date of September 18, 2026. Additionally, we plan to submit data from the ongoing TKI-naïve cohort in the Phase 2 portion of the

ARROS-1 clinical trial to the FDA to support a potential label expansion of zidesamtinib in TKI-naïve patients with advanced ROS1-positive NSCLC in the second half of 2026.

- ***Advance the ongoing clinical development of neladalkib, our second lead product candidate and a differentiated ALK-selective inhibitor, through the Phase 2 portion of our ALKOVE-1 study designed to support potential regulatory approval for patients with TKI pre-treated ALK-positive NSCLC.*** Clinical investigation is ongoing in the Phase 2 portion of our ALKOVE-1 study, a first-in-human, global Phase 1/2 clinical trial investigating neladalkib in advanced ALK-positive NSCLC and other solid tumors. Neladalkib has received FDA Breakthrough Therapy designation for the treatment of patients with locally advanced or metastatic ALK-positive NSCLC who have been previously treated with two or more ALK TKIs. In November 2025, we announced positive topline data for neladalkib in TKI pre-treated patients with advanced ALK-positive NSCLC from the ALKOVE-1 Phase 1/2 clinical trial. We have completed our pre-NDA meeting with the FDA and plan to move forward with an NDA submission of the data for TKI pre-treated patients with advanced ALK-positive NSCLC from our ALKOVE-1 study of neladalkib in the first half of 2026.
- ***Commercialize our product candidates, including, if approved, zidesamtinib and neladalkib, in key geographies and opportunistically pursue strategic collaborations to maximize the full potential of our pipeline.*** We retain full development and worldwide commercialization rights to our pipeline of precisely targeted therapies. We are building a fully integrated, commercial-stage biotechnology company capable of not only discovering and developing, but delivering new medicines for patients living with cancer. We are actively building the commercial infrastructure required, including our focused sales, market access, and marketing organization, to support our potential U.S. commercial launch of zidesamtinib for TKI pre-treated patients with ROS1-positive NSCLC in 2026, if approved, as well as planning for U.S. commercial launch readiness for neladalkib, as well as potential label expansions for both programs. In the future, we may enter into strategic collaborations around certain targets, product candidates, disease areas, or geographies, if we believe these collaborations could accelerate the development and commercialization of our product candidates and allow us to realize the full potential of our pipeline.
- ***Progress our ALKAZAR Phase 3 randomized, controlled trial of neladalkib versus ALECENSA (alectinib), designed to support potential regulatory approval for patients with TKI-naïve ALK-positive NSCLC.*** Clinical investigation is ongoing in our ALKAZAR clinical trial, a global, Phase 3, randomized, controlled trial evaluating neladalkib versus the current standard of care. The ALKAZAR clinical trial is designed to enroll approximately 450 patients with TKI-naïve ALK-positive NSCLC, randomized 1:1 to receive neladalkib monotherapy or ALECENSA (alectinib) monotherapy, reflecting input from collaborating physician-scientists and alignment with global regulatory agencies and patients.
- ***Progress our other development and discovery stage programs, including for HER2-altered NSCLC, while continuing to expand our pipeline of precisely targeted novel product candidates.*** We prioritize clinically proven kinase targets where the design of exquisitely selective inhibitors may overcome challenges of existing therapies including kinase resistance, kinase selectivity, and limited CNS activity. We intend to develop product candidates as monotherapy treatment and may also strategically pursue the development of synergistic combinations. We are progressing our HEROEX-1 Phase 1a/1b clinical trial of NVL-330 for patients with advanced HER2-altered NSCLC and plan to disclose a new development candidate by year-end 2026.
- ***Continue to partner with physician-scientists to characterize current and emerging medical needs for patients and the limitations of existing therapies.*** We prioritize clinically proven kinase targets where clear remaining or emerging medical needs for patients can be defined by our physician-scientist partners, and where we believe those needs can be addressed through the design of highly selective small molecule inhibitors. Combining clinical insight with our drug design capabilities and our development expertise, we seek to meet real-world medical needs through the development of detailed product profiles and well-defined selection criteria. Accordingly, we plan to disclose a new development candidate by year-end 2026. We believe this approach maximizes our opportunity to address the challenges of existing therapies and develop molecules that achieve deep, durable responses with minimal adverse events.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary products. While we believe that our technology, the expertise of our team, and our development experience and scientific knowledge provide us with competitive advantages, we face competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions.

Product candidates that we successfully develop and commercialize may compete with existing therapies and new therapies that may become available in the future, and we cannot predict what the standard of care will be as our product candidates progress through clinical development into commercialization. We believe the key competitive factors affecting the success of all of our programs are likely to be efficacy, including DOR, safety, and patient convenience. Potentially competitive therapies fall primarily into the following groups of treatment:

- traditional cancer therapies, including surgery, radiation, and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy or a combination of such methods;

- approved kinase inhibitors, including FDA-approved ROS1 TKIs (Xalkori, Rozlytrek, Augtyro, and Ibtrozi marketed by Pfizer, Roche, Bristol-Myers Squibb Company, and Nuvation Bio Inc., respectively), FDA-approved ALK TKIs (Xalkori, Zykadia, Alecensa, Alunbrig, Lorbrena and Ensacove, marketed by Pfizer, Novartis AG, Chugai Pharmaceutical Co. Ltd./Roche, Takeda Pharmaceutical Company Limited, Pfizer, and Xcovery Holdings, Inc., respectively), FDA-approved HER2 TKIs (Hernexeos and Hyrnuo, marketed by Boehringer Ingelheim and Bayer HealthCare Pharmaceuticals, respectively) and FDA-approved antibody drug conjugate (Enhertu, jointly marketed by Daiichi Sankyo and AstraZeneca);
- ROS1 TKIs in clinical development;
- ALK TKIs in clinical development;
- HER2ex20 TKIs in clinical development;
- TKIs not approved but recommended for use in the NCCN guidelines; and
- other therapies targeting kinases, including antibody or antibody-drug conjugate approaches, that are approved or in clinical development.

Many of our competitors, either alone or with their collaborators, have significantly greater financial resources, established presence in the market, and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Additional mergers and acquisitions may result in even more resources being concentrated in our competitors.

The availability of reimbursement from government and other third-party payors will also significantly affect the pricing and competitiveness of our products. Some cancer treatments are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. In addition, our competitors may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for our products, which could result in our competitors establishing a strong market position before we are able to enter the market. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our product candidates that we successfully introduce to the market will pose challenges.

Revenue Sharing Agreements

Revenue Sharing Agreement with Deerfield

We are party to an Amended and Restated Revenue Sharing Agreement with Deerfield Healthcare Innovations Fund, L.P. and Deerfield Private Design Fund IV, L.P. (collectively, Deerfield) pursuant to which we are obligated to pay Deerfield a fixed low single-digit percentage rate of net sales of certain commercial products discovered, identified or generated by us during the period commencing on February 2, 2017 and ending on the date that is the earlier of (i) five years after Deerfield's last investment in our capital stock and (ii) the fifth anniversary of our initial public offering. Any payments in respect of such products would be through the later of 12 years from the first commercial sale in a country or the expiration of the last-to-expire patent in that country. To date, we have not recorded any net sales and, as a result, have not paid any amounts under this agreement. There are no upfront fees or milestone payments required to be paid by us under this agreement.

Revenue Sharing Agreement with our scientific founder

We are party to an Amended and Restated Revenue Sharing Agreement with our scientific founder, Matthew Shair, Ph.D., pursuant to which we were obligated to pay Dr. Shair 1.5% of net sales of certain commercial products that either have a mechanism of action of (i) ROS1 inhibition and contain zidesamtinib or a backup compound substituted therefor in the event of a product development failure or (ii) ALK inhibition and contain neladalkib or a backup compound substituted therefor in the event of a product development failure, in each case through the later of 12 years from the first commercial sale in a country or the expiration of the last-to-expire patent in that country. Dr. Shair assigned this agreement to Royalty Pharma plc (Royalty Pharma) in December 2025 and, as a result, any payments we are obligated to make under the agreement will be made to Royalty Pharma. To date, we have not recorded any net sales and, as a result, have not paid any amounts under this agreement. There are no upfront fees or milestone payments required to be paid by us under this agreement.

Intellectual property

Our commercial success depends in part on our ability (i) to obtain and maintain patent and other proprietary and/or intellectual property rights and protection for our technology, inventions, and improvements; (ii) to protect and preserve the confidentiality of our trade secrets; (iii) to defend and enforce our proprietary and intellectual property rights, including any patents that we may own or license in the future; and (iv) to operate without infringing the valid and enforceable patents and other proprietary and/or intellectual property rights of third parties.

We wholly own Patent Cooperation Treaty (PCT) applications, U.S. patent applications, U.S. patents, U.S. provisional patent applications, foreign patents, and foreign patent applications relating to our lead and planned product candidates. We strive to protect our proprietary position by, among other methods, filing patent applications in the U.S. and in jurisdictions outside of the U.S. directed to our proprietary technology, inventions, improvements, and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates and continuing innovation to develop, strengthen and maintain our proprietary position in the field of oncology. Our strategic plans also include reliance on data exclusivity, market exclusivity, and patent term extensions when available.

Our ability to stop third parties from making, using, selling, offering to sell, or importing products identical or similar to ours will depend on the extent to which we have rights under valid and enforceable patents, trade secrets, or other intellectual property rights that cover these activities. The patent rights of biotechnology and pharmaceutical companies like ours are generally uncertain and can involve complex legal, scientific, and factual issues. Our and any future licensor's current and future patent applications may not result in the issuance of any patent in any particular jurisdiction, and the claims of any current or future issued patents, even if those claims are valid and enforceable, may not provide sufficient protection from competitors. Any owned or in-licensed patent rights we may obtain may not enable us to prevent others from replicating, manufacturing, using, or administering our product candidates for any indication. Moreover, the subject matter initially claimed in a patent application may be significantly reduced before a patent is issued, and a patent's scope can be reinterpreted after issuance. In addition, any patent we may own or in-license may be challenged, circumvented or invalidated by third parties. As a result, we cannot ensure that any of our product candidates will be protected by valid and enforceable patents.

We have filed certain patent applications directed generally to compositions of matter, pharmaceutical formulations, and therapeutic methods of using the foregoing related to our ROS1, ALK, and HER2 programs, as summarized below. We also possess substantial know-how and trade secrets relating to the development and commercialization of our product candidates, including related manufacturing processes and technology. In addition, we own certain registered trademarks and pending trademark applications in the U.S. and other countries.

With respect to our ROS1 program, we own one pending PCT patent application, five pending U.S. patent applications, three issued U.S. patents, 61 pending foreign patent applications, and three issued foreign patents directed to compositions of matter for our ROS1 inhibitory compounds (e.g., zidesamtinib) and related solid forms as well as methods of use. Any U.S. or foreign patent that has issued or may issue based on the pending patent applications is expected to expire no earlier than 2041, not including any patent term adjustments or patent term extensions that may be awarded. With respect to our ALK program, we own two pending PCT patent applications, three pending U.S. patent applications, two issued U.S. patents, two pending U.S. provisional patent applications, 60 pending foreign patent applications, and three issued foreign patents directed to compositions of matter for our ALK inhibitory compounds (e.g., neladalkib) and related solid forms as well as methods of use. Any U.S. or foreign patent that has issued or may issue based on the pending patent applications is expected to expire no earlier than 2041, not including any patent term adjustments or patent term extensions that may be awarded. With respect to our HER2 program, we own one pending U.S. patent application, one issued U.S. patent, 25 pending foreign patent applications, and two issued foreign patents directed to compositions of matter for our HER2 inhibitory compounds (e.g., NVL-330) and related methods of use. Any U.S. or foreign patent that has issued or may issue based on the pending patent applications is expected to expire no earlier than 2042, not including any patent term adjustments or patent term extensions that may be awarded.

Our pending and planned applications may not result in issued patents and we cannot provide any assurance that any patents that might be issued in the future will protect our current and future product candidates or provide us with any competitive advantage. Moreover, U.S. provisional patent applications are not eligible to become issued patents until, among other things, we file a non-provisional patent application within 12 months of the filing of the related provisional patent applications. With regard to our provisional patent applications, if we do not timely file one or more non-provisional patent applications, we may lose our priority date with respect to our provisional patent applications and therefore any patent protection on the inventions disclosed in such provisional patent applications. While we intend to timely file one or more non-provisional patent applications relating to our provisional patent applications, we cannot predict whether any such patent applications will result in the issuance of patent(s) that provide us with any competitive advantage. For more information regarding the risks related to our intellectual property, please see "Risk Factors—Risks related to our intellectual property."

Commercialization

We retain full development and worldwide commercialization rights to our product candidates. We are actively building the commercial infrastructure required, including our focused sales, market access, and marketing organization, to support our potential U.S. commercial launch of zidesamtinib for TKI pre-treated patients with ROS1-positive NSCLC in 2026, if approved, as well as planning for U.S. commercial launch readiness for neladalkib, as well as potential label expansions for both programs. We plan to commercialize zidesamtinib and neladalkib, if approved, on our own in the U.S. We intend to explore commercialization on our own, or potentially with a collaboration partner, in jurisdictions outside of the U.S. for these product candidates, if approved. Clinical data, the size of the addressable patient population, and the size of the commercial infrastructure and manufacturing needs all influence our current and future commercialization plans.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacturing if any of our product candidates obtain marketing approval. We also rely, and expect to continue to rely, on third parties to package, label, store and distribute our investigational product candidates, as well as our commercial products if marketing approval is obtained.

We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment, and personnel while also enabling us to focus our expertise and resources on the development and commercialization, if approved, of our product candidates.

All of our product candidates are small molecules and are manufactured in synthetic processes from available starting materials. The chemistry appears amenable to scale-up and does not currently require unusual equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Currently, active pharmaceutical ingredients (API) (i.e., drug substance) for zidesamtinib, neladalkib and NVL-330 are manufactured in accordance with current good manufacturing practices (cGMPs). The drug product formulation is being developed with the goal of producing tablets with consistent, immediate release dissolution profiles that can be reproducibly manufactured using automated equipment. All manufacturing activities for zidesamtinib, neladalkib and NVL-330 drug products are performed in accordance with cGMPs and we currently rely on the vendors performing these manufacturing activities as single-source contract manufacturing organizations (CMOs).

We are continuing to develop our supply chain for each of our product candidates and have or intend to put in place framework agreements under which third-party CMOs will generally provide us with necessary quantities of API and drug product on a project-by-project basis based on our development needs, as well as for commercial manufacturing needs if any of our product candidates obtain marketing approval.

As we advance our product candidates through development and, if approved, into commercialization, we will continue to explore adding additional backup suppliers across the supply chain, including for key starting material, API and drug product for each of our product candidates to protect against any potential supply disruptions.

We generally expect to rely on third parties for the manufacture of any companion diagnostics we may develop.

However, there are no assurances that our manufacturing and supply chain infrastructure will remain uninterrupted and reliable, or that the third parties we rely on will be able to satisfy our demand in a timely manner and not have supply chain disruptions due to stock-outs or raw material shortages and/or greater than anticipated demand or quality issues given the operational challenges and raw material shortages that have been experienced in the past.

Government regulation

The research, development, testing, manufacture, quality control, packaging, labeling, storage, record-keeping, distribution, import, export, promotion, advertising, marketing, sale, pricing and reimbursement of drug products are extensively regulated by governmental authorities in the U.S. and other countries and jurisdictions, including the European Union (EU). The processes for obtaining regulatory approvals in the U.S. and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory requirements, both pre-approval and post-approval, require the expenditure of substantial time and financial resources. The regulatory requirements applicable to drug product development, approval and marketing are subject to change, and regulations and administrative guidance often are revised or reinterpreted by the agencies in ways that may have a significant impact on our business.

U.S. Government Regulation of Drug Products

In the U.S., the FDA approves and regulates human drug products under the Federal Food, Drug, and Cosmetic Act (FDCA). A company, institution, or organization that takes responsibility for the initiation and management of a clinical development program for such products is typically referred to as a sponsor. The failure of a sponsor to comply with applicable U.S. requirements may result in FDA delays or refusal to approve pending NDAs, and may subject the sponsor to administrative or judicial sanctions, such as issuance of warning letters, or the imposition of fines, civil penalties, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or civil or criminal prosecution brought by the FDA and the U.S. Department of Justice or other governmental entities.

The FDA must approve our product candidates for therapeutic indications before they may be marketed in the U.S. A sponsor seeking approval to market and distribute a new drug product in the U.S. must satisfactorily complete each of the following steps:

- completion of preclinical laboratory tests, animal studies and formulation studies according to good laboratory practices (GLP) regulations or other applicable regulations;

- design of a clinical protocol and submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be updated when certain changes are made;
- approval by an independent institutional review board (IRB) or ethics committee representing each clinical trial site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practices (GCPs) and other clinical-trial related regulations to evaluate the safety and efficacy of the investigational product for each proposed indication;
- preparation and submission to the FDA of an NDA requesting marketing approval for one or more proposed indications, including payment of application user fees;
- payment of user fees pursuant to PDUFA;
- review of the NDA by an FDA advisory committee, where applicable;
- satisfactory completion of one or more FDA inspections 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 product's identity, strength, quality, and purity;
- satisfactory completion of any FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data submitted in support of the NDA; and
- FDA review and approval of the NDA, which may be subject to additional post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy (REMS), and any post-approval studies required by the FDA.

Preclinical Studies

Before a sponsor begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation, and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. These studies are typically referred to as IND-enabling studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the U.S. Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. An IND must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. The FDA will review an IND to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the investigational drug product. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial may proceed. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a partial clinical hold might state that a specific protocol or part of a protocol may not proceed, while other parts of a protocol or other protocols may do so. No more than 30 days after the imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following the issuance of a clinical hold or partial clinical hold, a clinical investigation may only resume once the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed or recommence. Occasionally, clinical holds are imposed due to manufacturing issues that may present safety issues for the clinical study subjects.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB, which must operate in compliance with FDA regulations, must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects and must monitor the trial

until completed. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data monitoring committee (DMC). This group provides authorization as to whether or not a trial may move forward at designated checkpoints based on review of available data from the study, to which only the DMC maintains access. Suspension or termination of development during any phase of a clinical trial can occur if the DMC determines that the participants or patients are being exposed to an unacceptable health risk.

Expanded Access

Expanded access, sometimes called "compassionate use," is the use of investigational new products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational products for patients who may benefit from investigational therapies. The FDA's regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational product for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its investigational products available for expanded access; however, as required by amendments to the FDCA included in the 21st Century Cures Act (the Cures Act), passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests with respect to product candidates in development to treat serious diseases or conditions, it must make that policy publicly available. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study for a covered investigational product; or 15 days after the investigational product receives designation from the FDA as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements which include, among other things, the requirement that all research subjects provide their informed consent in writing before they participate in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

- *Phase 1* clinical trials are initially conducted in a limited population, which may be healthy volunteers or subjects with the target disease, to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the product candidate's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.
- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage.

Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are typically well-controlled and closely monitored.

- *Phase 3* clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken using a larger patient population to further evaluate dosage, provide substantial evidence of clinical efficacy, and further test for safety in an expanded and diverse patient population at multiple geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a new prescription drug product. Such Phase 3 clinical trials are referred to as "pivotal" trials.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials, typically referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials, such as to verify clinical benefit in the case of products approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting mandatory Phase 4 clinical trials could result in withdrawal of FDA approval for products.

In March 2022, the FDA released final guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology product development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by the FDA. Expansion cohort trials can potentially bring efficiency to product development and reduce developmental costs and time.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the International Council for Harmonisation's recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

In December 2022, with the passage of the Food and Drug Omnibus Reform Act (FDORA), Congress required sponsors to develop and submit a diversity action plan (DAP) for each Phase 3 clinical trial or any other "pivotal trial" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans (DAPs). In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law, because FDORA specifically dictates that the form and manner for submission of DAPs are to be specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025 regarding diversity, equity and inclusion programs, the FDA removed this draft guidance from its website. This action raises questions about the applicability of statutory obligations to submit DAPs and the FDA's current thinking on best practices for clinical development.

Typically, clinical trials are designed in consultation with the FDA or foreign regulatory authorities during these development phases. The indications under development can influence the study designs employed during the conduct of clinical trials, such as for a first-line cancer treatment indication which may require head-to-head comparison data demonstrating clinical superiority or non-inferiority to currently available therapies. The timeline for first-line cancer indication development programs may also be longer than for indications sought in subsequent or later lines of treatment due to a desire for regulatory authorities to expedite access to treatments for patients whose cancer has progressed on prior treatments and in settings where there may be no available therapy option. As such, many new oncology products initially seek an indication for second or third-line treatment, which may be a smaller available treatment population in any oncology indication that has limited or no other therapy options, with subsequent development sought for those products in earlier front lines of treatment which target a larger treatment population and may require the conduct of additional clinical trials to provide comparative data against an available therapy option to show clinical superiority.

Clinical Studies Outside the U.S. in Support of FDA Approval

In connection with our clinical development program, we have trial sites outside the U.S. When a foreign clinical trial is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain regulatory requirements of the FDA in order to use the trial as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee (IEC) and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. The regulations further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

The acceptance by the FDA of trial data from clinical trials conducted outside the U.S. in support of U.S. approval 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 trial 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 trial is well-designed and well-conducted in accordance with GCP requirements, and the FDA is able to validate the data from the trial through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted.

Reporting Clinical Trial Results

Sponsors of clinical trials of certain FDA-regulated products, including prescription drugs, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health (NIH). In particular, information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017.

The Public Health Service Act grants the Secretary of Health and Human Services the authority to issue a notice of noncompliance to a responsible party for failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to correct the noncompliance and submit the required information. The FDA regularly issues notices of non-compliance, thereby signaling the government's willingness to enforce these requirements against non-compliant clinical trial sponsors. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

Interactions with the FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. Progress reports detailing the results of clinical trials must be submitted annually within 60 days of the anniversary dates that the IND went into effect and more frequently if serious adverse events occur. These reports must include a development safety update report. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND (pre-IND meeting), at the end of Phase 2 clinical trial (EOP2 meeting) and before an NDA is submitted (pre-NDA meeting). Meetings at other times may also be requested. There are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA meetings as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including for example meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. A type D meeting is focused on a narrow set of issues (should be limited to no more than two focused topics) and should not require input from more than three disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product.

These meetings provide an opportunity for the sponsor to share information about the data gathered to date with the FDA and for the FDA to provide advice on the next phase of development. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure.

Manufacturing and Other Regulatory Requirements

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

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the U.S. prior to being imported or offered for import into the U.S.

Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA.

Pediatric Studies

Under the Pediatric Research Equity Act (PREA), applications and certain types of supplements to applications must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor must submit an initial Pediatric Study Plan (PSP) within 60 days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and the FDA. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The sponsor and the FDA must reach agreement on a final plan. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs.

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial PSP or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-Phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The law now requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension, or have failed to request approval for a required pediatric formulation. It further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan drug designation, although the

FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued draft guidance that further describes the pediatric study requirements under PREA.

Expedited Review Programs

For certain drug products, the FDA is authorized to expedite the review and approval of applications in several ways. None of these expedited programs change the standards for approval, but they may help expedite the development and approval process governing product candidates.

- *Fast Track designation*. Candidate products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.
- *Breakthrough therapy designation.* To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.
- *Priority review.* A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention compared to marketed products. The FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.
- *Accelerated approval.* Drug products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, and 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 product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.

  In December 2022, Congress modified certain provisions governing accelerated approval of drug products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing the FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval trial of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner of the FDA or the Commissioner's designee and a written appeal, among other things.

  In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. While a randomized controlled trial is the preferred approach, the guidance states that there can be circumstances wherein a single-arm trial is appropriate in the development of a drug for accelerated approval. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. Subsequently, in December 2024 and January 2025, the FDA issued additional draft guidance relating to accelerated approval. This guidance describes the FDA's latest thinking on what it means to conduct a confirmatory trial with due diligence and how the FDA plans to interpret whether such a study needs to be underway at the time of approval. While this guidance is currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

- *Regenerative advanced therapy.* With passage of the Cures Act in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review, and accelerated approval based on surrogate or intermediate endpoints.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) thus authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved as well as for any new indication sought by the Section 505(b)(2) applicant.

Submission and Filing of NDAs

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, along with information relating to the product's chemistry, manufacturing, controls, safety updates, patent information, abuse information, and proposed labeling, are submitted to the FDA as part of an application requesting approval to market the product candidate for one or more indications. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of a drug product to the satisfaction of the FDA. The fee required for the submission and review of an application under PDUFA is substantial (for example, for fiscal year 2025, this application fee is $4,310,002), and the sponsor of an approved application is also subject to an annual program fee, currently set at $403,889 per eligible prescription product. These fees are typically adjusted annually, and exemptions and waivers may be available under certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the sponsor is a small business submitting its first human therapeutic application for review.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, the FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that the FDA determines that an application does not satisfy this standard, it will issue a Refuse to File (RTF) determination to the applicant. Typically, an RTF will be based on administrative incompleteness, such as clear omission of information or sections of required information; scientific incompleteness, such as omission of critical data, information, or analyses needed to evaluate safety and efficacy or provide adequate directions for use; or inadequate content, presentation, or organization of information such that substantive and meaningful review is precluded. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

After the submission is accepted for filing, the FDA begins an in-depth substantive review of the application. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective for its intended use, whether it has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months from the filing date in which to complete its initial review of a standard application that is a new molecular entity, and six months from the filing date for an application with "priority review." The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, it is not uncommon for FDA review of an application to extend beyond the PDUFA goal date.

In connection with its review of an application, the FDA will typically submit information requests to the sponsor and set deadlines for responses thereto. The FDA will also conduct a pre-approval inspection of the manufacturing facilities for the new product to

determine whether the manufacturing processes and facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. The FDA also may inspect the sponsor and one or more clinical trial sites to assure compliance with IND and GCP requirements and the integrity of the clinical data submitted to the FDA. To ensure cGMP and GCP compliance by its employees and third-party contractors, a sponsor may incur significant expenditure of time, money, and effort in the areas of training, record keeping, production, and quality control.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the NDA. That is because, under certain circumstances, principal investigators at a clinical trial site may also serve as scientific advisors or consultants to a sponsor and receive compensation in connection with such services. Depending on the level of that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of safety and efficacy of the investigational product.

Additionally, the FDA may refer an application, including applications for novel product candidates which present difficult questions of safety or efficacy, to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved and under what conditions. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations when making final decisions on approval. Data from clinical trials are not always conclusive, and the FDA or its advisory committee may interpret data differently than the sponsor interprets the same data. The FDA may also re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the sponsor during the review process.

The FDA also may require submission of a REMS if it determines that a REMS is necessary to ensure that the benefits of the product outweigh its risks and to assure the safe use of the product. The REMS could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS and the FDA will not approve the application without a REMS.

Decisions on NDAs

The FDA reviews an application to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that if the FDA determines, "based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, FDA may consider such data and evidence to constitute substantial evidence." This modification to the law recognized the potential for the FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, the FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. Although the FDA has not yet finalized that guidance, it did issue additional draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical study.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter (CRL) or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies, or manufacturing. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review. Sponsors may request the FDA for a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (*e.g.,* patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings, or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drug products within 30 days of approval of such products. To date, CRLs are not publicly available documents.

Post-approval Requirements

Following approval of a new prescription product, the manufacturer, the approved product, and the product's manufacturing locations are subject to pervasive and continuing regulation by the FDA, governing, among other things, monitoring and record-keeping activities, reporting of adverse experiences with the product and product problems to the FDA, product sampling and distribution, manufacturing, and promotion and advertising. Although physicians may prescribe legally available products for unapproved uses or patient populations (*i.e.,* "off-label uses"), manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products, if approved. In September 2021, the FDA published final regulations which describe the types of evidence that the FDA will consider in determining the intended use of a drug or biologic. Moreover, with passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. In addition, in January 2025, the FDA published final guidance outlining its policies governing the distribution of scientific information to healthcare providers about unapproved uses of approved products. The final guidance calls for such communications to be truthful, non-misleading and scientifically sound and to include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product. While this guidance only applies to communications about unapproved uses of approved products, it may be helpful in understanding the FDA's approach to communications about unapproved products.

If a company is found to have promoted off-label uses, it may become subject to administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the U.S. Department of Health and Human Services (HHS), as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes products, as well as adverse public relations and reputational harm. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Further, if there are any modifications to the product, including changes in indications, labeling, or manufacturing processes or facilities, the sponsor may be required to submit and obtain FDA approval of a new application or supplement, which may require the sponsor to develop additional data or conduct additional preclinical studies and clinical trials. Securing FDA approval for new indications is similar to the process for approval of the original indication and requires, among other things, submitting data from

adequate and well-controlled clinical trials to demonstrate the product's safety and efficacy in the new indication. Even if such trials are conducted, the FDA may not approve any expansion of the labeled indications for use in a timely fashion, or at all. There also are continuing, annual user fee requirements that are now assessed as program fees for certain products.

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

Other potential consequences include, among other things:

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

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws, the most recent of which is still in the process of being phased into the U.S. supply chain and regulatory framework. The Prescription Drug Marketing Act (PDMA) was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Today, both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. In November 2013, the federal Drug Supply Chain Security Act became effective in the U.S., mandating an industry-wide, electronic, interoperable system to trace prescription drugs through the pharmaceutical distribution supply chain with a ten-year phase-in process. Manufacturers were required by November 2023 to have such systems and processes. So as not to disrupt supply chains, the FDA has granted certain exemptions from enhanced drug distribution security requirements for eligible trading partners for particular periods of time.

Generic Drugs and Regulatory Exclusivity

In 1984, with passage of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs, and also enacted Section 505(b)(2). To obtain approval of a generic drug, a sponsor must submit an abbreviated new drug application (ANDA) to the FDA. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing conducted for a drug product previously approved under an NDA, known as the reference listed drug (RLD).

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug, and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA or 505(b)(2) application until any applicable period of regulatory exclusivity for the RLD has expired. The FDCA provides a period of five years of regulatory exclusivity for a new drug containing a new chemical entity (NCE). For the purposes of this provision, the FDA has consistently taken the position that an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, a generic or follow-on drug

application may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the sponsor may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of regulatory exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the sponsor and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as new indications, dosage forms, route of administration or combination of ingredients. Three-year regulatory exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; rather, this three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving follow-on applications for drugs containing the original active ingredient.

Five-year and three-year regulatory exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505(b)(1) of the FDCA; however, a sponsor submitting a traditional NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

As part of the submission of an NDA or certain supplemental applications, NDA sponsors are required to list with the FDA each patent with claims that cover the sponsor's product or an approved method of using the product. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. The FDA's regulations governing patent listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book. Specifically, the ANDA applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505(b)(2) NDA applicant is relying on studies conducted for an already approved product, the applicant also is required to certify to the FDA concerning any patents listed for the NDA-approved product in the Orange Book to the same extent that an ANDA applicant would.

If the generic drug or follow-on drug applicant does not challenge the innovator's listed patents, the FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new generic product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA owner and patent holders once the ANDA has been accepted for filing by the FDA. The NDA owner and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earliest of 30 months after the receipt of the Paragraph IV notice, expiration of the patent and a decision in the infringement case that is favorable to the ANDA or 505(b)(2) NDA applicant.

Orphan Drug Designation and Exclusivity

Orphan drug designation in the U.S. is designed to encourage sponsors to develop products intended for treatment of rare diseases or conditions. In the U.S., a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the U.S. or that affects more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available the product for the disease or condition will be recovered from sales of the product in the U.S.

Orphan drug designation qualifies a company for tax credits and potentially market exclusivity for seven years following the date of the product's approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development at the FDA based on acceptable confidential requests. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first approved product. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same disease or condition for seven years, except in certain limited circumstances. If a product designated as an orphan

drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

The period of market exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the disease or condition for which the product has been designated. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if the company with orphan drug exclusivity is not able to meet market demand or the subsequent product is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan drug exclusivity regardless of a showing of clinical superiority. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drug products that received orphan drug designation before enactment of amendments to the FDCA in 2017 but have not yet been approved by the FDA.

It is also possible that current or future litigation or action by Congress could change the scope of available orphan exclusivity. Any changes to the orphan drug provisions could change our opportunities for, or likelihood of success in obtaining, orphan drug exclusivity and could have a material adverse effect on our business, financial condition, results of operations, cash flows and prospects.

Pediatric Exclusivity

Pediatric exclusivity is a type of non-patent marketing exclusivity in the U.S. and, if granted, provides for the attachment of an additional six months of exclusivity to the term of any existing patent or regulatory exclusivity for drug products, including the orphan exclusivity and regulatory exclusivities available under the Hatch-Waxman provisions of the FDCA. The conditions for pediatric exclusivity include the FDA's determination that information relating to the use of a new product in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric clinical trials, and the sponsor agreeing to perform, and reporting on, the requested clinical trials within the statutory timeframe. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patents that cover the product are extended by six months. Although this is not a patent term extension, it effectively extends the regulatory period during which the FDA cannot approve another application.

Patent Term Restoration and Extension

In the U.S., a patent claiming a new product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent extension of up to five years for patent term lost during product development and FDA regulatory review. Assuming grant of the patent for which the extension is sought, the restoration period for a patent covering a product is typically one-half the time between the effective date of the IND involving human beings and the submission date of the NDA, plus the time between the submission date of the application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date in the U.S. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension in consultation with the FDA.

Companion Diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to the approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the therapeutic product and *in vitro* companion diagnostic device on issues related to co-development of the products.

The 2014 guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a product candidate generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption (IDE) regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a product are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND application alone, or both an IND- and IDE-application.

In April 2020, the FDA issued additional guidance which describes considerations for the development and labeling of companion diagnostic devices to support the indicated uses of multiple drug or biological oncology products, when appropriate. This guidance builds upon existing policy regarding the labeling of companion diagnostics. In its 2014 guidance, the FDA stated that if evidence is sufficient to conclude that the companion diagnostic is appropriate for use with a specific group of therapeutic products, the companion diagnostic's intended use/indications for use should name the specific group of therapeutic products, rather than specific products. The 2020 guidance expands on the policy statement in the 2014 guidance by recommending that companion diagnostic developers consider a number of factors when determining whether their test could be developed, or the labeling for approved companion diagnostics could be revised through a supplement, to support a broader labeling claim such as use with a specific group of oncology therapeutic products (rather than listing an individual therapeutic product(s)).

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the U.S., 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 pre-notification marketing clearance or approval from the FDA prior to commercial distribution.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval (PMA) simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the sponsor must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2025 the standard fee is $540,783 and the small business fee is $135,196.

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

Healthcare Compliance

In the U.S., biopharmaceutical manufacturers and their products are subject to extensive regulation at the federal and state level, such as laws intended to prevent fraud and abuse in the healthcare industry. Healthcare providers and third-party payors play a primary role in the recommendation, prescription, and coverage of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to healthcare providers, patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations include, but are not limited to, the following:

- federal false claims, false statements, and civil monetary penalties laws prohibiting, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment of government funds or knowingly making, or causing to be made, a false statement to get a false claim paid;
- the federal Anti-Kickback Statute, a broad criminal statute which prohibits, among other things, knowingly and willfully offering, soliciting, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce, or in return for, either the referral of an individual for, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under federal healthcare programs;
- the federal Physician Payment Sunshine Act, which requires applicable pharmaceutical and medical device manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, among others, to collect and report information on certain financial interactions with certain healthcare providers to the Centers for Medicare & Medicaid Services (CMS) for annual publication in a searchable form on a public website, as well as ownership and investment interests held by physicians and their immediate family members;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- analogous state laws and regulations, including: state anti-kickback and false claims laws; state laws requiring pharmaceutical companies to comply with specific compliance standards, restrict financial interactions between pharmaceutical companies and healthcare providers or require pharmaceutical companies to report information related to payments to healthcare providers or marketing expenditures; and state laws governing privacy, security and breaches of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- laws and regulations prohibiting bribery and corruption such as the U.S. Foreign Corrupt Practices Act (FCPA), which, among other things, prohibits U.S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations or foreign government-owned or affiliated entities, candidates for foreign public office, and foreign political parties or officials thereof.

Violations of these laws are punishable by criminal and/or civil sanctions, including, in some instances, exclusion from participation in federal and state healthcare programs, such as Medicare and Medicaid. Ensuring compliance is time consuming and costly. Similar healthcare laws and regulations exist in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of personal information.

Coverage and Reimbursement

In the U.S. and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government healthcare programs in the U.S. such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage and establish adequate reimbursement levels for the product. In the U.S., no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans, or federal healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations, and financial condition. Factors that payors consider in determining reimbursement include whether the product is (i) a covered benefit under its health plan; (ii) safe, effective, and medically necessary; (iii) appropriate for the specific patient; (iv) cost-effective; and (v) neither experimental nor investigational. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product and the level of coverage and reimbursement can differ significantly from payor to payor.

Net prices for drugs may be reduced by mandatory discounts or rebates required by federal healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government in order to receive coverage for their products under federal healthcare programs such as Medicare Part B and Medicaid. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by federal healthcare programs.

The containment of healthcare costs has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures and adoption of more restrictive policies in jurisdictions with existing controls and measures could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party payor reimbursement rates

may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of drug products, limiting coverage and reimbursement for medical products and other changes to the healthcare system in the U.S.

In March 2010, the U.S. Congress enacted the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the PPACA), which, among other things, includes changes to the coverage and payment for pharmaceutical products under government healthcare programs. Other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent statutory amendments, will remain in effect through the first eleven months of the President's fiscal year 2032 sequestration order unless additional congressional action is taken, with the exception of a temporary suspension, and later a temporary reduction instituted during the COVID-19 pandemic that expired on July 1, 2022.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On June 17, 2021, the U.S. Supreme Court dismissed a judicial challenge to the PPACA brought by several states who argued that, without the individual mandate, the entire PPACA was unconstitutional. The U.S. Supreme Court's dismissal of the lawsuit did not specifically rule on the constitutionality of the PPACA. Litigation and legislation over the PPACA may continue, with unpredictable and uncertain results.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the U.S. There have been several recent U.S. Congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. For example, on August 16, 2022, the Inflation Reduction Act of 2022 (IRA) was signed into law by former President Biden. The legislation requires manufacturers of certain drugs to engage in price negotiations with Medicare, with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation; and replaces the Part D coverage gap discount program with a new discounting program. The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for 10 high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years. When originally enacted, the IRA explicitly excluded from price negotiation orphan drugs designated for only one rare disease or condition and for which the only active approved indication is for such disease or condition. However, the One Big Beautiful Bill Act (OBBBA), signed into law in July 2025, amended the applicable statute to broaden the orphan drug exclusion to include products with more than one orphan designation and more than one approved indication. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law. The legislation also requires manufacturers to pay rebates for drugs in Medicare Parts B and D whose price increases exceed inflation and capped Medicare beneficiary out-of-pocket drug costs at $2,000 a year.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for 10 selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these 10 drugs became effective on January 1, 2026. In January 2025, CMS announced its selection of 15 additional drugs covered by Medicare Part D for the second cycle of negotiations, and in November 2025, CMS released negotiated prices for such products that will go into effect beginning January 1, 2027. While it remains to be seen how the drug pricing provisions imposed by the IRA will affect the broader pharmaceutical industry, several pharmaceutical manufacturers and other industry stakeholders have challenged the law, including through lawsuits brought against the HHS, the Secretary of the HHS, CMS, and the CMS Administrator challenging the constitutionality and administrative

implementation of the IRA's drug price negotiation provisions. This litigation is ongoing and the results, and potential impacts on our business, are uncertain.

In January 2025, CMS issued a public statement declaring that lowering the cost of prescription drugs is a top priority of the current presidential administration and CMS is committed to considering opportunities to bring greater pricing transparency. Moreover, President Trump has signed multiple executive orders addressing prescription drug pricing and access, and has exerted pressure on drug manufacturers to implement "most favored nation" pricing, including by suggesting that the administration may impose significant tariffs on pharmaceuticals if such manufacturers do not reach agreements to implement "most favored nation" pricing. Additionally, in November 2025, CMS announced a new voluntary payment initiative called the GENEROUS Model (GENErating cost Reductions for U.S. Medicaid Model) where drug manufacturers may voluntarily offer supplemental rebates to participating state Medicaid programs that are intended to provide such Medicaid programs with a "most favored nation" price for participating manufacturers' products. Most recently, in December 2025, CMS announced new mandatory payment models through two proposed rules, the Global Benchmark for Efficient Drug Pricing (GLOBE) and Guarding U.S. Medicare Against Rising Drug Costs (GUARD) models where manufacturers of certain Medicare Part B and Medicare Part D drugs will be assessed rebates if the prices for such products exceed those paid in economically comparable countries. It remains to be seen how these drug pricing initiatives will affect the broader pharmaceutical industry.

In addition, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program (SIP) to import certain prescription drugs from Canada into the U.S. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America (PhRMA) but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Several states have passed laws allowing for the importation of products from Canada. Other states have passed legislation establishing workgroups to examine the impact of a state importation program or submitted SIP proposals to the FDA for review and approval.

At the state level, individual states are increasingly aggressive in passing legislation and 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, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, and wholesale distributors, to disclose information about pricing of pharmaceuticals, including, but not limited to, information in connection with new product launches that exceed certain levels as identified in the relevant statutes. This is increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the U.S. and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the healthcare industry generally, under HIPAA, HHS has issued regulations to protect the privacy and security of protected health information (PHI) used or disclosed by covered entities including certain healthcare providers, health plans, and healthcare clearinghouses. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

In 2018, California passed into law the California Consumer Privacy Act (CCPA), which took effect on January 1, 2020, and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation (GDPR), including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA

also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act (CPRA), which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, several other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices, and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil, and administrative penalties, damages, fines, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Approval and Regulation of Medical Products in the EU

In addition to regulations in the U.S., we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products outside of the U.S. Whether or not we obtain FDA approval for a product candidate, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the 27-member EU, before we may commence clinical trials or market products in those countries or areas. In the EU, our product candidates also may be subject to extensive regulatory requirements. As in the U.S., medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained. Similar to the U.S., the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls.

With the exception of the EU/European Economic Area (EEA) applying the harmonized regulatory rules for medicinal products, the approval process and requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly between countries and jurisdictions and can involve additional testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Non-clinical Studies

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of GLP as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical Trials

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 (the CTR) became effective in the EU and replaced the prior Clinical Trials Directive 2001/20/EC (Clinical Trials Directive). The new CTR aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one EU Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU Portal and Database"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting EU Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted, or concerned EU Member States. Part II is assessed separately by each concerned EU Member State. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned member state. However, overall related timelines will be defined by the CTR.

The new CTR did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific clinical site after the applicable ethics committee has issued a favorable opinion.

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

Marketing Authorization

Marketing authorization applications (MAAs) can be filed either under the so-called centralized or national authorization procedures, albeit through the Mutual Recognition or Decentralized procedure for a product to be authorized in more than one EU member state.

The centralized procedure provides for the grant of a single marketing authorization (MA) following a favorable opinion by the EMA that is valid in all EU Member States, as well as Iceland, Liechtenstein, and Norway, which are part of the EEA. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, advanced-therapy medicines (such as gene-therapy, somatic cell-therapy or tissue-engineered medicines), and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases, and other immune dysfunctions and viral diseases. The centralized procedure is optional for products that represent a significant therapeutic, scientific, or technical innovation, or whose authorization would be in the interest of public health. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the sponsor in response to questions asked by the Committee for Medicinal Products for Human Use (CHMP). Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding stop-clocks.

There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- *Decentralized procedure*. Using the decentralized procedure, a sponsor may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure. The sponsor may choose a member state as the reference member state to lead the scientific evaluation of the application.
- *Mutual recognition procedure*. In the mutual recognition procedure, a medicine is first authorized in one EU Member State (which acts as the reference member state), in accordance with the national procedures of that country. Following this, further marketing authorizations can be progressively sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization produced by the reference member state.

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

Conditional Approval

In particular circumstances, EU legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5 and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use)) enables sponsors to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention, or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive, and (5) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Exceptional Circumstances

A MA may also be granted "under exceptional circumstances" when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved to medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk-benefit ratio is no longer favorable. Under these procedures, before granting the MA, the EMA or the competent authorities of the member states make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety, and efficacy. Except for conditional MAs, MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

Pediatric Studies

Prior to obtaining a marketing authorization in the EU, sponsors have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan (PIP), covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form, or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA (PDCO) may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate because (a) the product is likely to be ineffective or unsafe in part or all of the pediatric population; (b) the disease or condition occurs only in adult population; or (c) the product does not represent a significant therapeutic benefit over existing treatments for pediatric population. Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

PRIME Designation

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines (PRIME) scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises (SMEs) may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated agency contact and rapporteur from the CHMP or Committee for Advanced Therapies are appointed early in the PRIME scheme, facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance to the sponsor on the overall development and regulatory strategies.

Periods of Authorization and Renewals

A MA is valid for five years in principle and the MA may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety, and efficacy, including all variations introduced since the MA was granted, at least nine months before the marketing authorization ceases to be valid. Once renewed, the MA is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Regulatory Requirements after Marketing Authorization

As in the U.S., both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations. The holder of an EU marketing authorization for a medicinal product must, for example, comply with EU pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. The manufacturing process for medicinal products in the EU is also highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, including compliance with EU cGMP standards when manufacturing medicinal products and API.

In the EU, the advertising and promotion of approved products are subject to EU Member States' laws governing promotion of medicinal products, interactions with clinicians, misleading and comparative advertising, and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics (SmPC) as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion, which is prohibited in the EU.

Regulatory Exclusivity

In the EU, new products authorized for marketing (*i.e.,* reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic sponsors from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic sponsor from commercializing its product in the EU until 10 years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Orphan Drug Designation and Exclusivity

The criteria for designating an orphan medicinal product in the EU are similar in principle to those in the U.S. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition, (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment, and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. The term 'significant benefit' is defined in Regulation (EC) 847/2000 to mean a clinically relevant advantage or a major contribution to patient care.

Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to 10 years of market exclusivity for the approved therapeutic indication. During this ten-year market exclusivity period, the EMA or the competent authorities of the Member States of the EEA, cannot accept an application for a marketing authorization for a similar medicinal product for the same indication. A similar medicinal product is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The application for orphan designation must be submitted before the application for marketing authorization. The sponsor will receive a fee reduction for the MAA if the orphan designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity in the EU may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

(1) the second sponsor can establish that its product, although similar, is safer, more effective, or otherwise clinically superior; (2) the sponsor consents to a second orphan medicinal product application; or (3) the sponsor cannot supply enough orphan medicinal product.

Pediatric Exclusivity

If a sponsor obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate (SPC) or alternatively a one year extension of the regulatory market exclusivity from ten to eleven years, as selected by the marketing authorization holder.

Patent Term Extensions

The EU also provides for patent term extension through SPCs. The rules and requirements for obtaining an SPC are similar to those in the U.S. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of 15 years of marketing exclusivity for a drug. In certain circumstances, these periods may be extended for six additional months if pediatric exclusivity is obtained. Although SPCs are available throughout the EU, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the EU.

Reimbursement and Pricing of Prescription Pharmaceuticals

In the EU, similar political, economic, and regulatory developments to those in the U.S. may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the U.S. and the EU, reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, pharmaceutical firms may be required to conduct a clinical trial that compares the cost-effectiveness of the product to other available therapies.

The EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained.

Reference pricing used by various EU Member States, and parallel trade (*i.e.*, arbitrage between low-priced and high-priced Member States) can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any product candidates, if approved in those countries.

Approval of Companion Diagnostic Devices

In the EU, medical devices such as companion diagnostics must comply with the General Safety and Performance Requirements (SPRs) detailed in Annex I of the EU Medical Devices Regulation (Regulation (EU) 2017/745) (MDR), which came into force in May 2021 and replaced the previously applicable EU Medical Devices Directive (Council Directive 93/42/EEC). Compliance with SPRs and additional requirements applicable to companion medical devices is a prerequisite to be able to affix the Conformitè Europëenne mark of conformity to medical devices, without which they cannot be marketed or sold. To demonstrate compliance with the SPRs, a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. The MDR is meant to establish a uniform, transparent, predictable, and sustainable regulatory framework across the EU for medical devices.

Separately, the regulatory authorities in the EU also adopted a new In Vitro Diagnostic Regulation (Regulation (EU) 2017/746) (IVDR) for In vitro diagnostic medical devices (IVDs). The IVDR, among other things:

- strengthens the rules on placing devices on the market and reinforces surveillance once they are available;
- establishes explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance, and safety of devices placed on the market;

- improves the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number;
- establishes a central database to provide patients, healthcare professionals, and the public with comprehensive information on products available in the EU; and
- strengthens rules for the assessment of certain high-risk devices, such as implants, which may have to undergo an additional check by experts before they are placed on the market.

The IVDR became applicable in May 2022, but transitional periods for legacy devices have been extended, with deadlines on device class (e.g., Class D until December 31, 2027, Class C until December 31, 2028, and Class B/Class A sterile until December 31, 2029), subject to specified conditions. Certain provisions for in-house devices manufactured and used by health institutions apply as of May 26, 2028. The extended transition periods apply only to legacy devices that continue to comply with prior rules, undergo no significant design or intended-use changes, do not pose unacceptable risks, and for manufacturers implement an IVDR-compliant quality management system and submit a timely application to a notified body, where required.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EEA, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. In the United Kingdom (U.K.), the GDPR is retained in domestic law as the U.K. GDPR and sits alongside an amended version of the U.K. Data Protection Act 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues of the respective group of companies, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance. In July 2020 the Court of Justice of the European Union (CJEU) invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the U.S. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR.

In October 2022, former President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have challenged the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms.

Brexit and the Regulatory Framework in the United Kingdom

The U.K.'s withdrawal from the EU, commonly referred to as Brexit, took place on January 31, 2020. The EU and the U.K. reached an agreement on their new partnership in the Trade and Cooperation Agreement, which entered into force on May 1, 2021. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency (MHRA) became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland, and Wales under domestic law, whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol, as amended by a set of arrangements, known as the "Windsor Framework," agreed in February 2023.

As of January 1, 2025, the changes introduced by the Windsor Framework resulted in the MHRA being responsible for approving all medicinal products destined for the U.K. market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. The MHRA relies on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended) (HMR) as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the U.K.'s withdrawal from the EU.

As of January 1, 2024, a new international recognition procedure (IRP) applies that intends to facilitate approval of pharmaceutical products in the U.K. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators (RRs). The RRs notably include the EMA and regulators in the EEA Member States for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the

U.S.). The RR assessment must have undergone a full and standalone review. RR assessments based on reliance or recognition cannot be used to support an IRP application. A CHMP positive opinion or a mutual recognition/decentralized positive end of procedure outcome is an RR authorization for the purposes of IRP.

Other U.S. environmental, health, and safety laws and regulations

We may be 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. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our 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 for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development, or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties, or other sanctions.

Employees and Human Capital

As of December 31, 2025, we had 228 full-time employees, of which 144 are engaged in research and development. From time to time, we also retain independent contractors and other service providers to support our organization. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is positive.

We consider the intellectual capital of our employees to be an essential driver of our business. Our workforce expanded substantially during 2025; new employees were hired to support our clinical and preclinical pipeline and commercialization efforts, with additions in our research, clinical development, operations and general and administrative functions, including commercial. We expect to continue to add additional employees in 2026 with a focus on increasing expertise in commercialization and clinical and preclinical research and development as well as expanding critical capabilities across our organization.

We continually evaluate our business needs and opportunities and strive to balance in house expertise and capacity with outsourced expertise and capacity. Currently, we outsource substantially all clinical trial work to contract research organizations and manufacturing to CMOs.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and future employees. The principal purposes of our short-term and long-term incentive programs are to attract, retain and motivate employees and consultants. In addition, through the granting of stock-based compensation awards we seek to align our incentive compensation with the interests of our stockholders. We provide a comprehensive benefits package to help employees manage health, well-being, finances and life outside of work, including health, dental and vision insurance, life insurance, short-term and long-term disability insurance, paid sick leave, a 401(k) plan, a flexible spending account program and paid vacation time. We also strive to build an integrated, cohesive culture and safe work environment, designed so that the organization is structured and aligned to operate efficiently, decision making is timely and effective, and employees are supported, encouraged and motivated to do their best to support our mission and our values.

Information about our Executive Officers (as of February 19, 2026)

Name	Age	Position
James R. Porter, Ph.D.	50	Chief Executive Officer, President and Director
Alexandra Balcom, MBA, CPA	42	Chief Financial Officer and Treasurer
Deborah Miller, Ph.D., J.D.	50	Chief Legal Officer and Secretary
Darlene Noci, A.L.M.	49	Chief Development Officer
Christopher D. Turner, M.D.	58	Chief Medical Officer
Henry E. Pelish, Ph.D.	53	Chief Scientific Officer

James R. Porter, Ph.D., has served as our Chief Executive Officer and President and as a member of our board of directors since February 2020. Prior to that, Dr. Porter served as our Vice President, Product Development from April 2018 to January 2020 and worked as a consultant to the Company from January 2018 to April 2018. From July 2002 to December 2016, Dr. Porter held various roles at Infinity, including most recently as Vice President of Product Development. Over the course of over 14 years at Infinity, he contributed to the research and development programs of six different compounds entering clinical trials. As the duvelisib product

development team leader, Dr. Porter led a cross-functional development team from development candidate nomination through NDA submission, resulting in the FDA approval of COPIKTRA for patients with follicular lymphoma, small lymphocytic lymphoma and chronic lymphocytic leukemia. Following Infinity's licensing of duvelisib to Verastem, Inc., a biopharmaceutical company (Verastem), Dr. Porter served as Consultant, Product Development at Verastem from January 2017 to December 2017, where he led the transition, product development team and NDA submission for the duvelisib program. Dr. Porter received his B.A. in chemistry at the College of the Holy Cross and his Ph.D. in organic chemistry from Boston College.

Alexandra Balcom, MBA, CPA, has served as our Chief Financial Officer since January 2021. Ms. Balcom brings over 20 years of strategic, financial and operational experience in the biotechnology industry to her role. Before joining Nuvalent, she held various roles at SQZ Biotechnologies Company, a biotechnology company, from April 2017 to March 2021, including Vice President of Finance, where she was responsible for strategic planning, finance and accounting. Prior to that, Ms. Balcom served as Corporate Controller at Agios Pharmaceuticals Inc., a pharmaceutical company. Ms. Balcom was responsible for all financial functions of the company including strategic planning, treasury, tax, finance, and accounting. Earlier in her career, Ms. Balcom held positions at both Molecular Insight Pharmaceuticals Inc., a pharmaceutical company that was acquired by Progenics Pharmaceuticals, Inc., a biotechnology company, in 2013 and Coley Pharmaceutical Group, Inc., a biopharmaceutical company that was acquired by Pfizer in 2007. Ms. Balcom earned her B.B.A. in finance from the University of Massachusetts, Amherst and her MBA from Boston College. Ms. Balcom is also a certified public accountant in Massachusetts.

Deborah Miller, Ph.D., J.D., has served as our Chief Legal Officer since June 2021. Before joining Nuvalent, she held various roles at Sumitomo Dainippon Pharma America, Inc., a pharmaceutical company (SDPA), from April 2020 to June 2021, including Senior Vice President, Deputy General Counsel and Chief IP Counsel, where she was responsible for providing legal services to all of the North American companies of Sumitomo Dainippon Pharma Co., Ltd. (Sumitomo). Prior to that, Dr. Miller served as Deputy General Counsel & Chief IP Counsel at Sunovion Pharmaceuticals Inc., a subsidiary of SDPA, from March 2017 to April 2020, and held various roles at Infinity from March 2010 to March 2017, including Vice President, Deputy General Counsel and Chief Patent Counsel, where she built and managed the intellectual property group and supported various in-licensing, out-licensing and financing ventures. Earlier in her career, Dr. Miller was IP corporate counsel at Sepracor Inc. (currently, Sunovion Pharmaceuticals Inc.), a biopharmaceutical company, which was acquired by Sumitomo in 2010, and an associate at the law firm Nutter McClennen & Fish LLP. She received her B.A. in chemistry from Swarthmore College, her M.M.Sc. from Harvard Medical School, her Ph.D. in biological chemistry and molecular pharmacology from Harvard University and her J.D. from Suffolk University Law School.

Darlene Noci, A.L.M., has served as our Chief Development Officer since July 2022. Prior to that, she served as our Senior Vice President of Product Development & Regulatory Affairs from January 2021 until July 2022. Before joining Nuvalent, she founded her own regulatory consulting firm, Noci Strategic Consulting, LLC, in May 2018. Prior to that, Ms. Noci served as Vice President, Regulatory Affairs and Quality Assurance at X4 Pharmaceuticals, Inc., a biopharmaceutical company, from January 2016 to May 2018. Prior to that, Ms. Noci served as Global Regulatory Lead Strategist, Immuno-Oncology at EMD Serono, the North America biopharma business of Merck KgaA, Darmstadt, Germany, a pharmaceutical company, from June 2014 to January 2016, where she led the global regulatory strategy and portfolio for Bavencio, the company's anti-programmed death-ligand 1 antibody. Prior to that, she held various roles at several biotechnology companies, including Infinity, Sanofi and Genzyme (acquired by Sanofi in 2011). Ms. Noci received her B.A. from Adelphi University and her A.L.M. in government from Harvard University Extension School.

Christopher D. Turner, M.D., has served as our Chief Medical Officer since March 2021. Before joining Nuvalent, Dr. Turner served as Vice President of Clinical Development at Blueprint Medicines Corporation, a global precision therapy company, from June 2018 to March 2021, where he oversaw the development and approval of kinase inhibitor GAVRETO (pralsetinib) in RET-fusion positive NSCLC and RET-altered thyroid cancer. From July 2014 to May 2018, Dr. Turner served as Vice President of Clinical Science at Celldex Therapeutics, Inc., a biopharmaceutical company, where he led the development of novel antibody-drug conjugate and immune-oncology pipeline compounds. From July 2008 to July 2014, Dr. Turner held various roles at ARIAD Pharmaceuticals, Inc., a pharmaceutical company that was acquired by Takeda Oncology in 2017, including Head of Clinical Research, where he led the development of ICLUSIG (ponatinib), a kinase inhibitor therapy for patients with chronic myeloid leukemia, and ALUNBRIG (brigatinib), a kinase inhibitor therapy for patients with ALK positive NSCLC. Prior to that, Dr. Turner was Director of the Pediatric Neuro-Oncology Outcomes Clinic at the Dana-Farber Cancer Institute/Children's Hospital Boston and an Instructor of Pediatrics at Harvard Medical School. Dr. Turner is board certified in both Pediatrics and Pediatric Hematology and Oncology and is a Fellow of the American Academy of Pediatrics. He received his B.A. in biochemistry from Bowdoin College and his M.D. from the University of Rochester School of Medicine and Dentistry. He completed a residency in General Pediatrics at Children's National Medical Center in Washington, DC and fellowships in both Pediatric Hematology/Oncology and Pediatric Neuro-Oncology at Duke University Medical Center in Durham, North Carolina.

Henry E. Pelish, Ph.D., has served as our Chief Scientific Officer since July 2024. Prior to that, he served as our Senior Vice President, Drug Discovery from February 2023 until July 2024. Prior to that, he served as our Vice President, Drug Discovery from September 2022 until February 2023, Vice President, Biology from July 2019 until September 2022, and Senior Director, Biology from April 2018 until July 2019. Before his employment with Nuvalent, Dr. Pelish worked as a consultant to Nuvalent from February 2017 to April 2018. Dr. Pelish contributed scientifically to the creation of Nuvalent. Prior to April 2018, Dr. Pelish served as a Research Associate at Harvard University, where he contributed to the discovery of a new mechanism for targeting acute myeloid

leukemia cells that resulted in a licensing agreement and research collaboration with Merck. Dr. Pelish received a B.S. from Johns Hopkins, an M.S. from Stanford, and a Ph.D. in Chemistry and Chemical Biology from Harvard University.

Our Corporate Information

We were incorporated under the laws of the state of Delaware on January 25, 2017 under the name Nuvalent, Inc.

Our principal executive offices are located at One Broadway, 14th Floor, Cambridge, MA 02142 and our telephone number is (857) 357-7000. Our website address is *http://www.nuvalent.com*. The information contained on, or accessible through, our website does not constitute part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference.

Available Information

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

Item 1A. Risk Factors.

In evaluating the Company and our business, careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report and in other documents that we file with the SEC. Our business faces significant risks and uncertainties. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties were to actually occur, our business, prospects, financial condition or results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing the Company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any one factor or combination of factors may have on our business, prospects, financial condition or results of operations.

Risks related to our financial position and need for additional capital

We have a limited operating history, have no products approved for commercial sale and have not generated any revenue, which may make it difficult for investors to evaluate our current business and likelihood of success and viability.

We are a biopharmaceutical company with an operating history limited to research and development upon which investors can evaluate our business and prospects. We commenced significant operations in 2018, have no products approved for commercial sale and have never generated any revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. To date, we have devoted substantially all of our resources to research and development activities, including with respect to zidesamtinib (NVL-520), our ROS proto-oncogene 1 (ROS1)-selective inhibitor, neladalkib (NVL-655), our anaplastic lymphoma kinase (ALK)-selective inhibitor, NVL-330, our human epidermal growth factor receptor 2 (HER2)-selective inhibitor, and our discovery programs, business planning, establishing and maintaining our intellectual property portfolio, hiring personnel, raising capital, preparing for potential commercialization and providing general and administrative support for these operations.

In September 2025, we announced the completion of our New Drug Application (NDA) submission to the U.S. Food and Drug Administration (FDA) for zidesamtinib in tyrosine kinase inhibitors (TKI) pre-treated patients with locally advanced or metastatic (advanced) ROS1-positive non-small cell lung cancer (NSCLC) and subsequently, the FDA accepted for filing our NDA and assigned us a target action date of September 18, 2026 under the Prescription Drug User Fee Act (PDUFA). We cannot provide any assurances that the FDA will approve our NDA for zidesamtinib by the PDUFA target action date, or ever. We have not yet demonstrated our ability to successfully obtain marketing approvals, manufacture a commercial product at peak scale or have a third party do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, investors should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by clinical-stage biopharmaceutical companies such as ours. Any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by biopharmaceutical companies at our stage of development in rapidly evolving fields. As we approach the PDUFA target action date for zidesamtinib, we will also need to transition from a company with a primarily research and development focus to a company capable of undertaking commercial activities. We have not yet demonstrated an ability to successfully overcome such risks and difficulties, or to make such a transition. While we are in the process of establishing a commercial infrastructure in preparation for a commercial launch of zidesamtinib, if it is approved, and have been incurring costs in connection with such preparations, there can be no assurance that we will be able to obtain marketing approval for zidesamtinib or any of our other product candidates. Even if we are able to do so, we may not generate any meaningful return from the investments we have made and expect to make in the development of our product candidates or in connection with preparations for the commercial launch of our product candidates. We expect that our costs will continue to increase over time as we expand our operations, including our commercialization efforts. If we obtain marketing approval for zidesamtinib or our other product candidates, we will incur significant sales, marketing, manufacturing and distribution expenses. In addition, we may not be successful in building out the commercial, medical affairs and other functional capabilities that we believe will be necessary to operate as a fully integrated commercial-stage biopharmaceutical company, and our failure to do so could have an adverse effect on our anticipated development and commercialization timelines and on our financial condition and results of operations. If we do not adequately address these risks and difficulties or successfully make a transition to a commercial-stage company, our business will suffer.

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

We have incurred significant net losses in each reporting period since our inception, have not generated any revenue to date and have financed our operations principally through private placements and public offerings of securities. Our net losses were $425.4 million, $260.8 million and $126.2 million for the years ended December 31, 2025, 2024 and 2023, respectively. As of December 31, 2025, we had an accumulated deficit of $972.4 million. Our ability to generate revenue from product sales will depend heavily on the successful clinical development of, receipt of marketing approval from regulatory authorities for, and commercialization of one or more of our product candidates. 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 in order to discover, develop and market additional potential products.

We expect to incur significant expenses and significant net losses for the foreseeable future. We anticipate that our expenses will increase over time as we prepare for the potential commercialization of zidesamtinib, including due to the impact of increased headcount, and to support our clinical and commercialization activities and expanded infrastructure, among other things. If we obtain marketing approval of zidesamtinib, we expect to incur further increased sales, marketing, distribution and manufacturing expenses. Further, the net losses we incur may fluctuate 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 pace of our development and commercialization activities and 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, our ability to fund the development of our product candidates and our ability to achieve and maintain profitability and the performance of our stock.

Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve our objectives relating to the discovery, development and commercialization of our product candidates.

We rely on our team's expertise in chemistry, structure-based drug design, oncology drug development, business development and our patient-driven approach to develop our product candidates. Our business depends significantly on the success of our approach and the development and commercialization of the product candidates that we discover with this approach. We have been incurring commercialization expenses related to zidesamtinib, including costs associated with building a commercial infrastructure, and expect to incur additional commercialization expenses in advance of potentially receiving marketing approval for zidesamtinib. However, we currently have no products approved for commercial sale, and we have not generated any revenue to date. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives, including:

- successful and timely completion of preclinical and clinical development of our current and future product candidates;
- maintaining current and establishing new relationships with contract research organizations (CROs) and clinical sites for the clinical development of our current and future product candidates;
- timely receipt of marketing approvals from applicable regulatory authorities for our product candidates;
- developing an efficient and scalable manufacturing process for our product candidates, including the production of finished products that are appropriately packaged for sale if our product candidates obtain marketing approvals;
- maintaining current and establishing new 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 our product candidates, if approved;
- successful commercial launch following any marketing approval, including the development of a commercial infrastructure;
- maintaining an 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, including the willingness of physicians to use our product candidates, if approved, in lieu of (or in conjunction with) other approved therapies;
- satisfying any required post-marketing approval commitments to applicable regulatory authorities;
- identifying, assessing and developing new product candidates;
- obtaining, maintaining and expanding patent protection, trade secret protection and regulatory exclusivity, both in the United States (U.S.) and internationally;
- defending against third-party interference or infringement claims, if any;
- entering into, on favorable terms, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- obtaining coverage, adequate pricing and adequate reimbursement by third-party payors for our product candidates, if approved;
- 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. Even 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 Class A common stock 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 may require additional funding to finance our operations. If we are unable to obtain such funding 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, commercialization efforts, product development or other operations.

Since our inception, we have used substantial amounts of cash to fund our operations, and we expect to incur significant expenses for the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development of, initiate additional clinical trials of, seek marketing approval for, prepare for the commercialization of, and, if approved, commercialize our product candidates. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Even if one or more of our product candidates or any future product candidates that we develop are approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing and distribution activities. Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency (EMA) or other regulatory authorities to perform clinical trials or preclinical studies in addition to those that we currently anticipate. Other unanticipated costs may also arise. Because the success of our research, development and commercialization activities is highly uncertain, we cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of our product candidates or any future product candidates. We are not permitted to market or promote any product candidate before we receive marketing approval from the FDA, EMA or any comparable foreign regulatory authorities. Accordingly, we may need to obtain additional funding in order to continue our operations.

Based on our current operating plan, we believe that our existing cash, cash equivalents and marketable securities as of the date of this Annual Report will be sufficient to fund our operating expenses and capital expenditure requirements into 2029. Advancing the development of zidesamtinib, neladalkib, NVL-330 and our discovery programs and ultimately commercializing them, if approved, will require a significant amount of capital. Our existing cash, cash equivalents and marketable securities may not be sufficient to fund all of our product candidates through regulatory approval and into commercialization, if approved. We cannot be certain as to when, if ever, we will be able to generate substantial product revenues sufficient to fund our operations. We may, therefore, need to raise additional capital to complete the development and commercialization of our product candidates. Our estimate as to how long we expect our existing cash, cash equivalents and marketable securities to fund our operations does not include potential product revenue and 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.

Until such time, if ever, that we can generate substantial product revenues, we may be required to finance our funding needs through public or private equity financings, debt financings, collaborative agreements, licensing arrangements or other sources of financing, which may dilute our stockholders or restrict our operating activities. We do not have any committed external source of funds. Adequate additional funding may not be available to us on acceptable terms, or at all. Our ability to raise additional funds may be adversely impacted by general economic conditions, both inside and outside the U.S., including disruptions to, and instability and volatility in, the credit and financial markets in the U.S. and worldwide, including heightened inflation, interest rate and currency rate fluctuations, and economic slowdown or recession as well as concerns related to public health emergencies, natural disasters or geopolitical events, including actual or threatened tariffs or other changes in trade policy, civil or political unrest or military conflicts. In addition, market instability and volatility, high levels of inflation and interest rate fluctuations may increase our cost of financing or restrict our access to potential sources of future liquidity. To the extent that we raise additional capital through the sale of equity or convertible debt securities, each investor's ownership interests will be diluted, and the terms may include liquidation or other preferences that adversely affect each investor's rights as a stockholder. Debt financing may result in imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through upfront payments or milestone payments pursuant to 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 opportunistically 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.

Our failure to obtain funding 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 or drug development programs, clinical trials or commercialization efforts.

Risks related to the discovery, development and commercialization of our product candidates

Our future prospects are substantially dependent on zidesamtinib, neladalkib and NVL-330. If we are unable to advance these product candidates through development, obtain regulatory approval and ultimately commercialize such product candidates, or experience significant delays in doing so, our business will be materially harmed. Even if we obtain regulatory approval for such candidates, there is no assurance that our commercialization efforts will be successful or that we will be able to generate revenues or profits at the levels or on the timing we expect, if at all.

We are currently conducting Phase 1/2 clinical trials of zidesamtinib and neladalkib, a Phase 3 clinical trial of neladalkib, and a Phase 1 clinical trial of NVL-330. In November 2025, the FDA accepted for filing our NDA for zidesamtinib in TKI pre-treated patients with advanced ROS1-positive NSCLC and assigned us a target action date of September 18, 2026 under PDUFA. We cannot provide any assurances that the FDA will approve our NDA for zidesamtinib by the PDUFA target action date, or ever.

Our ability to generate product revenue will depend heavily on the successful clinical development of, receipt of marketing approval from regulatory authorities for, and commercialization of one or more product candidates. We are not permitted to market or promote any product candidate before we receive marketing approval from the FDA, EMA or any comparable foreign regulatory authorities, and we may never receive such marketing approvals.

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

- successful and timely completion of preclinical studies;
- submission of Investigational New Drug applications (INDs) in the U.S. and clinical trial applications (CTAs) and/or comparable applications outside the U.S. for regulatory authority review and agreement to proceed with our clinical trials;
- successful initiation and completion of clinical trials;
- successful and timely patient selection and enrollment in and completion of clinical trials;
- maintaining and establishing relationships with CROs and clinical sites for the clinical development of our product candidates both in the U.S. and internationally;
- maintaining and growing an organization of scientific, medical and other professionals who can develop and commercialize our product candidates;
- the frequency and severity of adverse events in clinical trials;
- obtaining positive data that support demonstration of efficacy, safety and tolerability profiles and durability of effect for our product candidates that are satisfactory to the FDA, EMA or any comparable foreign regulatory authority for marketing approval;
- the timely receipt of marketing approvals from applicable regulatory authorities;
- the timely identification, development and approval of companion diagnostic tests, if required;
- 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 and, if approved, commercialization of our product candidates;
- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the U.S. and internationally;
- the protection of our rights in our intellectual property portfolio;
- continuing to build sales, marketing and distribution capabilities and the successful launch of commercial sales of our product candidates if and when approved for marketing, whether alone or in collaboration with others;
- maintaining an acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors, including the willingness of physicians to use our product candidates, if approved, in lieu of (or in conjunction with) other approved therapies;
- our ability to compete with other therapies; and
- our ability to address any potential delays resulting from factors related to public health emergencies, natural disasters or geopolitical events.

We do not have complete control over many of these factors, including certain aspects of preclinical and 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 any product candidates from our lead programs, which would materially harm our business. If we do not receive marketing approvals for such product candidates, we may not be able to continue our operations.

Even if we obtain regulatory approval for any of our product candidates, we may never be able to successfully commercialize any product to achieve profitability. We have never marketed, sold or distributed for commercial use any pharmaceutical product. We may encounter issues, delays or other challenges in launching or commercializing a product candidate or generating revenues, if approved,

which could impair our ability to successfully commercialize the product or to generate revenues or profits or to meet our expectations with respect to the amount or timing of revenues or profits.

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

Before obtaining marketing approval from the FDA, EMA or other comparable foreign regulatory authorities for the sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and the ultimate outcome is uncertain. Failure can occur at any time during the preclinical study and clinical trial processes, there is a high risk of failure, and we may never succeed in developing marketable products.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent receipt of marketing approval or our ability to commercialize our product candidates, including:

- failure of our product candidates in preclinical studies or clinical trials to demonstrate safety and efficacy;
- receipt of feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- negative or inconclusive clinical trial results that may require us to conduct additional clinical trials or abandon certain research, discovery and/or drug development programs;
- the number of patients required for clinical trials being larger than anticipated, enrollment in these clinical trials being slower than anticipated, particularly if there are other trials enrolling the same or overlapping precisely targeted patient populations, or participants dropping out of these clinical trials at a higher rate than anticipated;
- third-party contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the suspension or termination of our clinical trials for various reasons, including non-compliance with regulatory requirements or a finding that our product candidates have undesirable adverse events or other unexpected characteristics or risks;
- the cost of clinical trials of our product candidates being greater than anticipated;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates being insufficient or inadequate;
- regulators determining that the requirements for approving our product candidates are different than what we expect or are different from regulatory precedent, including potentially in connection with feedback from the FDA regarding what data from our clinical trials may constitute pivotal data sufficient to support NDA submissions; and
- regulators revising the requirements for approving our product candidates.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we are currently contemplating, if we are unable to successfully complete clinical trials of our product candidates or other testing in a timely manner, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may incur unplanned costs, be delayed in seeking and obtaining marketing approval, if we receive such approval at all, receive more limited or restrictive marketing approval, be subject to additional post-marketing testing requirements or have the drug removed from the market after obtaining marketing approval.

Our discovery and development activities are focused on the development of targeted therapeutics for patients with cancer-associated genomic alterations, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs may never lead to approved or marketable products.

The discovery and development of targeted therapeutics for patients with cancer-associated genomic alterations is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop product candidates are evolving. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. Although we believe, based on our preclinical work and clinical trials to date, that the genomic alterations targeted by our programs are oncogenic drivers, clinical results may not confirm this hypothesis or may only confirm it for certain alterations or certain tumor types. The patient populations for our product candidates are limited to those with specific target alterations and may not be completely defined but are substantially smaller than the general treated cancer population, and we will need to screen and identify these patients with targeted alterations. Successful identification of patients is dependent on several factors, including achieving certainty as to how specific alterations respond to our product candidates and the ability to identify such alterations, which may require the use of companion diagnostic tests. Furthermore, even if we are successful in identifying patients, we cannot be certain that the resulting patient populations for each mutation will be large enough to allow us to successfully obtain approval for each mutation

type and commercialize our product candidates and achieve profitability. We do not know if our approach of focusing on treating patients with cancer-associated genomic alterations will be successful, and if our approach is unsuccessful, our business will suffer.

Any delays in the commencement or completion, or termination or suspension, of our current, planned or future clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before we can initiate clinical trials of any product candidate in any indication, we must submit the results of preclinical studies to the FDA, EMA or other comparable foreign regulatory authorities along with other information, including information about the product candidate's chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND or similar regulatory submission under which we must receive authorization to proceed with clinical development. The FDA, EMA or other comparable foreign regulatory authorities may require us to conduct additional preclinical studies for any product candidate before they allow us to initiate clinical trials under any IND, CTA or comparable application which may lead to additional delays and increase the costs of our preclinical development programs.

Before obtaining marketing approval from the FDA of any of our product candidates, including any future product candidates, in any indication, we must conduct extensive clinical studies to demonstrate safety and efficacy. Clinical testing is expensive, time consuming and uncertain as to outcome. In addition, we expect to rely in part on preclinical, clinical and quality data generated by our 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 are currently conducting Phase 1/2 clinical trials of zidesamtinib and neladalkib, a Phase 3 clinical trial of neladalkib, and a Phase 1 clinical trial of NVL-330. An IND submission must become effective prior to initiating any clinical trials in the U.S. for any of our future product candidates.

We could also encounter delays if a clinical trial is suspended or terminated by us, by an institutional review board (IRB) or independent ethics committee (IEC) of the institutions in which such trials are being conducted, by a data monitoring committee for such trial or by the FDA or 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 foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse events, failure to demonstrate a benefit from using a pharmaceutical, 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/IECs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Further, 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 be impacted. For example, in December 2022, with the passage of the Food and Drug Omnibus Reform Act (FDORA), Congress required sponsors to develop and submit a diversity action plan (DAP) for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for diversity action plans (DAPs). Unlike most guidance documents issued by the FDA, if the DAP guidance is finalized, it would have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are to be specified in FDA guidance.

In January 2025, in response to an executive order issued by President Trump, relating to diversity, equity and inclusion programs, the FDA removed the draft DAP guidance from its website. That action, along with similar actions by the Trump administration to remove certain other healthcare webpages, is currently the subject of ongoing litigation. Accordingly, in light of these ongoing actions, there is considerable uncertainty surrounding the draft DAP guidance and how the FDA will consider DAPs in connection with its review of NDAs.

Similarly, the regulatory landscape related to clinical trials in the European Union (EU) recently evolved. The Clinical Trials Regulation (EU) No 536/2014 (CTR), which was adopted in April 2014 and repealed the Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate CTA to be submitted in each member state, to both the competent national health authority and an IEC, 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.

Certain of our current or future scientific advisors or consultants who receive compensation from us may become investigators for our future clinical trials. Under certain circumstances, we may be required to report some of these relationships to the FDA. Although we expect any such relationships to be within the FDA's guidelines, the FDA 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 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 and may ultimately lead to the denial of marketing approval of our product candidates. If we experience delays in the completion of, or termination of, any clinical trial of any product candidate, the commercial prospects of such product candidate will be harmed, and our ability to generate product revenue will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenue, which may harm our business, financial condition, results of operations and prospects significantly.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later-stage clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities and we may not be able to commercialize our product candidates.

For each of our product candidates, we are required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use before we can seek marketing approvals for their commercial sale. Preclinical and clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Further, we have limited experience as a company in conducting and managing clinical trials, including later-stage clinical trials, necessary to support applications for marketing approval. Failure can occur at any time during the preclinical study and clinical trial processes, there is a high risk of failure, and we cannot guarantee that we will succeed in developing and commercializing marketable products.

The results of preclinical studies may not be predictive of the results of clinical trials of our product candidates, and the results of early clinical trials may not be predictive of the results of later-stage clinical trials. Although product candidates may demonstrate promising results in preclinical studies and early clinical trials, they may not prove to be safe or effective in subsequent clinical trials. Favorable results from certain animal studies may not accurately predict the results of other animal studies or of human trials, due to the inherent biologic differences in species, the differences between testing conditions in animal studies and human trials, and the particular goals, purposes, and designs of the relevant studies and trials. Similarly, certain of our hypotheses regarding the potential clinical and therapeutic benefits of our product candidates compared to other products or molecules in development are based on observations from the preclinical studies and early clinical trials that we have completed, and results from such preclinical studies and early clinical trials are not necessarily predictive of the results of later preclinical studies or clinical trials.

There is typically an extremely high rate of attrition from the failure of product candidates proceeding through preclinical studies and clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. Likewise, early, smaller-scale clinical trials may not be predictive of eventual safety or effectiveness in large-scale pivotal 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. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy, insufficient durability of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence preclinical studies and clinical trials are never approved as products. The development of our product candidates and our stock price may also be impacted by inferences, whether correct or not, that are drawn between the success or failure of preclinical studies or clinical trials of our competitors or other companies in the biopharmaceutical industry, in addition to our own preclinical studies and 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 dose and 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 adverse events that are unrelated to our product candidates. 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.

Any preclinical studies or clinical trials that we conduct may not demonstrate the safety and efficacy necessary to obtain regulatory approval to market our product candidates. If the results of our ongoing or future preclinical studies and clinical trials are inconclusive with respect to the safety and efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for such product candidates.

If we are unable to obtain marketing approval for any of our product candidates, the commercialization prospects and our business and financial prospects would be materially adversely affected.

In addition to zidesamtinib, neladalkib and NVL-330, our prospects depend in part upon discovering, developing and commercializing additional product candidates from our discovery programs, 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 zidesamtinib, neladalkib, NVL-330 and future product candidates from our discovery programs. A research candidate

can unexpectedly fail at any stage of development. The historical failure rate for research 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 research candidates that we may develop will depend on many factors, including the following:

- generating sufficient data to support the initiation or continuation of preclinical studies and 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 a product candidate for use in clinical trials;
- adverse events in clinical trials; and
- addressing any delays resulting from factors related to public health emergencies, natural disasters or geopolitical events.

Even if we successfully advance any research candidates into preclinical and clinical development, their success will be subject to all of the preclinical, clinical, regulatory and commercial risks described elsewhere in this "Risk Factors" section.

There can be no assurance that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from our product candidates.

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

Obtaining approval by the FDA, EMA 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 for our product candidates, the FDA, EMA 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 or may impose other prescribing limitations or warnings that limit the product candidate's commercial potential. Even if approved, we may be required to conduct additional studies to verify or confirm the clinical benefits of our products. We have not obtained regulatory approval for any product candidate, nor have we submitted for regulatory approval for any product candidate other than zidesamtinib, and it is possible that none of our product candidates will ever obtain regulatory approval. Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control.

Further, under the Pediatric Research Equity Act (PREA), an NDA or supplement to an NDA for certain drug products must contain data to assess the safety, potency and purity of the drug product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe, potent and pure, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety, potency and purity data need to be collected before the pediatric trials begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to publicly post the PREA Non-Compliance letter and the sponsor's response. The applicable legislation in the EU also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the EMA or to obtain a waiver or deferral from the conduct of these studies by this Committee.

For any of our product candidates for which we are seeking regulatory approval in the U.S. or the EU, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in an issuance and publication of a PREA Non-Compliance letter and associated reputational harm, our product candidate being considered misbranded and subject to relevant enforcement action, invalidation of the marketing application, and/or financial penalties.

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

- the FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or other comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, are only moderately effective or have undesirable or unintended adverse events, 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, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the clinical data of the clinical trial may fail to meet the level of statistical significance required to obtain approval of our product candidates by the FDA, EMA or other comparable foreign regulatory authorities;
- we may be unable to demonstrate to the FDA, EMA or other comparable foreign regulatory authorities that our product candidates' risk-benefit ratios for their proposed indications are acceptable;
- the FDA, EMA 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;
- the FDA, EMA or other comparable regulatory authorities may fail to approve companion diagnostic tests required for our product candidates;
- we may not obtain or maintain adequate funding to complete the clinical trial in a manner that is satisfactory to the FDA, EMA or other comparable foreign regulatory authorities; and
- the approval policies or regulations of the FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

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.

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

If our product candidates are associated with undesirable adverse events 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 adverse events or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related adverse events 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. There have been, and it is likely that there will be additional, adverse events associated with the use of our product candidates as is typically the case with oncology drugs. Results of our studies or trials could reveal a high and unacceptable severity and prevalence of these or other adverse events. In such an event, our trials could be suspended or terminated and the FDA, EMA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Drug-related adverse events could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, our product candidates may be used in populations for which safety concerns may be particularly scrutinized by regulatory authorities. Our product candidates may be studied in combination with other therapies, which 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 adverse events that are unrelated to our product candidates 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. For example, it is expected that some of the patients to be enrolled in our current or future clinical trials may die or experience major clinical events either during the course of our clinical trials or after participating in such trials for non-treatment related reasons.

If significant adverse events 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, EMA, other comparable foreign 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 events. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause adverse events that prevented their further development. Even if the adverse events do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable adverse events 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 obtain marketing approval, toxicities associated with such product candidates previously 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.

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

We have publicly disclosed interim, preliminary or topline data from our preclinical studies and clinical trials and we expect to do so in the future. These interim updates are based on preliminary analyses 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. For example, we may report responses in certain patients that are unconfirmed at the time and which do not ultimately result in confirmed responses to treatment after follow-up evaluations. 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 interim, preliminary or topline results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Interim, preliminary and topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the interim, preliminary or topline data we previously published. As a result, interim, preliminary and topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim, preliminary and topline data from clinical trials 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. Adverse changes between interim, preliminary or topline data and final data could significantly harm our business and prospects. Further, additional disclosure of interim, preliminary or topline data by us or by our competitors in the future could result in volatility in the price of our Class A common stock.

In addition, the information we choose to publicly disclose regarding a particular study or trial is typically selected from a more extensive amount of available information. Investors may not agree with what we determine is the material or otherwise appropriate information to include in our public disclosures, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the interim, preliminary or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, any of our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

If we experience delays or difficulties in the enrollment or maintenance of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to such trial's conclusion as required by the FDA, EMA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. We utilize genomic profiling of patients' tumors to identify suitable patients for recruitment into our clinical trials. For these clinical trials, we seek patients with specific genomic alterations that our product candidates are designed to precisely target. We cannot be certain (i) how many patients will have the requisite genomic alterations that qualify for inclusion in our clinical trials, (ii) that the number of patients enrolled in each program will suffice for regulatory approval or (iii) if regulatory approval is obtained, whether each specific ROS1, ALK or HER2 alteration will be included in the approved drug label. Additionally, we face competition, including from large pharmaceutical companies with significantly more resources than us, for enrollment of our precisely targeted patient populations, which may impact our ability to successfully recruit patients for our clinical trials. If our strategies for patient identification and enrollment prove unsuccessful, we may have difficulty enrolling or maintaining patients appropriate for our product candidates.

Patient enrollment may be affected if our competitors have ongoing clinical trials for programs 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' programs. Patient enrollment for our current or future 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, including biomarker-driven identification and/or certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have a biomarker-driven patient eligibility criteria;
- 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 or other product candidates being investigated for the indications we are investigating;
- clinicians' willingness to screen their patients for biomarkers to indicate which patients may be eligible for enrollment in our 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; 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 participation in our clinical trials through the treatment and any follow-up periods.

We have never commercialized a product candidate as a company before and currently lack substantially all of 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 as a company. While we are in the process of establishing a commercial infrastructure in preparation for a potential future product launch if one or more of our product candidates receives marketing approval, we may license certain rights with respect to our product candidates to collaborators, and, if so, we will rely on the assistance and guidance of those collaborators. For product candidates for which we retain commercialization rights and marketing approval, we will have to continue to build 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, if approved, on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, developing adequate educational and marketing programs to increase public acceptance of our approved product candidates, ensuring regulatory compliance of our Company, employees and third parties under applicable healthcare laws, 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 upon approval. 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 revenue from them or be able to reach or sustain profitability.

Even if one of our product candidates receives marketing approval, we or others may later discover that the product is less effective or tolerable than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of our collaborators, to market the product.

Clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we or others discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;

- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we, or our collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could harm our business and operations and could negatively impact our stock price.

We have limited resources and are currently focusing our efforts on zidesamtinib, neladalkib and NVL-330 in particular indications and advancing our discovery programs. As a result, we may fail to capitalize on other indications or product candidates that may ultimately have proven to be more profitable.

We are currently focusing our resources and efforts on our lead product candidates, zidesamtinib and neladalkib, for advanced ROS1-positive NSCLC and other solid tumors and advanced ALK-positive NSCLC and other solid tumors, respectively, on NVL-330 for advanced HER2-altered NSCLC, and on advancing our discovery programs. As a result, because we have limited resources, we may forgo or delay pursuit of opportunities for other indications or with other product candidates that may have greater commercial potential. 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 activities for zidesamtinib, neladalkib, NVL-330 and our discovery programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target markets for zidesamtinib, neladalkib, NVL-330 or any future product candidates we identify through our discovery programs, we may enter into collaboration, licensing or other strategic arrangements with the effect of relinquishing valuable rights in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

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

The pharmaceutical and biotechnology 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 product candidates 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 product candidates may need to compete with drugs physicians use off-label to treat the indications for which we seek approval. This may make it difficult for us to replace existing therapies with our product candidates.

In particular, there is intense competition in the field of oncology. We have competitors both in the U.S. 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 and retain qualified 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 and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We expect to face competition from existing products and products in development for each of our lead programs and in particular, our competitors that are developing product candidates often have the advantage of significant financial resources.

For zidesamtinib, there are currently four ROS1-targeted kinase inhibitors approved by the FDA for use in TKI-naïve ROS1-positive NSCLC: Xalkori (crizotinib), Rozlytrek (entrectinib), Augtyro (repotrectinib) and Ibtrozi (taletrectinib). Crizotinib has also received approval for treatment of ALK-positive NSCLC. Lorbrena (lorlatinib) is another therapy recommended for use in ROS1-positive NSCLC patients according to the National Comprehensive Cancer Network guidelines. Lorlatinib is a dual ALK/ROS1 inhibitor that has received marketing approval for the treatment of ALK-positive NSCLC and has demonstrated central nervous system activity as reported in its prescribing information.

For neladalkib, there are six ALK inhibitors approved by the FDA for the treatment of ALK-positive NSCLC: crizotinib, Zykadia (ceritinib), Alecensa (alectinib), Alunbrig (brigatinib), lorlatinib and Ensacove (ensartinib). All six have line-agnostic approvals for the treatment of ALK-positive NSCLC patients, including for patients who are TKI-naïve. Additionally, lorlatinib has demonstrated activity in patients that have progressed on crizotinib, alectinib, or ceritinib.

For NVL-330, there are two HER2 inhibitors approved by the FDA for the treatment of HER2-altered NSCLC: Hernexeos (zongertinib) and Hyrnuo (sevabertinib). Additionally, Enhertu (T-DXd), an antibody-drug conjugate, has been approved by the FDA for the treatment of HER2 mutant NSCLC.

Many of our competitors, either alone or with their collaborators, have significantly greater financial resources, established presence in the market, and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Large pharmaceutical and biotechnology companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing biotechnology product candidates. These companies also have significantly greater research and marketing capabilities than we do and may also have product candidates 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, EMA or other comparable foreign regulatory authorities or in discovering, developing and commercializing product candidates in our field before we do.

Our potential commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe adverse events, are more convenient, have a broader label, are marketed more effectively, are more widely reimbursed or are less expensive than any products that we may develop. Physicians may be more willing to prescribe our competitors' products for various reasons, and may rely on guidelines related to treatment of patients issued by medical societies, industry groups or other organizations, which may not include, and may never include, our products. Our competitors also may obtain marketing approval from the FDA, EMA 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 or make our development and marketing more complicated. 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.

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, as well as sophisticated quality assurance and quality control procedures. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. Contaminations can also lead to allegations of harm, including infections or allergic reactions, or closure of product facilities due to possible contamination.

If our third-party 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.

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. For example, we may introduce an alternative formulation of one or more of our product candidates during the course of our clinical trials. 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 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 impair our ability to generate revenue.

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, third-party 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 a product candidate is approved;
- restrictions on the use of product candidates in the labeling approved by regulatory authorities, such as boxed warnings or contraindications in labeling, or a Risk Evaluation and Mitigation Strategy (REMS), if any, which may not be required of alternative treatments and competitor products;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement by third-party payors, including government authorities;
- the ability to establish appropriate sales prices for our product candidates;
- willingness of physicians to use our product candidates, if approved, in lieu of (or in conjunction with) other approved therapies;
- the availability of an 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 undergo required diagnostic screening to determine treatment eligibility and of physicians to prescribe these therapies and diagnostic tests;
- the effectiveness of sales and marketing efforts;
- unfavorable publicity relating to our product candidates; and
- the approval of other new therapies for the same indications.

If any of our product candidates are approved but do 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.

The market opportunities for any product candidates we develop, if approved, may be limited to certain smaller patient subsets and may be smaller than we estimate them to be.

When cancer is detected early (referred to as localized disease), conventional treatments, which include chemotherapy, hormone therapy, surgery and radiation therapy and/or selected targeted therapies, may be adequate to cure the patient in many cases. However, once cancer has spread to other areas (advanced or metastatic disease), cancer treatments may not be sufficient to provide a cure but often can significantly prolong life without curing the cancer. First-line therapies designate treatments that are initially administered to patients with advanced or metastatic disease, while second- and third-line therapies are administered to patients when the prior therapies lose their effectiveness. The FDA, EMA and other regulatory bodies often approve cancer therapies for a particular line of treatment. Typically, drug approvals are initially granted for use in later lines of treatment, but with additional evidence of significant efficacy from clinical trials, biopharmaceutical companies can successfully seek and gain approval for use in earlier lines of treatment.

We plan to initially seek approval of zidesamtinib, neladalkib, NVL-330 and any other future product candidates in most instances for previously treated patients with advanced or metastatic cancer where at least one prior therapy has limited clinical benefit or where tumors have developed resistance to such therapy. For those product candidates that prove to be sufficiently safe and effective, if any, we would potentially expect to seek approval ultimately as a first line TKI therapy. There is no guarantee that our product candidates, even if approved for previously treated patients would be approved for an earlier line of therapy, and prior to any such approvals we may have to conduct additional clinical trials that may be costly, time-consuming and subject to risk.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive a particular line of therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new data and studies may change the estimated incidence or prevalence of the cancers that we are targeting, especially if new therapies that are approved while we advance our product candidates affect the treatment paradigm and/or the size of the target population. The potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. Consequently, even if our product candidates are approved, the number of patients that may be eligible for treatment with our product

candidates may turn out to be much lower than expected. In addition, we have not yet conducted market research to determine how treating physicians would expect to prescribe a product that is approved for multiple tumor types if there are different lines of approved therapies for each such tumor type. Even if we obtain significant market share for our products, if approved, if the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications.

Even if we are able to commercialize any of our product candidates, the drugs may become subject to unfavorable third-party coverage and reimbursement practices, as well as pricing regulations.

Patients rely on insurance coverage by third-party payors (third-party payors include federal healthcare programs such as Medicare and Medicaid and commercial insurance companies such as Blue Cross Blue Shield, Humana, Cigna, etc.), to pay for products. The availability and extent of coverage and adequate reimbursement by third-party payors, including federal healthcare programs, 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 U.S. and internationally, on the extent to which the costs of such product candidates will be covered and reimbursed by third-party payors. No uniform policy exists for coverage and reimbursement in the U.S. 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 U.S., for example, principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services (CMS), an agency within the U.S. Department of Health and Human Services (HHS). CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor's determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate. As a result, the coverage determination process is often time-consuming and costly. Factors payors consider in determining reimbursement include: (i) a covered benefit under its health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost-effective; and (v) neither experimental nor investigational. This process may 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.

As federal and state governments implement additional healthcare cost containment measures, including measures to lower prescription drug pricing, we cannot be sure that our products, if approved, will be covered by private or public payors, and if covered, whether the reimbursement will be adequate or competitive with other marketed products. Such other actions by federal and state governments and health plans may put additional downward pressure on pharmaceutical pricing and healthcare costs, which could negatively impact coverage and reimbursement for our products if approved, our revenue, and our ability to compete with other marketed products and to recoup the costs of our research and development. For further discussion, see "— Current and future legislation may increase the difficulty and cost for us to obtain reimbursement for our product candidates;" and "— The prices of prescription pharmaceuticals in the U.S. and foreign jurisdictions are the subject of considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed for marketing."

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.

In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or products, will apply to companion diagnostics. Additionally, if any companion diagnostic provider is unable to obtain reimbursement or is inadequately reimbursed, that may limit the availability of such companion diagnostic, which would negatively impact prescriptions for our product candidates, if approved.

Outside the U.S., the commercialization of therapeutics is 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 countries of the EU, medical product prices are subject to varying price control mechanisms as part of national health systems. In

these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing approval. 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 U.S. 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 U.S., the reimbursement for our products may be reduced compared with the U.S. 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 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.

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 and other risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability and other claims or incidents, such as cyber incidents and breaches, could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an FDA, EMA or other regulatory authority investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs. FDA, EMA 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 and other insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to advancing our product candidates into later stages of development or 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, product liability, and other types of insurance (such as cyber insurance) is becoming increasingly expensive and difficult to obtain. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability or other claims or incidents, including data breach and incidents, that could have an adverse effect on our business and financial condition.

Risks related to regulatory approval and other legal compliance matters

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

Our product candidates are and will continue to be 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 U.S. and in many foreign jurisdictions before a new drug can be approved for marketing. 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.

Although the FDA accepted for filing our NDA for zidesamtinib in TKI pre-treated patients with advanced ROS1-positive NSCLC and assigned us a target action date of September 18, 2026 under PDUFA, we have not completed the regulatory approval process with the FDA, EMA or any other regulatory authority. The time required to obtain approvals from the FDA, EMA 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 does, change 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 applicable FDA, EMA or other regulatory policy during the period of drug development, clinical trials and regulatory review.

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

- the FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or other comparable foreign regulatory authorities may determine that our product candidates are not safe and effective or have undesirable or unintended adverse events, 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, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- we may be unable to demonstrate to the FDA, EMA or other comparable foreign regulatory authorities that our product candidates' risk-benefit ratios for their proposed indications are acceptable;
- the FDA, EMA 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, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from any particular product candidates we are developing and for which we are 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, promote and advertise the drug or the labeling or other restrictions. In addition, the FDA has the authority to require a REMS plan as part of approving an NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. 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.

In addition, we could be adversely affected by several significant administrative law cases decided by the U.S. Supreme Court in 2024. In Loper Bright Enterprises v. Raimondo, for example, the U.S. Supreme Court overruled Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc., which previously required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U.S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the U.S. Administrative Procedure Act (APA). Additionally, in Corner Post, Inc. v. Board of Governors of the Federal Reserve System, the U.S. Supreme Court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, Securities and Exchange Commission v. Jarkesy, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty, delays and other impacts, any of which could adversely impact our business and operations.

Finally, substantial uncertainty remains as to how, if at all, the current presidential administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The impending uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates.

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.

We may develop our current or future product candidates in combination with other therapies, which would expose us to additional risks.

We may develop our current or future product candidates in combination with one or more currently approved cancer therapies or therapies in development. Even if any of our current or future product candidates 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, EMA or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any of our product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our product candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our product candidates or our own products being removed from the market or being less successful commercially.

We may also evaluate our current or future product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA, EMA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval.

If the FDA, EMA or other comparable foreign regulatory authorities do not approve or withdraw their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with any of our current or future product candidates, we may be unable to obtain approval of or successfully market any one or all of the current or future product candidates we develop. Additionally, if the third-party providers of therapies or therapies in development used in combination with our current or future product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our current or future product candidates, or if the cost of combination therapies are prohibitive, 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.

We have conducted and intend to continue conducting certain of our clinical trials globally. However, the FDA and other foreign equivalents may not accept data from such trials, in which case our development plans may be delayed, which could materially harm our business.

We have conducted and intend to continue conducting certain of our clinical trials globally. The acceptance by the FDA or other regulatory authorities of study data from clinical trials conducted outside of their respective jurisdictions 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 good clinical practice (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 would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Conducting clinical trials outside the U.S. also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- diminished protection of intellectual property in some countries; and
- interruptions or delays in our trials resulting from geopolitical events, including actual or threatened tariffs or other changes in trade policy, civil or political unrest or military conflicts.

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 or EMA 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 U.S., 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 U.S., 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 potential product candidates will be harmed.

Further, we could face heightened risks with respect to obtaining marketing authorization in the United Kingdom (U.K.) as a result of the withdrawal of the U.K. from the EU, commonly referred to as Brexit. The U.K. is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency (MHRA) is responsible for approving all medicinal products destined for the U.K. market (i.e., Great Britain and Northern Ireland). In April 2025, the U.K. Parliament adopted amendments to improve and strengthen the U.K.'s clinical trials regulatory regime; they will take effect in April 2026. These changes were needed since the current U.K. requirements are based upon the now-repealed EU Clinical Trials Directive (2001/20/EC), which has been replaced by the European Clinical Trials Regulation (Regulation EU No 536/2014) (EU CTR). Since the U.K. left the EU prior to the date on which the EU CTR took effect, the U.K. legal framework did not benefit from the same revisions as occurred at EU level.

At the same time, a new international recognition procedure (IRP) will apply, which intends to facilitate approval of pharmaceutical products in the U.K. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators (RRs). The RRs notably include the EMA and regulators in the European Economic Area (EEA) Member States for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals may force us or our collaborators to restrict or delay efforts to seek regulatory approval in the U.K. for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is anticipated in 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term. On June 4, 2025, the European Council adopted its position on the proposed overhaul of the EU general pharmaceutical legislative framework, which is known as the new Pharma Package. This proposal will be the subject of additional negotiations and technical meetings, with the objective of reaching agreement on issues such as the regulatory data protection framework and the access and supply obligations.

Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit, the ongoing review of EU pharmaceutical legislation or otherwise, may force us to restrict or delay efforts to seek regulatory approval for our product candidates in the U.K., the EU or other foreign jurisdictions, which could significantly and materially harm our business. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for our product candidates may be withdrawn. If we fail to comply with the applicable regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects could 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 ongoing 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 and regulatory inspection. 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, EMA 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 ongoing compliance with current good manufacturing practices (cGMPs) 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, EMA and other regulatory authorities for compliance with cGMP regulations and standards. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the U.S. prior to being imported or offered for import into the U.S. If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a

regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, failure to comply with FDA, EMA 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;
- imposition of restrictions on operations, including costly new manufacturing requirements;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions; and
- requirements to conduct additional post-market clinical trials to assess the safety of the product.

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

The FDA, EMA and other regulatory authorities 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, EMA and other regulatory authorities 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 in the U.S. for uses that are not approved by the FDA as reflected in the product's approved labeling, or in other jurisdictions for uses that differ from the labeling or uses approved by the applicable regulatory authorities. While physicians may prescribe products for off-label uses, the FDA, EMA and other regulatory authorities actively enforce laws and regulations that prohibit the promotion of off-label uses by companies, including promotional communications made by companies' sales force with respect to off-label uses that are not consistent with the approved labeling, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in January 2025, the FDA published final guidance outlining the FDA's non-binding policies governing the distribution of scientific information on unapproved uses of approved products to healthcare providers. This final guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths, weaknesses, validity and utility of the information about the unapproved use of the approved product. If a company engages in such communications consistent with the guidance's recommendations, the FDA indicated that it will not treat such communications as evidence of unlawful promotion of a new intended use for the approved product. In addition, under recent guidance from the FDA and the Pre-Approval Information Exchange Act, signed into law as part of the Consolidated Appropriations Act (CAA), companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We may engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. We will need to carefully navigate the FDA's

various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.

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, EMA or comparable regulatory authority to obtain clearance or approval of a companion diagnostic test in connection with approval of any of our product candidates or a group of therapeutic products, and we do not obtain or we face delays in obtaining clearance or approval of a diagnostic test, we may not be able to commercialize the product candidate and our ability to generate revenue may be materially impaired.

If we are required by the FDA, EMA or a comparable regulatory authority to obtain clearance or approval of a companion diagnostic test in connection with approval of any of our product candidates, such companion diagnostic test would be used during our more advanced phase clinical trials as well as in connection with the commercialization of our product candidates. To be successful in developing and commercializing product candidates in combination with these companion diagnostics, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to ensuring the safe and effective use of a novel therapeutic product or new 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. In certain circumstances (for example, when a therapeutic product is intended to treat a serious or life-threatening condition for which no satisfactory available therapy exists or when the labeling of an approved product needs to be revised to address a serious safety issue), however, the FDA may approve a therapeutic product without the prior or contemporaneous marketing authorization of a companion diagnostic. In this case, approval of a companion diagnostic may be a post-marketing requirement or commitment.

Co-development of companion diagnostics and therapeutic products is critical to the advancement of precision medicine. Whether initiated at the outset of development or at a later point, co-development should generally be conducted in a way that will facilitate obtaining contemporaneous marketing authorizations for the therapeutic product and the associated companion diagnostic. If a companion diagnostic is required to identify patients who are most likely to benefit from receiving the product, to be at increased risk for serious adverse events as a result of treatment with a particular therapeutic product, or to monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness, then the FDA has required marketing approval of all companion diagnostic tests essential for the safe and effective use of a therapeutic product for cancer therapies. Various foreign regulatory authorities also regulate in vitro companion diagnostics as medical devices and, under those regulatory frameworks, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of any future diagnostics we may develop, which we expect will require separate regulatory clearance or approval prior to commercialization in those countries.

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 genomic alteration or mutation alteration that the companion diagnostic was developed to detect. If the FDA, EMA or a comparable regulatory authority requires clearance or approval of a companion diagnostic for any of our product candidates, whether before, concurrently with approval, or post-approval of the product candidate, we, and/or future collaborators, may encounter difficulties in developing and obtaining clearance or approval for these companion diagnostics. The process of obtaining or creating such diagnostic is time consuming and costly. The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to a product candidate to obtain pre-market approval (PMA), simultaneously with approval of the therapeutic candidate. The PMA process, including the gathering of preclinical and clinical data and the submission and review by the FDA, can take several years or longer. It involves a rigorous pre-market review during which the sponsor must prepare and provide 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. After a device is placed on the market, it remains subject to significant regulatory requirements, including requirements governing development, testing, manufacturing, distribution, marketing, promotion, labeling, import, export, record-keeping, and adverse event reporting.

Any delay or failure by us or third-party collaborators to develop or obtain regulatory clearance or approval of a companion diagnostic could delay or prevent approval or continued marketing of our related product candidates. Further, in April 2020, the FDA issued new guidance on developing and labeling companion diagnostics for a specific group of oncology therapeutic products, including recommendations to support a broader labeling claim rather than individual therapeutic products. We will continue to evaluate the impact of this guidance on our companion diagnostic development and strategy. This guidance and future issuances from the FDA, EMA and other regulatory authorities may impact our development of a companion diagnostic for our product candidates and could result in delays in regulatory clearance or approval or a change in the determination for whether or not a companion diagnostic is still required for our product candidates. We may be required to conduct additional studies to support a broader claim or more narrowed

claim for a subset population. Also, to the extent other approved diagnostics are able to broaden their labeling claims to include any of our future approved product candidates covered indications, we may no longer need to continue our companion diagnostic development plans or we may need to alter those companion diagnostic development strategies, which could adversely impact our ability to generate revenue from the sale of our companion diagnostic test.

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

Where appropriate, we plan to pursue approval from the FDA, EMA or comparable foreign regulatory authorities through the use of accelerated registration pathways. 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, EMA or comparable regulatory authorities, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA, EMA or such other regulatory authorities may seek to withdraw accelerated approval.

Where appropriate, we plan to pursue accelerated development strategies in areas of medical need. We may seek an accelerated approval pathway for one or more of our product candidates from the FDA, EMA or comparable foreign regulatory authorities. Under the accelerated approval provisions in the Federal Food, Drug, and Cosmetic Act, and the FDA's implementing regulations, 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 verify 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. Further, the FDA has issued guidances outlining its current thinking and approach to accelerated approval. While these guidances are currently only in draft form and will ultimately not be legally binding even when finalized, we would need to observe the FDA's guidances closely should our products qualify for accelerated approval.

Finally, there can be no assurance that we will satisfy all FDA requirements, including new provisions, that govern accelerated approval. For example, with passage of FDORA in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to the FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing the FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval study of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting

with the Commissioner of the FDA or the Commissioner's designee and a written appeal, among other things. We will need to fully comply with these and other requirements in connection with the development and approval of any product candidate that is granted accelerated approval.

In the EU, a "conditional" marketing authorization may be granted in cases where all the required safety and efficacy data are not yet available. A conditional marketing authorization is subject to conditions to be fulfilled for generating missing data or ensuring increased safety measures. A conditional marketing authorization is valid for one year and has to be renewed annually until fulfillment of all relevant conditions. Once the applicable pending studies are provided, a conditional marketing authorization can become a "standard" marketing authorization. However, if the conditions are not fulfilled within the timeframe set by the EMA, the marketing authorization will cease to be renewed.

Prior to seeking accelerated approval, we will seek feedback from the FDA, EMA or comparable foreign regulatory authorities and will otherwise evaluate our ability to seek and receive such accelerated approval. 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 feedback from the FDA, EMA or comparable foreign regulatory authorities, 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 any other form of expedited development, review or approval, 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, EMA 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 seek certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review in the U.S., and PRIME (priority medicines) in the EU, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

Zidesamtinib has received FDA Breakthrough Therapy designation for the treatment of patients with advanced ROS1-positive NSCLC who have previously been treated with two or more ROS1 TKIs, and neladalkib has received FDA Breakthrough Therapy designation for the treatment of patients with locally advanced or metastatic ALK-positive NSCLC who have been previously treated with two or more ALK TKIs. We may seek certain designations for our other current or future product candidates or other designations for zidesamtinib and neladalkib that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, early and frequent interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development. Sponsors may also have greater interactions with the FDA and the FDA may initiate review of sections of the NDA of a product candidate with Breakthrough Therapy designation before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of data submitted by the sponsor, that a product with Breakthrough Therapy designation may be effective.

We may also seek Fast Track designation for one or more of our product candidates. The FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. Like with Breakthrough Therapy designation, sponsors with Fast Track products may have greater FDA interactions and the FDA may initiate review of sections of a Fast Track product's NDA before the application is complete if it determines, after its preliminary data evaluation, that the product may be effective.

We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate intended to treat a serious condition and, if approved, offers a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation shortens the goal for the FDA to review an application within six months, rather than the standard review period of ten months.

These designations require a sponsor to submit an application for review and approval by the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if our product candidates qualify for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

In the EU, we may seek PRIME for some of our product candidates in the future. PRIME is a voluntary program launched by the EMA that is aimed at enhancing the scientific and regulatory support for the development and accelerated assessment of new product candidates that target an unmet medical need. PRIME is aimed to offer early and proactive support to sponsors to optimize the generation of robust data on the product's benefits and risks and enable accelerated regulatory assessment of new marketing applications. To be eligible for PRIME, a product candidate must meet the eligibility criteria in respect to its potential to offer a major therapeutic advantage over existing treatments, or benefit patients who do not have any treatment options. The benefits of PRIME include the appointment of a Committee for Medicinal Products for Human Use rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. We may apply for PRIME and it may not be granted. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

We may not be able to obtain orphan drug designation or obtain or maintain orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA, EMA or other comparable foreign regulatory authorities, from approving competing products.

Regulatory authorities in some jurisdictions, including the U.S. and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of researching and developing the drug will be recovered from sales in the U.S. Our target indications may include diseases with large patient populations or may include orphan indications. Zidesamtinib has received orphan drug designation for ROS1-positive NSCLC. Neladalkib has received orphan drug designation for ALK-positive NSCLC. There can be no assurances that we will be able to obtain orphan designation for our other current product candidate or candidates we may discover and develop in the future.

In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product candidate that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product candidate is entitled to orphan drug exclusivity. Orphan drug exclusivity in the U.S. provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances. The applicable exclusivity period is 10 years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug designation for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the U.S. may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to ensure that we will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process or entitles the product candidate to Priority Review.

It is also possible that current or future litigation or action by Congress could change the scope of available orphan exclusivity. Any changes to the orphan drug provisions could change our opportunities for, or likelihood of success in obtaining, orphan drug exclusivity and could materially affect our business, financial condition, results of operations, cash flows and prospects.

Current and future legislation may increase the difficulty and cost for us to obtain reimbursement for our product candidates.

In the U.S. and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

Further, since enactment of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the PPACA), there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017 (Tax Act), Congress repealed the "individual mandate." Litigation and legislation over the PPACA may continue, with unpredictable and uncertain results.

The American Taxpayer Relief Act of 2012 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. Further, with passage of the Inflation Reduction Act of 2022 (IRA) in August 2022, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars. This provision is limited in terms of the number of pharmaceuticals whose prices can be negotiated in any given year and it only applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years. Drugs and biologics that have been approved for a single rare disease or condition are categorically excluded from price negotiation. With the passage of the One Big Beautiful Bill Act (OBBBA) in July 2025, Congress extended this exemption to drugs and biologics with more than one orphan drug designation and more than one approved indication. In addition, the legislation provides that if pharmaceutical companies raise prices in Medicare faster than the rate of inflation, they must pay rebates back to the government for the difference. The IRA also capped Medicare beneficiary out-of-pocket drug costs at an estimated $2,000 a year beginning in 2025.

These laws and other healthcare reform measures may result in additional reductions in Medicare and other healthcare funding and otherwise affect the reimbursement we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in reimbursement from private payors. Accordingly, 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.

The prices of prescription pharmaceuticals in the U.S. and foreign jurisdictions are the subject of considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed for marketing.

The prices of prescription pharmaceuticals have been the subject of considerable discussion in the U.S. There have been several recent U.S. Congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

In October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program (SIP) to import certain prescription drugs from Canada into the U.S. Several states have passed laws allowing for the importation of drugs from Canada, while others have passed legislation establishing workgroups to examine the impact of a state SIP. In May 2025, the FDA announced that it would offer individual states the opportunity to submit a draft proposal for pre-review and meet with the agency to obtain initial feedback from the FDA prior to formally submitting their SIP proposal. The intent of these meetings is to assist states in developing their proposals by further clarifying requirements, enhancing the quality of proposals submitted to the agency and ultimately shortening the review timeline.

On August 16, 2022, the IRA was signed into law by former President Biden. This requires manufacturers of certain drugs to engage in price negotiations with Medicare, with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation; and replaces the Part D coverage gap discount program with a new discounting program. The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least nine years and biologics that have been licensed for 13 years. When originally enacted, the IRA explicitly excluded from price negotiation orphan drugs designated for only one rare disease or condition and for which the only active approved indication is for such disease or condition. However, the OBBBA, signed into law in July 2025, amended the applicable statute to broaden the orphan drug exclusion to include products with more than one orphan designation and more than one approved indication. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law. The legislation also requires manufacturers to pay rebates for drugs in Medicare Parts B and D whose price increases exceed inflation and capped Medicare beneficiary out-of-pocket drug costs at $2,000 a year.

The first cycle of negotiations for the Medicare Drug Price Negotiation Program commenced in the summer of 2023. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for 10 selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these 10 drugs became effective on January 1, 2026.

In January 2025, CMS announced its selection of 15 additional drugs covered by Medicare Part D for the second cycle of negotiations, and in November 2025, CMS released negotiated prices for such products that will go into effect beginning on January 1, 2027. While it remains to be seen how the drug pricing provisions imposed by the IRA will affect the broader pharmaceutical industry, several pharmaceutical manufacturers and other industry stakeholders have challenged the law, including through lawsuits brought against the HHS, the Secretary of the HHS, CMS, and the CMS Administrator challenging the constitutionality and administrative implementation of the IRA's drug price negotiation provisions. This litigation is ongoing and the results, and potential impacts on our business, are uncertain.

Accordingly, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

In April 2025, President Trump issued an executive order which directs HHS to take steps to reduce the prices of pharmaceutical products (the Order). The Order repeats many of the proposals advanced during the first Trump administration, including directing the FDA to streamline and improve its existing drug importation program so as to make it easier for states to obtain approval without sacrificing the safety or quality of drug products. With respect to the IRA's Medicare drug pricing program, the Order, among other things, calls for alignment in "the treatment of small molecule prescription drugs with that of biological products, ending the distortion that undermines relative investment in small molecule prescription drugs, coupled with other reforms to prevent any increase in overall costs to Medicare and its beneficiaries."

Subsequently, in May 2025, President Trump issued an additional executive order (the Additional Order) calling on pharmaceutical manufacturers to voluntarily reduce the prices of medicines in the U.S. The Additional Order directs the Secretary of HHS to communicate most-favored-nation (MFN) price targets to pharmaceutical manufacturers to bring prices in line with comparably developed nations. Since the Additional Order, the Trump administration has continued to exert pressure on drug manufacturers to implement "most favored nation" pricing, including by suggesting that the administration may impose significant tariffs on pharmaceuticals if such manufacturers do not reach agreements to implement "most favored nation" pricing. Additionally, in November 2025, CMS announced a new voluntary payment initiative called the GENEROUS Model (GENErating cost Reductions fOr U.S. Medicaid Model) where drug manufacturers may voluntarily offer supplemental rebates to participating state Medicaid programs that are intended to provide such Medicaid programs with a "most favored nation" price for participating manufacturers' products. Most recently, in December 2025, CMS announced new mandatory payment models through two proposed rules, the Global Benchmark for Efficient Drug Pricing (GLOBE) and Guarding U.S. Medicare Against Rising Drug Costs (GUARD) models where manufacturers of certain Medicare Part B and Medicare Part D drugs will be assessed rebates if the prices for such products exceed those paid in economically comparable countries. It remains to be seen how these drug pricing initiatives will affect the broader pharmaceutical industry.

At the U.S. state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. This is increasingly true with respect to products approved pursuant to the accelerated approval pathway. State Medicaid programs and other payers are developing strategies and implementing significant coverage barriers, or refusing to cover these products outright, arguing that accelerated approval drugs have insufficient or limited evidence despite meeting the FDA's standards for accelerated approval.

In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription product and other healthcare programs. These measures could reduce the ultimate demand for our products, if approved, or put pressure on our product pricing. In addition, in some countries, including member states of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take a significant amount of time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices, and in certain instances render commercialization in certain markets infeasible or disadvantageous from a financial perspective. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our products to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or government authorities may lead to further pressure on the prices or reimbursement levels. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the commercial launch of our products could be delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more products, and there could be a material adverse effect on our business.

We are or may become subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

There are multiple privacy and data security laws that may impact our business activities in the U.S. and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the healthcare industry generally, for example, under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), HHS has issued regulations to protect the privacy and security of protected health information used or disclosed by specific covered entities including certain healthcare providers, health plans and healthcare clearinghouses. We are not currently classified as a covered entity or business associate under HIPAA. Thus, we are not directly subject to HIPAA's requirements or penalties. However, healthcare providers, including certain research institutions from which we may obtain patient or subject health information, may be subject to privacy, security, and breach notification requirements under HIPAA. Additionally, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face criminal penalties if we knowingly receive individually identifiable health information from a HIPAA covered entity, business associate or subcontractor that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. In addition, we may maintain sensitive personally identifiable information, including health and genetic information, that we receive throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who may enroll in patient assistance programs if we choose to implement such programs. As such, in addition to risks and obligations related to HIPAA, we also may be subject to various state laws regulating the use or disclosure of this information or requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA.

Furthermore, certain health privacy laws, data breach notification laws, consumer protection laws and genetic information laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Individuals from whom we or our collaborators may obtain health information, as well as the healthcare providers who may share this information with us, may have statutory or contractual rights that limit the ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Additionally, the collection and use of personal data, including data concerning health, in the EU is governed by the General Data Privacy Regulation (GDPR), which extends the geographical scope of EU data protection law to non-EU entities under certain conditions and imposes substantial obligations upon companies and new rights for individuals, as discussed below in "—Processing of personal data is governed by restrictive laws and regulations in the jurisdictions in which we operate."

Brexit may adversely impact our ability to obtain regulatory approvals for our product candidates in the EU, result in restrictions or imposition of taxes and duties for importing our product candidates into the EU, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the EU.

Disruptions at the FDA and other government agencies from funding cuts, personnel losses, regulatory reform, government shutdowns and other developments could hinder our ability to obtain guidance from the FDA regarding our clinical development programs and develop and secure approval of our product candidates in a timely manner, which would negatively impact our business.

The FDA and comparable regulatory agencies in foreign jurisdictions, such as the EMA, play an important role in the development of our product candidates by providing guidance on our clinical development programs and reviewing our regulatory submissions, including INDs, requests for special designations and marketing applications. If these oversight and review activities are disrupted, then our ability to develop and secure timely approval of our product candidates could be impacted in a negative manner, accordingly.

For example, the regulatory reform measures being implemented by the Trump administration across the government, some of which ordered the loss of FDA leadership and personnel, could lead to disruptions and delays in FDA guidance, review and approval of our product candidates. In March 2025, the Secretary of HHS announced a reorganization and Reduction in Force (RIF) across HHS of approximately 20,000 employees (82,000 to 62,000), with the FDA's workforce to decrease by 3,500 full-time employees. Shortly thereafter, thousands of employees at the FDA were fired. In addition, President Trump has issued a number of executive orders that could have a significant impact on the manner in which the FDA conducts its operations and engages in regulatory and oversight activities. If current or future orders or executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Further, while the FDA's review of marketing applications and other activities for new drugs and biologics is largely funded through the user fee program established under PDUFA, it remains unclear how the administration's RIF and budget cuts will impact this

program and the ability of the FDA to provide guidance and review our product candidates in a timely manner. For example, while the FDA RIF did not reportedly specifically target FDA reviewers, many operations, administrative and policy staff that help support such reviews were affected and those losses could lead to delays in PDUFA reviews and related activities. In addition, while currently unclear, there is a risk that the RIF and budget cutbacks could threaten the integrity of the PDUFA program itself. That is because, for the FDA to obligate user fees collected under PDUFA in the first place, a certain amount of non-user fee appropriations must be spent on the process for the review of applications plus certain other costs during the same fiscal year. For example, one company disclosed in June 2025 that the FDA had notified it that a previously disclosed PDUFA goal date would not be met due to heavy workload and limited resources. While the impact of these staffing disruptions remains uncertain, there can be no assurance that staff responsible for managing the PDUFA program will not be impacted and that companies will not experience delays in processing of NDAs and BLAs that may result in a longer than expected review period or delayed PDUFA dates.

In addition, government funding of the Securities and Exchange Commission (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. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities.

At the same time, disruptions at the FDA and other government agencies may result from public health events similar to the COVID-19 pandemic. For example, during the pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

Accordingly, if any of the foregoing developments and others impact the ability of the FDA to provide us with guidance regarding our clinical development programs or delay the agency's review and processing of our regulatory submissions, including INDs and NDAs, our business would be negatively impacted. Further, any future government shutdown could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

If our product candidates are licensed for marketing and receive federal healthcare reimbursement, any relationships we may have with healthcare providers will be subject to applicable healthcare fraud and abuse laws and regulations, which could expose us to criminal and civil penalties and exclusion from participation in government healthcare programs.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we are able to obtain marketing approval. Any arrangements we have with healthcare providers, third-party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we conduct clinical research, market, sell and distribute any products for which we obtain marketing approval. These include the following:

- *Anti-Kickback Statute.* The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), 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, lease or order of a good, facility, item or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid.
- *False Claims Laws.* The federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions against individuals or entities for, among other things, knowingly presenting or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties.
- *HIPAA.* HIPAA imposes criminal and civil liability for, among other things, executing a scheme or making materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Additionally, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations on covered entities and their business associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information.
- *Transparency Requirements.* The federal Physician Payments Sunshine Act requires certain manufacturers of 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 report annually to CMS information related to payments or transfers of value made to physicians, other healthcare providers and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members.

- *Analogous State and Foreign Laws.* Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors and are generally broad and are enforced by many different federal and state agencies as well as through private actions.

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. 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 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. Our failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that any business arrangements we have with third parties and our business generally will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm and the curtailment or restructuring of our operations.

Processing of personal data is governed by restrictive laws and regulations in the jurisdictions in which we operate.

We are or may become subject to many cybersecurity, privacy and data protection laws in the U.S. and around the world. In the U.S., we are subject to numerous federal and state laws governing the collection, processing, use, transmission, disclosure, and sale (collectively, Processing) of personal data (which may also be referred to as personal information, personally identifiable information, and/or non-public personal information).

There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission (FTC) and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws are also being considered at both the state and federal levels. For example, the FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the Federal Trade Commission Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The FTC is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements.

New laws are also being considered and implemented at the state level. For example, the California Consumer Privacy Act (CCPA) went into effect on January 1, 2020, and established a new privacy framework for covered businesses such as ours. The CCPA imposed many requirements on businesses that process the personal information of California residents. Further, in November 2020, California voters passed the California Privacy Rights Act (CPRA), which significantly expanded the CCPA to incorporate additional GDPR-like provisions and create a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. While certain of our business activities will not be subject to these laws, it remains unclear how various provisions of the CCPA and CPRA will be interpreted and enforced.

In addition to California, several other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). There are also states that are currently regulating health information specifically, or considering passing new laws to do so. These laws and regulations may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws

regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business.

In addition, outside of the U.S., we are subject to foreign rules and regulations. Many countries outside of the U.S. maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the EEA, and the processing of personal data that takes place in the EEA, is subject to the GDPR, which became effective on May 25, 2018. This provision expanded the scope of data protection in the EU to foreign companies who process the personal data of EU residents, imposed a strict data protection compliance regime with stringent penalties for noncompliance and included new rights for data subjects such as the "portability" of personal data. In particular, under the GDPR, fines of up to €20 million, or up to 4% of the annual global revenue of the noncompliant company, whichever is greater, could be imposed for violations of certain of the GDPR's requirements. If we were found to be in breach of the GDPR, the potential penalties we might face could have a material adverse impact on our business, financial condition, results of operations, and cash flows. Compliance with the GDPR requires time and expense and may require us to make changes to our business operations.

While the GDPR applies uniformly across the EU, each EU Member State is permitted to issue nation-specific data protection legislation, which has created inconsistencies on a country-by-country basis. Brexit has created further uncertainty and could result in the application of new data privacy and protection laws and standards to our operations in the U.K., our handling of personal data of users located in the U.K., and transfers of personal data between the EU and the U.K. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act of 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR. A decision from the European Commission appears to deem the U.K. as being "essentially adequate" for purposes of data transfer from the EU to the U.K., although this decision may be re-evaluated in the future. Further, despite the current effectiveness of the Data Protection Act of 2018 in the U.K., it is still unclear whether transfer of data from the EEA to the U.K. will remain lawful under the GDPR. The U.K. and the U.S. also have agreed on a framework for personal data to be transferred between the U.K. and the U.S., called the U.K.-U.S. Data Bridge, but this may be challenged in the future as well.

There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. On July 16, 2020, the European Court of Justice invalidated the EU-U.S. Privacy Shield Framework, a mechanism under which personal data could be transferred from the EEA to U.S. entities that had self-certified under the Privacy Shield Framework. In October 2022, former President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield, for which the European Commission adopted an adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. The uncertainty around this issue has the potential to impact our business at the international level.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and any eventual sale and distribution of commercial products. Such laws may have potentially conflicting requirements or burdensome obligations that would make compliance challenging or expensive. Such changes may also require us to modify our products and features, and may limit our ability to make use of the data that we collect, may require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies.

In addition to these provisions restricting the transfer of personal information to the U.S., a new U.S. law also restricts the transfer of certain kinds of personal data in certain situations outside of the U.S. to "countries of concern," including but not limited to China. On April 8, 2025, the U.S. Department of Justice's National Security Division implemented the Data Security Program Rule under Executive Order 14117 and the International Emergency Economic Powers Act. This rule establishes restrictions on certain data-related transactions involving U.S. persons and entities, particularly those that may result in access to U.S. government-related data or bulk sensitive personal data of U.S. persons by foreign adversaries or entities under their control. The rule effectively imposes export control-like restrictions on the transfer, sale, or sharing of sensitive data—including genomic, geolocation, biometric, health, financial, and other personal data—to or with entities in countries of concern, as well as entities and persons associated with those countries. It also imposes additional due diligence obligations on U.S. companies concerning personal data they collect, store, or transmit. Failure to comply with the Data Security Program Rule could result in civil or criminal penalties, reputational harm, and restrictions on our ability to engage in certain business activities. Compliance may require us to modify our data handling practices, implement new controls, or terminate existing relationships with certain foreign vendors, customers, or partners. These changes could increase our operational costs, limit our market opportunities, and adversely affect our financial performance. Additionally, the scope and interpretation of the rule may evolve, and future guidance or enforcement actions could impose further obligations or restrictions.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to Process data (including personal data), or in some cases, impact our ability to operate in certain jurisdictions. Any actual or alleged failure to comply with U.S. or international laws and regulations relating to privacy, data

protection, and data security could result in governmental investigations, proceedings and enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity, harm to our reputation, and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to Process the information or impose other obligations or restrictions in connection with our Processing of information, and we may otherwise face contractual restrictions applicable to our Processing of information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

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 or may have engaged in misconduct or other improper activities. Misconduct by these parties could include failures to comply with SEC, FDA, EMA or comparable foreign regulatory authority regulations, provide accurate information to regulatory authorities, comply with federal and state healthcare fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, research, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations 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. We have adopted a code of conduct and engage contractors that agree to undertake certain measures with respect to their employees, but it is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. 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, 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.

Our business activities may be subject to the U.S. Foreign Corrupt Practices Act (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.

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 others to give 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 are 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 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 or domestic 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 our products would likely adversely affect our business.

Risks related to employee matters, managing our growth and other risks related to our business

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

Historically, our team was primarily focused on research and development of small molecule kinase inhibitors. More recently, we began to establish a commercial infrastructure in preparation for a future product launch if one or more of our product candidates receives marketing approval, including the hiring of sales, marketing and other commercially focused personnel. We continue to build this commercial infrastructure. To succeed, we must recruit, hire, retain, manage and motivate qualified clinical, scientific, technical, sales and marketing, and management personnel, and we face significant competition for experienced personnel. Personnel with the required skills and experience may be scarce or may not be available at all. In addition, competition for these skilled personnel is intense and recruiting and retaining skilled employees is difficult, particularly for a precommercial-stage company such as ours. Even if we are successful in identifying, attracting, hiring and retaining qualified employees, recent market changes, including labor shortages, and rising inflation have increased employee-related costs substantially, which may negatively affect our operating results.

We are highly dependent on the principal members of our management, commercial and scientific and medical staff. If we do not succeed in attracting and retaining qualified personnel in these positions, 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.

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 higher compensation, 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.

Additionally, we rely on our physician-scientist partners and other scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. Most of these advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. In particular, if we are unable to maintain consulting or employment relationships with our physician-scientist partners and other scientific and clinical advisors, or if they provide services to our competitors, our development and commercialization efforts will be impaired and our business will be significantly harmed. For example, if we are no longer able to access our network of physician-scientists, our ability to define and characterize patients' needs for future product candidate development may be negatively affected.

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

We expect to continue to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug and clinical development, regulatory affairs, medical affairs, commercialization, sales and marketing. As of December 31, 2025, we had 228 full time employees. This growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining, retaining and motivating our current and additional employees;
- managing our internal development efforts effectively, including the preclinical, clinical, FDA, EMA and other comparable foreign regulatory authorities' review process for zidesamtinib, neladalkib, NVL-330 and our discovery programs, while complying with any contractual obligations to contractors and other third parties;
- managing increasing operational and managerial complexity;
- preparing for potential commercialization of our product candidates; 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 zidesamtinib, neladalkib, NVL-330 and any future product candidates developed from our discovery programs and other 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. Any inability to manage such growth could delay the execution of our business plans or disrupt our operations.

Further, 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 research, clinical development and manufacturing. There can be no assurance 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 preclinical studies and clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval for our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing third-party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

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

Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants or potential future collaborators, may fail or suffer actual or suspected 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, and potentially significant delays in our delivery to market.

Despite the implementation of security measures in an effort to protect systems that store our data, given their size and complexity and the increasing amount of information maintained on our internal information technology systems and external processing and storage systems (i.e., cloud), and those of our third-party CROs, other contractors (including sites performing our clinical trials) and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. The risk of a security breach or disruption through cyber-attacks has generally increased as the number, intensity and sophistication of attempted attacks from around the world have increased. For example, companies have experienced an increase in phishing and social engineering attacks from third parties. Also, a majority of our employees are working remotely. As a result, we may have increased cybersecurity and data security risks, due to increased use of home wi-fi networks and virtual private networks, as well as increased disbursement of physical machines. While we implement IT controls to reduce the risk of a cybersecurity or data security breach, there is no guarantee that these measures will be adequate to safeguard all systems.

To the extent that any disruption or security breach were to result in a loss, destruction, unavailability, alteration or dissemination of, or damage to, our data (including confidential information and personal data) or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our product candidates could be delayed. There can be no assurance that our data protection efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other third parties, will prevent significant breakdowns or breaches in systems or other cyber incidents that cause loss, destruction, unavailability, alteration or dissemination of, or damage to, our data that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data, as well as claims or investigations from regulators or other third parties. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal data), which could result in financial, legal, business, and reputational harm to us. For example, any such event that leads to unauthorized access, use, or disclosure of personal data, including personal data regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to financial exposure related to investigation of the incident (including cost of forensic examinations), subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of data, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Notifications, follow-up actions, claims and investigations related to a security incident could impact our reputation and 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 expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security breach. 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 incident were to result in a loss, destruction or alteration of, or damage to, our data (including personal 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 privacy and security laws from countries outside of the U.S.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in or, failure or security breach of our systems or third-party systems where information important to our business operations or commercial development is stored. 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.

Changes in and uncertainty surrounding U.S. trade policy could have a material adverse impact on our business, financial condition and results of operations.

As a result of numerous changes in tariffs and trade restrictions that have been announced and/or implemented by the Trump administration since taking office, and other countries in response to the Trump administration's actions, and the underlying uncertainty currently surrounding international trade, we could experience a negative impact on our costs of materials or supply chain disruptions and delays. If we are unable to obtain necessary raw materials or product components in sufficient quantity and in a timely manner due to disruptions in the global supply chain caused by macroeconomic events and conditions, the development, testing and clinical trials of our product candidates may be delayed or rendered infeasible, and regulatory approval or commercial launch of any resulting product may be delayed, which could significantly harm our business. We cannot yet predict the effect of recently imposed U.S. tariffs, or of possible future U.S. tariffs, including, but not limited to, tariffs on pharmaceuticals, pharmaceutical ingredients, including finished drug products, medical countermeasures, critical inputs such as active pharmaceutical ingredients (API) and key starting materials, and derivative products of those items, on imports, or the extent to which other countries will impose quotas, duties, tariffs, taxes or other similar restrictions upon imports or exports in the future, nor can we predict future trade policy or the terms of any renegotiated trade agreements and their impact on our business.

Changes in U.S. and international trade policies, particularly with respect to China, may adversely impact our business and operating results.

Some of our manufacturers and suppliers are located in China. Trade tensions and conflicts between the U.S. and China have been escalating in recent years and, as such, we are exposed to the possibility of product supply disruption and increased costs and expenses in the event of changes to the laws, rules, regulations and policies of the governments of the U.S. or China, or as a result of geopolitical unrest or unstable economic conditions. Certain Chinese biotechnology companies may become subject to trade restrictions, sanctions, other regulatory requirements or proposed legislation by the U.S. government, which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting their supply of material to us. For example, in February 2024, U.S. lawmakers called for investigations into and the imposition of possible trade sanctions against certain Chinese biotechnology companies, including WuXi AppTec and WuXi Biologics (collectively, WuXi), over alleged ties to the Chinese military. In December 2025, Congress enacted a law, which, subject to certain grandfather provisions, will restrict U.S. federal agencies from procuring or obtaining "biotechnology equipment or services" from certain Chinese companies designated as "biotechnology companies of concern." It will also prohibit U.S. federal agencies from entering into, extending, or renewing contracts with any entity that either uses biotechnology equipment or services provided by a company designated as a biotechnology company of concern in performance of the contract or enters into any contract with a third party that requires either party to use biotechnology equipment or services produced or provided by a company designated as a biotechnology company of concern. In addition, it prohibits an executive agency from obligating or expending a loan or grant to procure biotechnology equipment or services produced or provided by a "biotechnology company of concern."

Sustained uncertainty about or further escalating trade and political tensions between the U.S. and China may prevent or hinder the export of materials or technical information among us, our contract development and manufacturing organizations (CDMOs) and other relevant third parties, such as pharmaceutical partners, or could result in trade or retaliatory restrictions that may hinder or potentially inhibit our ability to rely on CDMOs and other service providers that operate in China. Further, regulatory or legislative action taken by the U.S. to impose restrictions on transactions with China, like the restrictions described above, could have the potential to severely restrict the ability of companies like ours to contract with Chinese biotechnology companies of concern, which could have adverse effects on the development of our product candidates and our business operations.

Any unfavorable government policies on international trade, such as export controls, capital controls or tariffs, may increase the cost of manufacturing our product candidates, affect the demand for our drug products (if and once approved), the competitive position of our product candidates, and the import or export of raw materials and finished product candidate used in our and our collaborators' preclinical studies and clinical trials, particularly with respect to any product candidates and materials that we import from China, including pursuant to our manufacturing service arrangements with WuXi. If any new tariffs, export controls, legislation and/or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if either the U.S. or Chinese government

takes retaliatory trade actions due to the recent trade tension, such changes could have an adverse effect on our business, financial condition and results of operations.

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

We lease office space for our corporate headquarters, which is located in Cambridge, Massachusetts. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major flood, fire, earthquake, power loss, telecommunications failure, terrorist activity, pandemics 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.

Artificial intelligence presents risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information and personal data.

Issues in the use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. Our vendors may incorporate generative artificial intelligence tools into their offerings without disclosing this use to us, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If any of our vendors experience an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

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

While we have begun to establish a commercial infrastructure in preparation for a future product launch if one or more of our product candidates receives marketing approval, in order to successfully commercialize any product candidates, if approved, we must successfully build robust 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 a full 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. Further, we may underestimate the size of the sales or marketing force required for a successful product launch and may need to expand our sales and marketing force earlier and at a higher cost than we anticipated. 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 and such arrangements may prove to be less profitable than commercializing the product on our own. 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.

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

We may seek regulatory approval of our product candidates outside of the U.S. 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, such as the lack of pathways for accelerated drug approval, may result in foreign regulatory approvals taking longer and being more costly than obtaining approval in the U.S.;
- foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials or our interpretation of data from preclinical studies or clinical trials;

- approval policies or regulations of foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- the impact of pandemics or other public health emergencies, natural disasters and geopolitical events on our ability to produce our product candidates and conduct clinical trials in foreign countries;
- 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 legal requirements applicable to privacy, data protection, information security and other matters;
- 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;
- complexities associated with managing multiple payor reimbursement regimes and government payors in foreign countries;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- 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 U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical events, including war and terrorism, trade policies, treaties and tariffs.

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

Changes in tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, the U.S. Treasury Department and other applicable tax authorities. Changes to tax laws (which changes may have retroactive application), including the OBBBA passed in July 2025, could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations.

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

Our federal net operating loss (NOL) carryforwards may be unavailable to offset future taxable income because of restrictions under U.S. tax law. Under the Tax Act as amended by the Coronavirus Aid, Relief, and Economic Security Act, our federal NOLs generated in tax years beginning after December 31, 2017 may be carried forward indefinitely but the utilization of our federal NOL carryforward is limited to 80% of current year taxable income. As of December 31, 2025, we had available federal NOL carryforwards of approximately $503.2 million and available state NOL carryforwards of approximately $531.1 million.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a cumulative change in the corporation's ownership by "5-percent shareholders" that exceeds 50 percentage points (by value) over a rolling three-year period), the corporation's ability to use its pre-change NOL carryforwards and certain other pre-change tax attributes to offset its post-change taxable income 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 annual limitations, if any, that could result from such changes in ownership. There is also a risk that due to regulatory changes, such as suspensions on the use of NOL carryforwards, or other unforeseen reasons, our existing NOL carryforwards could expire or otherwise be unavailable to offset future income tax liabilities. Because our ability to utilize our NOL carryforwards and certain other tax attributes could be limited as described above, we may not be able to utilize a material portion of our NOL carryforwards and certain other tax attributes, which could have a material adverse effect on our cash flows and results of operations.

Risks related to our intellectual property

Derivation 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 proceedings provoked by third parties or brought by us or declared by the U.S. Patent and Trademark Office (USPTO) may be necessary to determine the priority of inventions with respect to one or more of our patents or patent applications or those of our future licensors. An unfavorable outcome may require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be adversely affected if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of derivation 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 development programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

If we are unable to obtain, maintain and enforce patent protection for our technology and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain protection of the intellectual property rights we own (either solely and jointly with others), or may in the future license from third parties (in particular, worldwide patents relating to any proprietary technology and product candidates we develop). We seek to protect our proprietary position by filing patent applications in the U.S. and select other countries related to our technologies and product candidates that are important to our business and by in-licensing intellectual property related to such technologies and product candidates. We do not yet have issued patents for all of our most advanced product candidates in all markets in which we may commercialize them, but we continue to actively pursue patent protection for our technology and product candidates in certain jurisdictions around the world. However, 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, or the methods of use or manufacture of those products. If we are unable to obtain and maintain meaningful patent protection in jurisdictions important to our business for our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, or other proprietary technologies, our business, financial condition, results of operations and prospects could be adversely affected.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain or defend all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances involving technology that we may license from third parties, we may not have the sole right to control the preparation, filing and prosecution of patent applications or to maintain, enforce and defend the in-licensed patents. Therefore, any in-licensed patents and applications may not be prepared, filed, prosecuted, maintained, defended and enforced in a manner consistent with the best interests of our business.

The patent rights of pharmaceutical and biotechnology companies, like ours, generally are highly uncertain, involve complex legal and factual questions and have been the subject of much litigation in recent years. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents, particularly those related to oncology, has emerged in the U.S. The relevant patent laws and their interpretation outside of the U.S. are also uncertain. Various courts, including the U.S. Supreme Court, have rendered decisions that affect the scope of patent eligibility of certain inventions or discoveries relating to biotechnology. These decisions conclude, among other things, that abstract ideas, natural phenomena and laws of nature are not themselves patent eligible subject matter. Precisely what constitutes a law of nature or abstract idea is uncertain, and certain aspects of our technology could be considered ineligible for patenting under applicable law. In addition, the scope of patent protection outside the U.S. is uncertain, and laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. or vice versa. For example, European patent law precludes the patentability of methods of treatment of the human body. We cannot predict whether the patent applications we are currently pursuing will issue as patents that protect our technology and product candidates, in whole or in part, in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Changes in either the patent laws or interpretation of the patent laws in the U.S. or other countries may diminish the value of our patents and our ability to obtain, protect, maintain, defend and enforce our patent rights, narrow the scope of our patent protection and, more generally, affect the value or narrow the scope of our patent rights.

Further, third parties may have intellectual property rights relating to our product candidates of which we are unaware. 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. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases are not published at all. Therefore, neither we nor our future licensors can know with certainty whether either we or our future licensors were

the first to make the inventions claimed in the patent applications we own or any patents or patent applications we may own or in-license in the future, or that either we or any of our future licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our owned and future in-licensed patent rights are uncertain. For example, currently unpublished patent applications may later publish and limit our ability to obtain valid and enforceable patents.

Moreover, any issued patents we do obtain or in-license may be challenged, invalidated, or circumvented. We or our future licensors may be subject to a third-party pre-issuance submission of prior art to the USPTO, or to a foreign patent office, or become involved in opposition, derivation, revocation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by any patents we obtain 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. Moreover, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents we may obtain. For these reasons and others, we may face competition with respect to our product candidates.

Additionally, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned and any future in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us, or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and any patents we do obtain may be challenged in the courts or patent offices in the U.S. and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which 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 technology and product candidates. Such challenges also may result in substantial cost and require significant time from our management and employees, even if the eventual outcome is favorable to us. Furthermore, our competitors may be able to circumvent any patents we obtain or in-license in the future by developing similar or alternative technologies or products in a non-infringing manner. For these reasons, even if we are successful in obtaining patents or in-licensing patents in the future, our patent portfolio may not provide us with sufficient rights to exclude others from using or commercializing technology and products similar or identical to any of our technology and product candidates for any period of time.

Patent terms may not protect our competitive position for an adequate amount of time.

Issued patents can provide protection for varying periods of time, depending, for example, upon the type of patent, 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. However, patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the statutory expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. The term of a patent outside of the U.S. varies in accordance with the laws of the foreign jurisdiction. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are approved for use or commercialized.

If we do not obtain patent term extension in the U.S. under the Hatch-Waxman Act and in foreign countries under similar legislation, which if granted could extend the term of our marketing exclusivity for any product candidates we may develop, our business may be materially and adversely affected.

In the U.S., the term of a patent that covers an FDA-approved drug may be eligible for limited patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. In addition, the patent term of only one patent applicable to an approved drug may be extended, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Similar provisions are available in Europe and certain other non-U.S. jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on any patents that issue covering those product candidates, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted and, even if granted, the length of such extensions. We may not be granted patent term extension either in the U.S. or in any foreign country, even where we obtain a patent that is eligible for patent term extension, if, for example, an applicable government authority determines that we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy

applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we obtain such an extension, it may be for a shorter period than we had sought. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially and adversely affected.

Furthermore, for any patents we may in-license in the future, we may not have the right to control prosecution, including filing with the USPTO, of a petition for patent term extension under the Hatch-Waxman Act. Thus, if a patent we in-license in the future is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed or whether the requested extension is obtained from the USPTO.

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

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

Changes in either the patent laws or interpretation of patent laws in the U.S. or other jurisdictions could increase the uncertainties and costs surrounding the prosecution of our owned and any future in-licensed patent applications and the maintenance, enforcement or defense of any issued patents we may obtain or in-license.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. For example, the USPTO regularly revises its policies and procedures for patent examination. Future political changes may impose new difficulties in obtaining patent protection. This combination of events has increased uncertainty with respect to the validity and enforceability of patents once obtained. Similarly, foreign courts and patent offices have made, and will likely continue to make, changes in how the patent laws in their respective jurisdictions are interpreted. We cannot predict future changes in the interpretation of patent laws or changes to patent laws that might be enacted into law by U.S. and foreign legislative bodies. Those changes may materially affect our patents or patent applications and our ability to obtain patent protection in the future.

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

Competitors and other third parties may infringe, misappropriate or otherwise violate patents or other intellectual property that we own or license. As a result, we or our future licensors may need to file infringement, misappropriation or other intellectual property claims, which can be expensive and time-consuming. Any claims we assert against others could provoke them to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property rights. 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 the extent to which we obtain and enforce patent claims that cover our technology, inventions, and improvements.

Furthermore, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability. In a patent infringement proceeding, the perceived infringers could counterclaim that the patents we or our licensors have asserted are invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are common. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may institute such claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions, such as opposition proceedings in the European Patent Office. The outcomes of allegations of invalidity or unenforceability are unpredictable. With respect to validity, for example, even if we are successful in obtaining patents or in-licensing patents, we cannot be certain that there is no invalidating prior art of which the patent examiner and we or our future licensing partners were unaware during prosecution.

An adverse result in any such proceeding could put one or more of the patents that we may own or in-license in the future at risk of being invalidated or interpreted narrowly, and could put any of our present or future owned or in-licensed patent applications at risk of not yielding an issued patent. A court may also refuse to stop the third party from using the technology at issue in a proceeding, for example, on the basis that our owned or in-licensed patents do not cover that technology. Furthermore, if the breadth or strength of protection provided by our patent applications and any future patents is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products, diagnostic tests or services.

In addition, interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patent applications or any future patents. 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 adversely affected if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation 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 litigation could have a material adverse effect on our ability to raise funds as needed to continue our clinical trials, continue our discovery programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information or trade secrets could be compromised by disclosure during litigation. Any of the foregoing could allow third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations and prospects.

Third parties may allege that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the pharmaceutical and biotechnology industries. We may become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and product candidates, including interference proceedings, post grant review, inter partes review and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, including our competitors, exist in the fields in which we are pursuing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our technologies or product candidates may be subject to claims that they infringe the patent rights of third parties. Our competitors and others may have significantly larger and more mature patent portfolios than we have. In addition, future litigation may be initiated by patent holding companies or other third parties who have no relevant product or service revenue and against whom our future patents, if any, may provide little or no deterrence or protection. Competitors may also assert that our product candidates infringe their intellectual property rights as part of a business strategy to impede our successful entry into those markets.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources and management attention to defend. The risks of being involved in such litigation and proceedings may increase if and as our product candidates near commercialization and as we gain greater visibility as a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of merit. Because patent applications can take many years to issue, pending patent applications may result in issued patents that our product candidates infringe. For example, there may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the discovery, use or manufacture of our product candidates or technologies. We may not be aware of all such intellectual property rights potentially relating to our technology and product candidates, or we may incorrectly conclude that third-party intellectual property is invalid or that our activities and product candidates do not infringe the intellectual property rights of third parties. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third party's intellectual property rights. Parties making claims against us may also obtain injunctive or other equitable relief. For example, if any third-party patents were held to cover the manufacturing process of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidates. In the event of a successful claim of infringement against us, we may also have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, indemnify customers, collaborators or other third parties, seek new regulatory approvals, and redesign our infringing products, which may not be possible or practical. If we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we may be required to obtain a license from such third party to continue developing, manufacturing and marketing our technology and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and could require us to make substantial licensing and royalty payments. Claims that we have misappropriated the confidential information, trade secrets or other intellectual property rights of third parties could have a similar material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to obtain licenses from third parties on commercially reasonable terms, our business could be adversely affected.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from the third parties. The in-licensing and acquisition of third-party intellectual property

rights is a competitive area, and a number of more established companies are also pursuing strategies to in-license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. Furthermore, companies that perceive us to be a competitor may be unwilling to sell, assign or license rights to us. In addition, we expect that competition for the in-licensing or acquisition of third-party intellectual property rights for product candidates that are attractive to us may increase in the future, which may mean fewer suitable opportunities for us as well as higher acquisition or licensing costs. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, such as substantial licensing or royalty payments, our business could be materially and adversely affected. If we are unable to obtain a necessary license, the third parties owning such intellectual property rights could seek an injunction prohibiting our sales or we may be unable to otherwise develop or commercialize the affected product candidates, which could materially harm our business. 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.

If we are unable to obtain rights to required third-party intellectual property rights, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations, and prospects significantly.

If we fail to comply with our obligations in any future intellectual property licenses with third parties that we may enter into, or otherwise experience disruptions to our business relationships with our future licensors, we could lose intellectual property rights that are important to our business.

We may in the future enter into licensing and funding arrangements with third parties that may impose, among other things, diligence, development, and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with those obligations, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements, or our counterparties may require us to grant them certain rights. Such an occurrence could materially adversely affect the value of any product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, which would have a material adverse effect on our business, financial condition, results of operations, and prospects, or impede, delay or prohibit the further development or commercialization of, one or more product candidates that rely on such agreements.

For example, disputes may arise regarding intellectual property that is or becomes subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other matters of contract interpretation;
- whether and the extent to which our technology and processes infringe the intellectual property rights of the licensor that are not subject to the licensing agreement;
- whether our licensor or its licensor had the right to grant the license agreement;
- whether third parties are entitled to compensation or equitable relief, such as an injunction, for our use of the intellectual property rights without their authorization;
- our involvement in the prosecution of licensed patents and our licensors' overall patent enforcement strategy;
- the amounts of royalties, milestones or other payments due under the license agreement;
- the sublicensing of patent and other rights under collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If we do not prevail in such disputes, we may lose any or all of our rights under such license agreements.

In addition, intellectual property license agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we may license prevent or impair our ability

to maintain our licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected technology and product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our future licensors may rely on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents and patent applications we may in-license. If other third parties have ownership rights to patents and/or patent applications we may in-license, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our in-licensed patents in order to enforce such patents against third parties, and we may not receive such cooperation. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Despite our efforts, our future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize product candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors could seek regulatory approval for and market products and technologies identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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

Third parties may attempt to develop and commercialize competitive products in foreign countries where we do not have any patent protection and/or where legal recourse may be limited. This may have a significant commercial impact on our foreign business operations.

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive. 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 U.S., and even where such protection is nominally available, adequate judicial and governmental enforcement of such intellectual property rights may be lacking. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling our inventions in such countries or importing products made using our inventions into the U.S. 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 do obtain patent protection or future licenses but enforcement is not as strong as that in the U.S. These products may compete with our products, and our 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 certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of any patents we do obtain or in-license or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect, to the same extent as the U.S. or at all, inventions that constitute new methods of treatment.

Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put any patents we obtain at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We work with third-party contractors located in China to develop certain of our intellectual property. On December 1, 2020, the Chinese government implemented a new Export Control Law which regulates the export of certain technologies outside of China. As currently implemented, we do not believe the Export Control Law applies to our product candidates, and we do not expect it to impact our business; however, the Export Control Law could be amended in the future in a way that could adversely affect our business.

Many countries, including India, China and certain countries in Europe, 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 patents. If we do obtain or in-license patents and we or any of 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.

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

We or our future licensors may be subject to claims that current or former employees, collaborators, CROs, universities or other third parties have an interest in our owned or future in-licensed patents and patent applications, trade secrets or other intellectual property as an inventor, co-inventor, owner or co-owner. For example, we or our future licensors may have inventorship or ownership disputes that arise from conflicting obligations of employees, consultants, CROs or others who are involved in developing our product

candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of any owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, we may be required to pay monetary damages and we may also lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to protect our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Additionally, if residents of other countries can claim inventorship of our patents and patent applications, we may be required to fulfill additional obligations. For example, some countries, including China, require a patent owner to provide remuneration to inventors who assign rights to inventions developed during course of their employment. Litigation may be necessary to defend against claims based on foreign inventors. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property discovered through government funded programs 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.

We may in the future develop, acquire, or license intellectual property rights that have been generated through the use of U.S. government funding or grants. Pursuant to the Bayh-Dole Act of 1980, the U.S. government has certain rights in inventions developed with government funding. 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: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). If the U.S. government exercises its "march-in" rights in any future intellectual property rights that are generated through the use of U.S. government funding or grants, we could be forced to license or sublicense intellectual property developed by us or that we may license on terms unfavorable to us, and there can be no assurance that we would receive compensation from the U.S. government for the exercise of such 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 U.S. 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 U.S. 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 covered by such intellectual property. Any exercise by the government of any of the foregoing rights could harm our competitive position, business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of such third parties, or that they have wrongfully used or disclosed alleged trade secrets of their current or former employers, or that we have misappropriated their intellectual property, or that they own what we regard as our own intellectual property.

Many of our employees, physician-scientist partners, consultants and contractors are or were previously employed at or engaged by universities or other pharmaceutical or biotechnology companies, including our competitors or potential competitors. Many of them executed proprietary rights, non-disclosure and/or non-competition agreements in connection with such previous employment or engagement. Although we try to ensure that the individuals who work for us do not use the intellectual property rights, proprietary information, know-how or trade secrets of others in their work for us, we may be subject to claims that we or they have, inadvertently or otherwise, used, infringed, misappropriated or otherwise violated the intellectual property rights, or disclosed the alleged trade secrets or other proprietary information, of these former employers, competitors or other third parties. We may also be subject to claims that we have improperly used or obtained such trade secrets. Litigation may be necessary to defend against these claims. Any litigation or the threat of litigation may adversely affect our ability to hire employees or engage consultants and contractors. A loss of key personnel or their work product could hamper or prevent us from developing and commercializing products and product candidates, which could have an adverse effect on our business, results of operations, or prospects.

In addition, while it is our policy to require our employees, physician-scientist partners, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in obtaining such an agreement from each party who in fact develops intellectual property that we regard as our own. Our intellectual property assignment agreements with them may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Additionally, assignment agreements and related agreements may be interpreted under the laws of a foreign country, which may be unpredictable. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If we fail in prosecuting or defending any such claims, we may be required to pay monetary damages, and we may also lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive position and prospects. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

If we are unable to protect the confidentiality of our trade secrets and other proprietary information, our business and competitive position would be adversely affected.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information to maintain our competitive position. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, advisors and other third parties. We cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, our unpublished patent applications or other confidential research, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and 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 U.S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate such trade secrets, from using that technology or information to compete with us.

Furthermore, we expect that, over time, our trade secrets, know-how and proprietary information may be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel to and from academic and industry scientific positions. Consequently, without costly efforts to protect our proprietary technology, we may be unable to prevent others from exploiting that technology, which could affect our ability to expand in domestic and international markets. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely affected.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. These security measures may be breached or otherwise accessed in an unauthorized manner, and we may not have adequate remedies for any breach.

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

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. As a means to enforce our trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition or cancellation proceedings. This can be time-consuming and expensive, particularly for a company of our size. In addition, in an infringement proceeding, a court may decide that a trademark of ours is not valid or is unenforceable, or may determine another trademark is not infringing our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these trademarks or trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trademarks or trade names similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trademark or trade name infringement claims brought by owners of other registered trademarks or trade names that incorporate variations of our trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks and trade names may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Our current trademark applications and additional trademark applications we may file in the future may not proceed to registration and/or may be opposed by third parties. Even if such applications proceed to registration, third parties may challenge our use of such trademarks or seek to invalidate our registration in the future. Other companies in our industry may be using trademarks that are similar to ours and may in the future allege that the use of our trademarks in connection with our products infringes or otherwise violates their trademark rights. Trademark-granting authorities may decide to investigate our trademarks on their own initiative if they believe that there may be potential issues to be resolved. In addition, failure to maintain our trademark registrations, or to obtain new trademark registrations in the future, could limit our ability to protect and enforce our trademarks and impede our marketing efforts in the countries in which we operate. Over the long term, if we are unable to establish brand recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected.

Risks related to our dependence on third parties

We rely on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.

We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, contract manufacturing organizations (CMOs), and strategic partners (collectively, partners) to conduct and support our preclinical studies and our clinical trials under agreements with us and plan to continue to do so for our future preclinical studies and clinical trials. These third parties have had and will continue to have a significant role in the conduct of our preclinical studies and clinical trials and the subsequent collection and analysis of data. For example, our partners contribute highly enabling technologies and services that include: (i) numerous physician-scientists at leading CROs, (ii) support for our translational research efforts, (iii) crystallography to enable structure-based drug discovery, (iv) biochemical and cell-based assays to guide lead generation and optimization, and (v) patient-derived, cell and xenograft models to translate our findings to the clinical setting.

These third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we have limited ability to control the amount or timing of resources that any such third party will devote to our preclinical studies or our clinical trials. The third parties we rely on for these services may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could affect their performance on our behalf. Some of these third parties may terminate their engagements with us at any time. We also have to negotiate budgets and contracts with CROs, clinical trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. If we need to enter into alternative arrangements with, or replace or add any third parties, it would involve substantial cost and require extensive management time and focus, or involve a transition period, and may delay our drug development activities, as well as materially impact our ability to meet our desired clinical development timelines.

Our heavy reliance on these third parties for such drug development and clinical trial activities reduces our control over these activities. As a result, we have less direct control over the conduct, timing and completion of preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCP standards, regulations for conducting, recording and reporting the results of clinical trials to assure that data and reported results are reliable and accurate and that the rights, integrity and confidentiality of trial participants are protected. The EMA also requires us to comply with similar standards. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials substantially comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations and require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients, may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, or if these third parties need to be replaced, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials, and expect to continue to do so for additional preclinical studies, clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quality and quantities of our product candidates 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. If we were to experience an unexpected loss of supply of any of our 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 preclinical studies or clinical trials.

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

- the failure of the third party to manufacture our product candidates according to our schedule and specifications, 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, including cGMP;
- 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 our contract manufacturing partners and are dependent on these contract manufacturing partners for general project management, in-person oversight and for compliance with cGMP regulations for manufacturing both API and finished drug products. To date, we have obtained API and drug product for our product candidates from a limited group of third-party contract manufacturers, and we continue to develop our supply chain for each of our product candidates. As we advance our product candidates through development and into commercialization, if approved, we will continue to take steps to protect against any potential supply disruptions through the use of a safety stock strategy and by maintaining relationships and contracting with additional suppliers. However, we may be unsuccessful in maintaining or putting in place additional framework agreements or protecting against potential supply disruptions.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the U.S. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or comparable regulatory authorities, 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, EMA 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 will need to find alternative manufacturing facilities, and those new facilities would need to be inspected and approved by the FDA, EMA or a comparable regulatory authority prior to commencing manufacturing, 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.

If any third-party manufacturer with whom we contract fails to perform its obligations, we may be forced to enter into an agreement with a different third-party manufacturer, which we may not be able to do on reasonable terms, if at all. As a result, our clinical trial supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our product candidates may be unique or proprietary to the original third-party manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change third-party manufacturers for any reason, we will be required to verify that the new third-party manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new third-party manufacturer could negatively affect our ability to develop product candidates or commercialize our anticipated products in a timely manner or within budget. Furthermore, a third-party manufacturer may possess technology related to the manufacture of our product candidate that such third-party manufacturer owns independently. This would increase our reliance on such third-party manufacturer or require us to obtain a license from them in order to have another third-party manufacturer manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior

clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. Our current and anticipated future dependence upon others for the manufacture of our product candidates 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.

Our manufacturing process needs to comply with FDA regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays in or termination of our clinical programs and suspension or withdrawal of any regulatory approvals.

In order to commercially produce our products either at a third party's facility or in any facility of ours, we will need to comply with the FDA's cGMP regulations and guidelines. We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We are subject to inspections by the FDA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill-finish, packaging, or storage of our precision medicines as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our product candidates, including leading to significant delays in the availability of our precision medicines for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

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 evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, product candidates, 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, products and product candidates 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, 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.

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

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

environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

If we decide to establish collaborations, 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 may require additional cash to fund expenses. We may 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 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 depends, 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 preclinical studies or clinical trials, the likelihood of approval by the FDA, EMA 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 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 discovery 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 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.

If we enter into any collaboration arrangements with any third parties for the development and commercialization of our product candidates, we will likely 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 revenue 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 would 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 de-emphasize 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 business combination or 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;
- we may grant exclusive rights to our collaborators that would prevent us from collaborating with others;

- 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;
- collaborators may not provide us with timely and accurate information regarding development progress and activities under the collaboration or may limit our ability to share such information, which could adversely impact our ability to report progress to our investors and otherwise plan our own development of our product candidates;
- collaborators may own or co-own intellectual property covering our products or product candidates that result from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks related to ownership of our common stock

The market price of our Class A common stock may be volatile, and our investors could lose all or part of their investment.

The trading price of our Class A common stock has been and is likely to continue to be highly volatile and subject to wide fluctuations in response to various factors, many 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 Class A common stock, regardless of our actual operating performance. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report, these factors include, without limitation:

- the timing and results of INDs, NDAs, 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;
- our success in commercializing our drug candidates, if approved;
- regulatory actions with respect to our products or product candidates or our competitors' products or product candidates;
- actual or anticipated changes in our growth rate relative to our competitors;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning our 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;
- 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;
- the impact of any public health emergencies, natural disasters, or geopolitical events, including actual or threatened tariffs or other changes in trade policy, civil or political unrest or military conflicts; and
- general economic, political, industry and market conditions.

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 Class A common stock.

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 Class A common stock may 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.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award, and recognize the cost as an expense over the employee's requisite service period. Compensation cost for stock-based awards with performance-based vesting conditions is recognized on a straight-line basis over the requisite service period for each separately vesting portion of the underlying stock award when the performance-based vesting condition is deemed probable to occur. As the variables that we use as a basis for valuing these awards change over time, including our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and cost of, and level of investment in, research and development activities relating to our programs, which will change from time to time;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- the cost of manufacturing our current product candidates and any future product candidates, which may vary depending on FDA, EMA or other comparable foreign regulatory authority guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies or other assets;
- the timing and outcomes of preclinical studies and clinical trials for our product candidates, or competing product candidates;
- the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;
- competition from existing and potential future products that compete with our product candidates, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any delays in regulatory review or approval of our product candidates;
- the level of demand for any of our product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future products that compete with our product candidates;
- our ability to commercialize our product candidates, if approved, inside and outside of the U.S., either independently or working with third parties;

- our ability to establish and maintain collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing, volatile and instable global economic and political environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our Class A common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

Global credit and financial markets have experienced extreme instability, volatility and disruptions in the past several years due to a number of factors, including the COVID-19 pandemic, ongoing military conflicts, bank failures and other market-influencing developments, including severely diminished liquidity and credit availability, declines in consumer confidence, increases in interest rates, declines in economic growth, increases in unemployment rates, increases in inflation and uncertainty about international trade policy and economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions, whether due to changes in trade policy, public health emergencies, military conflicts, bank failures or otherwise, will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive.

Failure to secure additional financing, as needed, in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans or commercialization efforts. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. Our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Our principal stockholders own a significant percentage of our stock and can exert significant control over matters subject to stockholder approval. Two of our directors are affiliated with one of our principal stockholders.

Our holders of 5% or more of our capital stock and their respective affiliates beneficially own a substantial amount of our outstanding Class A common stock and Class B common stock and a substantial amount of our Class A voting stock. Two of our directors, Joseph Pearlberg, M.D., Ph.D. and Cameron A. Wheeler, Ph.D., are affiliated with Deerfield Management Company, L.P., certain affiliates of which, collectively, constitute our largest stockholder. Our principal stockholders, acting together or on their own, could exert significant control over matters requiring stockholder approval. For example, they may be able to impact elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that investors may feel are in their best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with each investor's 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 Class A common stock.

The dual class structure of our common stock and the option of the holders of shares of our Class B common stock to convert into shares of our Class A common stock may limit our Class A common stockholders' ability to influence corporate matters.

Our Class A common stock has one vote per share, while our Class B common stock is non-voting. Nonetheless, each share of our Class B common stock may be converted at any time into one share of Class A common stock at the option of its holder, subject to the limitations provided for in our third amended and restated certificate of incorporation, as amended, that prohibit the conversion of our Class B common stock into shares of Class A common stock to the extent that, upon such conversion, such holder and any other persons with whom such holder's beneficial ownership would be aggregated for purposes of Section 13(d) of the Exchange Act would beneficially own in excess of 4.9% or 9.9%, as applicable, based on the holder's election of any class of our securities registered under the Exchange Act. Consequently, if holders of Class B common stock exercise their option to make this conversion, such exercise will have the effect of increasing the relative voting power of those prior holders of our Class B common stock (subject to the ownership limitation described in the previous sentence) and increasing the number of outstanding shares of our voting common stock, and

correspondingly decreasing the relative voting power of the current holders of our Class A common stock, which may limit our Class A common stockholders' ability to influence corporate matters. Because our Class B common stock is generally non-voting, stockholders who own more than 10% of our common stock overall but 10% or less of our Class A common stock will not be required to report changes in their ownership from transactions in our common stock pursuant to Section 16(a) of the Exchange Act and would not be subject to the short-swing profit provisions of Section 16(b) of the Exchange Act.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our 2021 Stock Option and Incentive Plan (2021 Plan), could result in dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

Additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities, investors may be materially diluted by such sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock.

Pursuant to our 2021 Plan, our management is authorized to grant stock options and restricted stock units, among other award types, to our employees, directors and consultants. If the number of shares reserved under our 2021 Plan is increased pursuant to the terms of our 2021 Plan, our stockholders may experience dilution, which could cause our stock price to fall.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

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

Until such time, if ever, as we can generate substantial product revenues, we may need to finance our cash needs through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through future strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates or grant licenses on terms unfavorable to us.

We incur significant costs as a result of operating as a public company, and our management is devoting substantial time to related compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses. We are and will continue to be subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and Nasdaq. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, significant legal and financial compliance costs, and making some activities more time consuming. We have had to hire additional accounting, finance, and other personnel in connection with our status as a public company, and our management and other personnel devote a substantial amount of time to these compliance initiatives and we cannot accurately predict or estimate the amount or timing of additional costs we may incur to respond to these requirements.

In addition, as a public company we are required to incur additional costs and obligations in order to comply with SEC rules that implement Section 404 of the Sarbanes-Oxley Act. Under these rules, we are required to maintain effective disclosure and financial controls and to make a formal assessment of the effectiveness of our internal control over financial reporting. In addition, we are subject to Section 404(b) of the Sarbanes-Oxley Act, which requires us to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. Compliance with Section 404 has been and will continue to be both costly and time-consuming for our management.

If we experience material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

We may in the future discover material weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of

controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. Accordingly, we cannot assure our stockholders that we will not in the future identify material weaknesses.

If we have a material weakness in our internal controls over financial reporting, we may not be able to produce timely and accurate financial statements. If that were to happen, our investors could lose confidence in our reported financial information, the market price of our stock could decline, and we could be subject to sanctions or investigations by the stock exchange on which our Class A common stock is listed, the SEC or other regulatory authorities.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the fact that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

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

The market price of our Class A 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.

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

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

Anti-takeover 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 Class A common stock.

Our third amended and restated certificate of incorporation, as amended, and amended and restated 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, include:

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

In addition, Section 203 of the General Corporation Law of the State of Delaware (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 third amended and restated certificate of incorporation, as amended, our amended and restated bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by 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 amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of, or a claim based on, fiduciary duty owed by any of our current or former directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our third amended and restated certificate of incorporation or our amended and restated bylaws or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein (the Delaware Forum Provision). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the U.S. shall be the sole and exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act (the Federal Forum Provision). In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

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

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We have developed and implemented a cybersecurity risk management program intended to protect the confidentiality, integrity and availability of our critical systems and information. Our cybersecurity risk management program includes a cybersecurity Incident Response Plan (IRP). Our cybersecurity risk management program is a key component of our overall risk management process, and includes similar characteristics, reporting channels and governance processes to those that apply across other legal, compliance, strategic, operational and financial risk areas within the Company.

We design and assess our program based on the National Institute of Standards and Technology Cybersecurity Framework (NIST CSF). This does not imply that we meet any particular technical standards, specifications, or requirements, only that we use the NIST CSF as a guide to help us identify, assess, and manage cybersecurity risks relevant to our business.

Our cybersecurity risk management program includes:

- risk assessments designed to help identify material cybersecurity risks to our critical systems, information, products, services, and our broader enterprise IT environment;
- a security team principally responsible for managing (1) our cybersecurity risk assessment processes, (2) our security controls, and (3) our response to cybersecurity incidents;
- the use of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security controls;

- cybersecurity awareness training of our employees, incident response personnel and senior management;
- a cybersecurity IRP that includes procedures for responding to cybersecurity incidents; and
- a third-party risk management process for service providers, suppliers and vendors.

We have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected or are reasonably likely to materially affect us, including our operations, business strategy, results of operations or financial condition.

Cybersecurity Governance

Our board of directors considers cybersecurity risk as part of its risk oversight function and has delegated to its audit committee oversight of cybersecurity and other information technology risks. The audit committee oversees management's implementation of our cybersecurity risk management program.

The audit committee receives reports from management on our cybersecurity risks at least annually. In addition, management updates the audit committee regarding all material cybersecurity incidents, as well as any incidents with lesser impact potential that management, in its discretion, determines may be relevant for audit committee review. The audit committee reports to the board of directors regarding its activities, including those related to cybersecurity.

Our management team, including our Chief Financial Officer, working closely with our Vice President, Information Technologies and our Director, Cybersecurity and Compliance (collectively, our Cybersecurity Oversight Team), is responsible for assessing and managing our material risks from cybersecurity threats. Our Cybersecurity Oversight Team has primary responsibility for our overall cybersecurity risk management program and supervises both our internal cybersecurity personnel and our retained external cybersecurity consultants. Our Cybersecurity Oversight Team's experience includes a combined 50+ years in the pharmaceutical industry and information technology. This includes software and systems development, cybersecurity program oversight and overall IT management. Our Cybersecurity Oversight Team has over two decades of experience dedicated to supporting enterprise architecture and over a decade of experience specializing in cybersecurity, implementing cybersecurity frameworks, assessing and managing cybersecurity risks and executing incident response plans.

Our Cybersecurity Oversight Team supervises efforts to prevent, detect, mitigate and remediate cybersecurity risks and incidents through various means, which include briefings from internal security personnel; threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us; and alerts and reports produced by security tools deployed in the IT environment.

Pursuant to our IRP, all of our employees are trained to report a suspected cybersecurity incident or breach to our information technology team. Reporting guidelines under the IRP describe how to report an incident and what details to include. As a first step under the IRP, our information technology team assesses the reported risk or breach and escalates it to our Incident Response Team (IRT), as appropriate. The IRT is comprised of the members of our Cybersecurity Oversight Team and other critical business function leaders, including members of our legal and communications teams. Following notification from our information technology team, the IRT is responsible for continuing to assess the suspected risk or breach to determine its potential impact on our organization, systems and data. Based on that assessment, the IRT may raise the incident or breach to other members of management or the audit committee for further review and triage.

Item 2. Properties

We lease office space for our corporate headquarters, which is located in Cambridge, Massachusetts. We believe our leased office space is adequate for our current needs and that suitable additional or alternative space will be available in the future on commercially reasonable terms, if required.

Item 3. Legal Proceedings.

As of December 31, 2025, we were not party 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.

Certain Information Regarding the Trading of Our Common Stock

Our Class A common stock trades under the symbol "NUVL" on the Nasdaq Global Select Market and has been publicly traded since July 29, 2021. Prior to this time, there was no public market for our Class A common stock. Our Class B common stock is not listed or traded on any stock exchange.

Holders of Our Common Stock

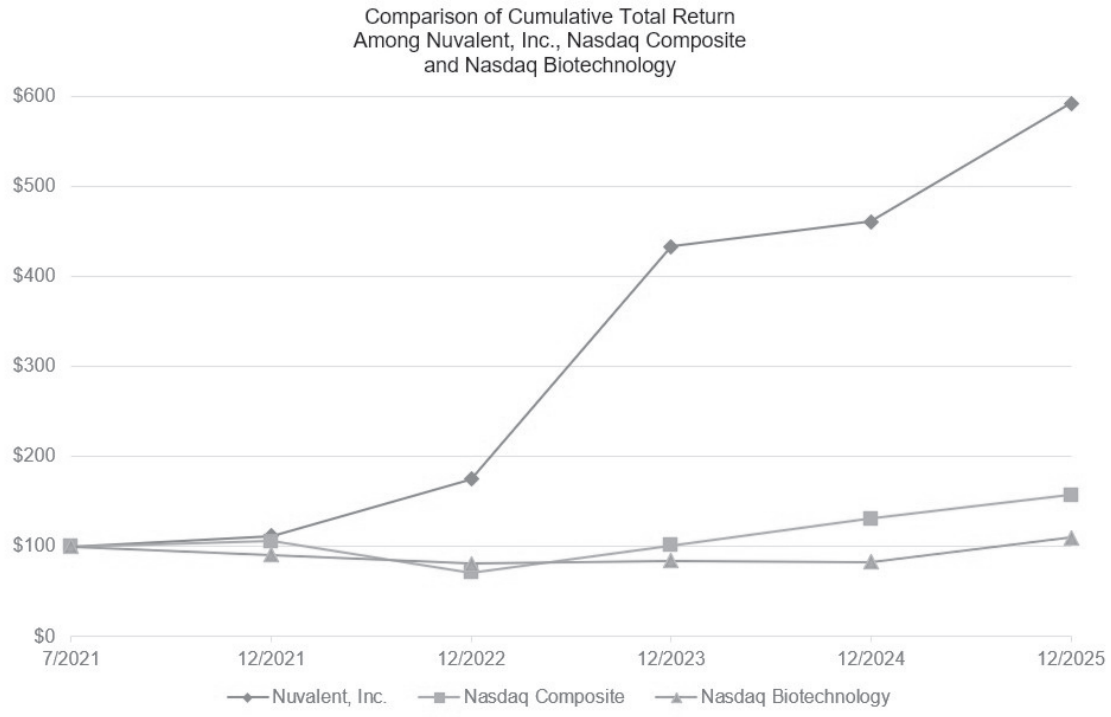
As of February 19, 2026, there were approximately 5 holders of record of shares of our Class A common stock and 2 holders of record of shares of our Class B common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividends

We have never declared or paid cash dividends on our common stock since our inception. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Stock Performance Graph

The stock performance graph below compares the performance of our common stock to The Nasdaq Biotechnology Index (Nasdaq Biotechnology) and The Nasdaq Composite Index (Nasdaq Composite) from July 29, 2021 to December 31, 2025. The comparisons assume an investment of $100 in our Class A common stock and in each of the foregoing indices, and assume reinvestment of dividends, if any. The comparisons shown in the stock performance graph below are based upon historical data and are not necessarily indicative of, nor are they intended to forecast, the potential future performance of our common stock. The following stock performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission for purposes of Section 18 of the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.



Recent Sales of Unregistered Securities

There were no shares of equity securities sold or issued by us during the period covered by this Annual Report that were not registered under the Securities Act, and that were not previously reported in an Annual Report on Form 10-K, Quarterly Report on Form 10-Q or Current Report on Form 8-K.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period from October 1, 2025 to December 31, 2025.

Item 6. [Reserved.]

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. For a detailed discussion of our business environment, please read Item 1. Business, included in this Annual Report. As a result of many factors, including those factors set forth in Item 1A. Risk Factors of this Annual Report, our actual results could differ materially from the results described in, or implied by, the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company focused on creating precisely targeted therapies for patients with cancer. We leverage our team's deep expertise in chemistry and structure-based drug design to develop innovative small molecules that are designed with the aim to overcome the limitations of existing therapies for clinically proven kinase targets.

Limitations faced by currently available kinase inhibitors can include (i) kinase resistance, or the emergence of new mutations in the kinase target that can enable resistance to existing therapies, (ii) kinase selectivity, or the potential for existing therapies to inhibit other structurally similar kinase targets and lead to off-target adverse events, and (iii) limited brain penetrance, or the ability for the therapy to treat disease that has spread or metastasized to the brain. By prioritizing target selectivity, we believe our drug candidates have the potential to overcome resistance, avoid dose-limiting off-target adverse events, address brain metastases, and drive more durable responses. This may result in the potential to drive deeper, more durable responses with minimal adverse events, and we believe these potential benefits may support opportunities for clinical utility earlier in the treatment paradigm.

Candidate Overview

Zidesamtinib (NVL-520)

Our first lead product candidate, zidesamtinib (NVL-520), is being developed for patients with ROS proto-oncogene 1 (ROS1)-positive non-small cell lung cancer (NSCLC). Zidesamtinib is a novel ROS1-selective inhibitor designed with the aim to address the clinical challenges of emergent treatment resistance, central nervous system (CNS)-related adverse events, and brain metastases that may limit the use of currently available ROS1 tyrosine kinase inhibitors (TKIs). Zidesamtinib has received U.S. Food and Drug Administration (FDA) Breakthrough Therapy designation for the treatment of patients with locally advanced or metastatic (advanced) ROS1-positive NSCLC who have previously been treated with two or more prior ROS1 TKIs, and orphan drug designation for ROS1-positive NSCLC.

Our ARROS-1 clinical trial is a first-in-human global Phase 1/2, multicenter, open-label, dose-escalation and expansion study evaluating zidesamtinib as an oral monotherapy in patients with advanced ROS1-positive NSCLC and other solid tumors. Dosing was initiated in the Phase 1 portion of the ARROS-1 clinical trial in January 2022. From January 2022 to August 2023, the Phase 1 portion of the ARROS-1 trial enrolled 104 patients (99 NSCLC, 5 other solid tumors).

In September 2023, we announced the initiation of the Phase 2 portion of the ARROS-1 clinical trial, following alignment with the FDA on a recommended Phase 2 dose (RP2D) of 100 mg once daily (QD). The Phase 2 portion of the ARROS-1 clinical trial is designed to evaluate the safety and activity of zidesamtinib in patients with advanced ROS1-positive NSCLC and other solid tumors, examining several specific cohorts of patients based on the prior anti-cancer therapies that such patients have received. The Phase 2 cohorts have been designed to support potential registration in TKI-naïve and/or TKI pre-treated ROS1-positive NSCLC patients.

Between September 2023 and June 16, 2025, 435 patients were enrolled in the Phase 2 portion of the ARROS-1 clinical trial. In June 2025, we announced positive pivotal data for zidesamtinib in TKI pre-treated patients with advanced ROS1-positive NSCLC from the global ARROS-1 Phase 1/2 clinical trial, and in September 2025, we presented the pivotal dataset at the International Association for the Study of Lung Cancer 2025 World Conference on Lung Cancer. The primary efficacy analysis population for this pivotal dataset consisted of 117 TKI pre-treated patients with advanced ROS1-positive NSCLC with measurable disease who received zidesamtinib at the RP2D by May 31, 2024, with duration of response (DOR) follow-up of at least 6 months available for nearly all responders.

In June 2025, we also shared preliminary data from the Phase 2 TKI-naïve cohort in the ARROS-1 clinical trial, in which enrollment is ongoing. Encouraging preliminary data were available for 35 TKI-naïve patients with advanced ROS1-positive NSCLC treated with zidesamtinib at RP2D as of August 31, 2024. As of June 16, 2025, a total of 104 patients had been enrolled in the ongoing TKI-naïve cohort of the ARROS-1 trial.

In November 2025, the FDA accepted for filing our New Drug Application (NDA) for zidesamtinib for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who received at least 1 prior ROS1 TKI. The application has been assigned a Prescription Drug User Fee Act target action date of September 18, 2026. Additionally, we plan to submit data from the ongoing TKI-naïve cohort in the Phase 2 portion of the ARROS-1 clinical trial to the FDA to support a potential label expansion of zidesamtinib in TKI-naïve patients with advanced ROS1-positive NSCLC in the second half of 2026.

Neladalkib (NVL-655)

Our second lead product candidate, neladalkib (NVL-655), is being developed for patients with anaplastic lymphoma kinase (ALK)-positive NSCLC. Neladalkib is a brain-penetrant ALK-selective inhibitor designed with the aim to address the clinical challenges of emergent treatment resistance, CNS-related adverse events, and brain metastases that may limit the use of first-generation (1G; crizotinib), second-generation (2G; ceritinib, alectinib, or brigatinib), and third-generation (3G; lorlatinib) ALK inhibitors. Neladalkib has received FDA Breakthrough Therapy designation for the treatment of patients with locally advanced or metastatic ALK-positive NSCLC who have been previously treated with two or more ALK TKIs, and orphan drug designation for ALK-positive NSCLC.

Our ALKOVE-1 clinical trial is a first-in-human global Phase 1/2, multicenter, open-label, dose-escalation and expansion study evaluating neladalkib as an oral monotherapy in patients with advanced ALK-positive NSCLC and other solid tumors. Dosing was initiated in the Phase 1 portion of the ALKOVE-1 clinical trial in June 2022. From June 2022 to February 2024, the Phase 1 portion of the ALKOVE-1 clinical trial enrolled 133 patients (131 NSCLC, 2 other solid tumors).

In February 2024, we announced the initiation of the Phase 2 portion of the ALKOVE-1 clinical trial, following alignment with the FDA on a RP2D of 150 mg QD. The Phase 2 portion of the ALKOVE-1 clinical trial is designed to evaluate the safety and activity of neladalkib in several expansion cohorts of patients defined based on the number and type of prior anti-cancer therapies they have received. The Phase 2 cohorts are designed with registrational intent for TKI pre-treated patients with ALK-positive NSCLC and to enable preliminary evaluation for patients with ALK-positive NSCLC who are TKI-naïve.

In July 2025, we announced the initiation of the ALKAZAR Phase 3 clinical trial with registrational intent for TKI-naïve patients with advanced ALK-positive NSCLC. The ALKAZAR clinical trial is a global, randomized, controlled trial designed to evaluate neladalkib versus the current standard of care. Patients are randomized 1:1 to receive neladalkib monotherapy or ALECENSA (alectinib) monotherapy, reflecting input from collaborating physician-scientists and alignment with global regulatory agencies. The ALKAZAR clinical trial is designed to enroll approximately 450 patients with TKI-naïve ALK-positive NSCLC. The primary endpoint is progression-free survival (PFS) based on Blinded Independent Central Review (BICR). Secondary endpoints include overall survival, PFS based on investigator's assessment, time to intracranial response, and BICR assessment of intracranial objective response rate, intracranial duration of response, objective response rate, DOR, time to intracranial progression, and safety.

At the European Society for Medical Oncology Congress in October 2025, we presented preliminary data for neladalkib in patients with advanced ALK-positive solid tumors outside of NSCLC from the ongoing ALKOVE-1 clinical trial. Neladalkib demonstrated encouraging preliminary activity across a diverse set of ALK TKI-naïve and previously treated advanced ALK-positive solid tumors, and was considered generally safe and well-tolerated with a preliminary overall safety profile consistent with its ALK-selective, tropomyosin receptor kinase-sparing design, and with previously reported data.

In November 2025, we announced positive topline data for neladalkib in TKI pre-treated patients with advanced ALK-positive NSCLC from the global ALKOVE-1 Phase 1/2 clinical trial. The primary analysis population for this topline dataset consisted of 253 TKI pre-treated patients with advanced ALK-positive NSCLC with measurable disease who received neladalkib at the RP2D by September 30, 2024, with DOR follow-up of at least 6 months available for nearly all responders.

In November 2025, we also shared preliminary data from the Phase 2 exploratory cohort for TKI-naïve patients with advanced ALK-positive NSCLC from the ALKOVE-1 study. Encouraging preliminary data were available for 44 TKI-naïve patients with advanced ALK-positive NSCLC treated with neladalkib at RP2D as of August 29, 2025.

We have completed our pre-NDA meeting with the FDA and plan to move forward with an NDA submission of the data for TKI pre-treated patients with advanced ALK-positive NSCLC from our ALKOVE-1 study of neladalkib in the first half of 2026. We plan to present detailed study results at a future medical meeting.

NVL-330

Our third product candidate, NVL-330, is a brain-penetrant human epidermal growth factor receptor 2 (HER2)-selective inhibitor designed with the aim to address the combined medical needs of treating tumors driven by HER2 mutations and alterations, including HER2 exon 20 insertion mutations (HER2ex20), treating brain metastases, and avoiding treatment-limiting adverse events including due to off-target inhibition of wild-type epidermal growth factor receptor (EGFR). Preclinical data have shown that NVL-330 inhibited a broad range of HER2 oncogenic alterations, including HER2ex20, in cell-based assays, was brain penetrant and was selective for HER2 oncogenic alterations over the structurally related wild-type EGFR. Additionally, new preclinical data were presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in October 2025, further supporting NVL-330's potentially differentiated brain-penetrant profile. Compared to several currently available and investigational HER2 TKIs in the same preclinical assays, NVL-330 demonstrated a favorable efflux ratio and brain partitioning, metrics that are potentially positive predictors of brain exposure in humans. In preclinical models of intracranial activity, NVL-330 induced deep intracranial regression in mice. In the same models, the approved therapies Enhertu (T-DXd) and Hernexeos (zongertinib) did not induce intracranial regression at their clinically relevant doses. Additionally, NVL-330 induced intracranial tumor regression in mice that had progressed in the CNS on zongertinib.

We are currently enrolling patients in the HEROEX-1 clinical trial, a global Phase 1a/1b, multicenter, open-label, dose-escalation and expansion trial evaluating NVL-330 in pre-treated patients with advanced HER2-altered NSCLC, including those with HER2ex20 mutations. In July 2024, we announced that the first patient was dosed with NVL-330 in the HEROEX-1 trial. The HEROEX-1 trial is evaluating the overall safety and tolerability of NVL-330. Additional objectives include determination of the RP2D, characterization of the pharmacokinetic profile, and preliminary evaluation of anti-tumor activity.

Discovery Programs

We have prioritized a number of additional small molecule research programs following an assessment of medical need. Research for these programs is ongoing, and we plan to disclose a new development candidate by year-end 2026.

Financial Overview

Since commencing significant operations in 2018, we have focused substantially all of our efforts and financial resources on research and development activities for our programs, including zidesamtinib, neladalkib and NVL-330, establishing and maintaining our intellectual property portfolio, organizing and staffing our Company, business planning, raising capital, preparing for potential commercialization and providing general and administrative support for these operations. We do not have any products approved for sale and have not generated revenue from product sales or any other source.

We have incurred significant net losses since our inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development of, receipt of marketing approval from regulatory authorities for, and eventual commercialization of our product candidates. We reported net losses of $425.4 million, $260.8 million and $126.2 million for the years ended December 31, 2025, 2024 and 2023, respectively. As of December 31, 2025, we had an accumulated deficit of $972.4 million. We expect to incur significant expenses for the foreseeable future in connection with ongoing activities, particularly if and as we:

- continue to advance zidesamtinib, neladalkib and NVL-330 in clinical development;
- advance the development of our discovery programs;
- expand our pipeline of product candidates through our product discovery and development efforts;
- seek regulatory approvals for our product candidates;
- continue to build a sales, marketing and distribution infrastructure to commercialize any approved product candidates and incur related commercial manufacturing costs;
- implement operational, financial and management systems;
- attract, hire and retain additional clinical, scientific, management, sales and marketing and administrative personnel;
- maintain, expand, protect and enforce our intellectual property portfolio, including patents, trade secrets and know-how;
- acquire or in-license other product candidates and technologies; and
- operate as a public company.

We will not generate revenue from product sales unless and until we successfully complete clinical development of, obtain regulatory approval for and successfully commercialize one or more of our product candidates. As a result, we may need additional funding 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 expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. Our ability to raise additional funds may be adversely impacted by general economic conditions, both inside and outside the U.S., including disruptions to, and instability and volatility in, the credit and financial markets in the U.S. and worldwide, including heightened inflation, interest rate and currency rate fluctuations, and economic slowdown or recession as well as concerns related to public health emergencies, natural disasters or geopolitical events, including actual or threatened tariffs or other changes in trade policy, civil or political unrest or military conflicts. In addition, market instability and volatility, high levels of inflation and interest rate fluctuations may increase our cost of financing or restrict our access to potential sources of future liquidity. Our failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on our business, results of operations or financial condition, including requiring us to have to delay, reduce or eliminate our product development or commercialization efforts. Insufficient liquidity may also require us to relinquish rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our development efforts.

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

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $1.4 billion. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements into 2029. Our existing cash, cash equivalents and marketable securities may not be sufficient to fund all of our product candidates through regulatory approval, and we may need to raise additional capital to complete the development and commercialization of our product candidates. See *"—Liquidity and Capital Resources."*

Components of Our Results of Operations

Operating expenses

Our operating expenses are comprised of research and development expenses and general and administrative expenses.

Research and development expenses

Research and development expenses consist primarily of salaries and related costs, including stock-based compensation, for personnel engaged in research and development functions; costs incurred in connection with the advancement of our discovery programs and product candidates in preclinical and clinical studies, including under agreements with contract research organizations (CROs); and the cost of developing and scaling our manufacturing process, including under agreements with contract manufacturing organizations (CMOs), to manufacture drug substance and drug product for use in our research and preclinical and clinical studies and manufacture commercial-scale validation batches in preparation for the commercial launch of our product candidates that obtain regulatory approval.

We track our direct external research and development expenses on a program-by-program basis, including costs incurred with our CROs and CMOs, in connection with our preclinical, clinical and manufacturing activities. Costs incurred prior to nominating a development candidate are included in discovery programs. We do not allocate employee costs or other indirect costs to specific product development programs because these costs are deployed across multiple programs and, as such, are not separately classified.

We expect to incur substantial research and development expenses as we continue to advance zidesamtinib, neladalkib and NVL-330 in clinical development, and expand our discovery, research and preclinical activities in the near term and in the future. Although the ALKAZAR Phase 3 clinical trial, the Phase 2 portions of our ARROS-1 and ALKOVE-1 clinical trials and the HEROEX-1 Phase 1 clinical trial are ongoing, at this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any product candidates we may develop. A change in the outcome of any number of variables with respect to product candidates we may develop could significantly change the costs and timing associated with the development of that product candidate. The duration, costs and timing of preclinical studies and clinical trials and development of our product candidates will depend on a variety of factors, including:

- the timing and progress of development activities relating to zidesamtinib, neladalkib, NVL-330 and any future product candidates from our discovery programs, including any additional costs that may result from delays in enrollment or other factors;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to maintain our current research and development programs and to establish new ones;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the number of trials required for regulatory approval;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible subjects and initiate clinical trials;
- the number of subjects that participate in the trials and per subject trial costs;
- potential additional safety monitoring requested by regulatory authorities;
- the duration of subject participation in the trials and follow-up;
- the successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to applicable regulatory authorities;
- the receipt of approvals from applicable regulatory authorities;
- the timing, receipt and terms of any marketing approvals and post-marketing approval commitments from applicable regulatory authorities;

- the extent to which we establish collaborations, strategic partnerships or other strategic arrangements with third parties, if any, and the performance of any such third party;
- establishing commercial manufacturing capabilities including making arrangements with CMOs; and
- development and timely delivery of commercial-grade drug formulations that can be used in our clinical trials and for commercial launch.

Any changes in the outcome of any of these factors could significantly impact the costs, timing and viability associated with the development of our product candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, for personnel in executive, finance, commercial and administrative functions. General and administrative expenses also include professional fees for legal, patent, consulting, investor and public relations and accounting and audit services, as well as expenses relating to commercialization preparation activities. We anticipate that our general and administrative expenses will increase over time as we increase our headcount to support the growth of our organization as well as prepare for the commercial launch of our product candidates that obtain regulatory approval.

Other income (expense)

Change in fair value of related party revenue share liability

We have a revenue sharing agreement with Deerfield Healthcare Innovations Fund, L.P. and Deerfield Private Design Fund IV, L.P. (collectively, Deerfield), each an investor in the Company, to pay Deerfield a fixed low single-digit percentage rate of net sales of certain commercial products. We account for the liability to Deerfield at fair value with changes recognized in the consolidated statements of operations and comprehensive loss.

Interest income and other income (expense), net

Interest income and other income (expense), net consists of interest income earned on our cash, cash equivalents and marketable securities and other income (expense) unrelated to our core operations.

Results of Operations

The following discussion and analysis of our results of operations includes a comparison of the year ended December 31, 2025 to the year ended December 31, 2024. For the discussion and analysis of our results of operations for the year ended December 31, 2024 compared to the year ended December 31, 2023, refer to Part II, Item 7 “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our Annual Report on Form 10-K for the year ended December 31, 2024 filed with the Securities and Exchange Commission (SEC) on February 27, 2025 (the 2024 Form 10-K), which is incorporated herein by reference.

Comparison of the Years Ended December 31, 2025 and 2024

The following table summarizes our results of operations for the years ended December 31, 2025 and 2024 (in thousands):

	Year Ended December 31,		
	2025	2024	Change
Operating expenses			
Research and development	$ 306,970	$ 217,774	$ 89,196
General and administrative	107,337	62,594	44,743
Total operating expenses	414,307	280,368	133,939
Loss from operations	(414,307)	(280,368)	(133,939)
Other income (expense)			
Change in fair value of related party revenue share liability	(55,220)	(17,940)	(37,280)
Interest income and other income (expense), net	44,735	38,316	6,419
Total other income (expense), net	(10,485)	20,376	(30,861)
Loss before income taxes	(424,792)	(259,992)	(164,800)
Income tax provision	585	764	(179)
Net loss	$ (425,377)	$ (260,756)	$ (164,621)

Research and development expenses

The following table summarizes our research and development expenses for the years ended December 31, 2025 and 2024 (in thousands):

	Year Ended December 31,		
	2025	2024	Change
Direct external research and development expenses by program:			
Zidesamtinib	$ 59,519	$ 62,110	$ (2,591)
Neladalkib	105,446	67,778	37,668
NVL-330	21,819	8,293	13,526
Discovery programs	11,875	9,178	2,697
Unallocated research and development expenses:			
Personnel-related (including stock-based compensation)	95,987	62,594	33,393
Other	12,324	7,821	4,503
Total research and development expenses	$ 306,970	$ 217,774	$ 89,196

Research and development expenses were $307.0 million for the year ended December 31, 2025, compared to $217.8 million for the year ended December 31, 2024. The increase in direct external research and development expenses related to neladalkib of $37.7 million was primarily due to costs related to the ongoing Phase 2 portion of the ALKOVE-1 clinical trial and the Phase 3 ALKAZAR clinical trial, which was initiated in July 2025, and professional services. The increase in direct external research and development expenses related to NVL-330 of $13.5 million was primarily due to costs related to the ongoing HEROEX-1 Phase 1 clinical trial and manufacturing costs. The increase in personnel-related expenses of $33.4 million was primarily due to an increase of $16.7 million in stock-based compensation expense and an increase in headcount. For the years ended December 31, 2025 and 2024, stock-based compensation expense was $48.1 million and $31.4 million, respectively.

General and administrative expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2025 and 2024 (in thousands):

	Year Ended December 31,		
	2025	2024	Change
Personnel-related (including stock-based compensation)	$ 63,678	$ 42,106	$ 21,572
Professional and consultant fees	15,033	10,854	4,179
Commercial preparation and other	28,626	9,634	18,992
Total general and administrative expenses	$ 107,337	$ 62,594	$ 44,743

General and administrative expenses were $107.3 million for the year ended December 31, 2025, compared to $62.6 million for the year ended December 31, 2024. The increase in personnel-related expenses of $21.6 million was primarily due to an increase in headcount and an increase of $9.2 million in stock-based compensation expense. For the years ended December 31, 2025 and 2024, stock-based compensation expense was $38.4 million and $29.2 million, respectively. The increase in commercial preparation and other expenses of $19.0 million was primarily due to costs incurred in preparation for the potential commercial launch of our product candidates.

Other income (expense)

Change in fair value of related party revenue share liability

The change in fair value of the related party revenue share liability was $55.2 million and $17.9 million for the years ended December 31, 2025 and 2024, respectively. For the years ended December 31, 2025 and 2024, the change in fair value of the related party revenue share liability was due to changes in certain assumptions in the model used to calculate fair value such as the probability and timing of obtaining regulatory approval due to the progression of our product candidates in clinical development towards potential commercialization, and estimated future product revenues.

Interest income and other income (expense), net

Interest income and other income (expense), net for the years ended December 31, 2025 and 2024, consisted primarily of interest income of $44.8 million and $38.4 million, respectively. The increase in interest income was primarily due to an increase in cash, cash equivalents and marketable securities.

Liquidity and Capital Resources

Since our inception, we have incurred significant net losses. We have not yet commercialized any of our product candidates and our ability to generate revenue from product sales will depend heavily on the successful clinical development of, receipt of marketing

approval from regulatory authorities for, and eventual commercialization of one or more of our product candidates. Through December 31, 2025, we have funded our operations primarily with proceeds from the sales of convertible preferred stock, the issuance of convertible notes, debt financing from stockholders and proceeds from the sale of common stock in our public offerings. As of December 31, 2025, we had cash, cash equivalents and marketable securities of $1.4 billion and accounts payable and accrued expenses and other current liabilities of $91.2 million.

In November 2025, we issued and sold 4,950,496 shares of our Class A common stock in an underwritten public offering at a public offering price of $101.00 per share. We received net proceeds of $471.8 million, after deducting equity issuance costs and underwriting discounts and commissions.

The following discussion and analysis of a summary of our cash flows includes a comparison of the year ended December 31, 2025 to the year ended December 31, 2024. For the discussion and analysis that compares our summary of cash flows for the year ended December 31, 2024 to the year ended December 31, 2023, refer to Part II, Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our 2024 Form 10-K, which is incorporated herein by reference.

Cash Flows

The following table summarizes our cash flows for each of the years ended December 31, 2025 and 2024 (in thousands):

	Year Ended December 31,	
	2025	2024
Net cash used in operating activities	$ (275,209)	$ (185,064)
Net cash used in investing activities	(124,077)	(573,514)
Net cash provided by financing activities	515,340	568,882
Net increase (decrease) in cash and cash equivalents	$ 116,054	$ (189,696)

Operating activities

During the year ended December 31, 2025, operating activities used $275.2 million of cash, resulting from our net loss of $425.4 million adjusted for non-cash items, primarily stock-based compensation expense of $86.5 million, change in fair value of related party revenue share liability of $55.2 million and net accretion on marketable securities of $11.1 million, and net cash provided by changes in our operating assets and liabilities of $19.2 million. Our net loss was primarily due to clinical trial and manufacturing costs to support the development of our product candidates, personnel-related expenses due to the growth of our Company, costs related to professional services and costs incurred in preparation for the potential commercial launch of our product candidates, partially offset by interest income due to our cash, cash equivalents and marketable securities. Net cash provided by changes in our operating assets and liabilities was primarily due to increases in accounts payable and accrued expenses and other liabilities of $36.1 million, partially offset by increases in other assets and prepaid expenses and other current assets of $16.9 million.

During the year ended December 31, 2024, operating activities used $185.1 million of cash, resulting from our net loss of $260.8 million adjusted for non-cash items, including stock-based compensation expense of $60.6 million, change in fair value of related party revenue share liability of $17.9 million and net accretion on marketable securities of $14.7 million, and net cash provided by changes in our operating assets and liabilities of $11.8 million. Net cash provided by changes in our operating assets and liabilities was due to an increase in accrued expenses and other current liabilities of $26.9 million, partially offset by an increase in prepaid expenses and other current assets of $7.6 million, a decrease in accounts payable of $4.0 million, and an increase in other assets of $3.4 million.

Changes in prepaid expenses and other current assets, other assets, accounts payable, and accrued expenses and other liabilities were generally due to growth in our business, the advancement of our research and development programs and the timing of vendor invoicing and payments.

Investing activities

During the year ended December 31, 2025, net cash used in investing activities was $124.1 million, primarily due to purchases of marketable securities of $1.1 billion, partially offset by proceeds from maturities of marketable securities of $932.8 million.

During the year ended December 31, 2024, net cash used in investing activities was $573.5 million, primarily due to purchases of marketable securities of $1.0 billion, partially offset by proceeds from maturities of marketable securities of $450.5 million.

Financing activities

During the year ended December 31, 2025, net cash provided by financing activities was $515.3 million, primarily due to proceeds from an underwritten public offering of $472.5 million, net of underwriting discounts and commissions, and proceeds from the exercise of options to purchase common stock of $42.0 million.

During the year ended December 31, 2024, net cash provided by financing activities was $568.9 million, primarily due to proceeds from an underwritten public offering of $540.5 million, net of underwriting discounts and commissions, and proceeds from the exercise of options to purchase common stock of $28.8 million.

Funding Requirements

We expect to incur significant expenses in connection with our ongoing activities, particularly as we advance our preclinical, clinical, and commercialization preparation activities for our product candidates in development and any future product candidates. The timing and amount of our operating expenditures will depend largely on:

- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our discovery programs and product candidates, including the advancement of zidesamtinib, neladalkib and NVL-330 throughout clinical development;
- the clinical development plans we establish for our product candidates, including zidesamtinib, neladalkib and NVL-330;
- the number and characteristics of product candidates that we discover and develop through our product discovery and research efforts;
- the terms of any collaboration agreements we may choose to pursue;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, the European Medicines Agency and other comparable foreign regulatory authorities;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale outsourced manufacturing activities; and
- the cost of continuing to build sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own.

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $1.4 billion. We expect that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements into 2029. Our existing cash, cash equivalents and marketable securities may not be sufficient to fund all of our product candidates through regulatory approval, and we may need to raise additional capital to complete the development and commercialization of our product candidates. Our estimate as to how long we expect our existing cash, cash equivalents and marketable securities to fund our operations does not include potential product revenue and is based on assumptions that may prove to be wrong, 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 product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including those listed above.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. 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 acquisitions or capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, 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 or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Other Commitments

We have an obligation under a revenue sharing agreement with Deerfield to pay Deerfield a fixed low single-digit percentage rate of net sales of certain commercial products. We are also party to a revenue sharing agreement with our scientific founder, Matthew Shair, Ph.D., pursuant to which we were obligated to pay Dr. Shair 1.5% of net sales of certain commercial products. In December 2025, Dr. Shair assigned the revenue sharing agreement to Royalty Pharma plc (Royalty Pharma) and, as a result, any payments we are obligated to make under this agreement will be made to Royalty Pharma. See Note 10 in the notes to the consolidated financial statements included elsewhere in this Annual Report for additional information regarding our obligations under the revenue sharing agreements.

We lease office space for our corporate headquarters, which is located in Cambridge, Massachusetts. We enter into contracts in the normal course of business with our CMOs, CROs and other third parties to support research and development, commercial preparation, and other business activities. These contracts are generally terminable by us for convenience or for breach after reasonable cure periods.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Critical Accounting Policies and Significant Judgments and Estimates

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

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

Related party revenue share liability

We account for the related party revenue share liability with Deerfield at fair value. The revenue sharing agreement with Deerfield obligates us to pay a fixed low single-digit percentage rate of net sales of certain commercial products. In accordance with Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) Topic 825, *Financial Instruments*, we elected the fair value option. Each reporting period, we remeasure the liability to estimated fair value using a discounted cash flow model based on the most recent assumptions such as the probability and timing of product approval, future product revenues and discount rate. These assumptions are estimates and can change based on factors such as the progression of our product candidates in clinical development and potential commercialization, current market conditions, competition, estimated clinical benefit and pricing. Changes to these assumptions can result in a material impact to our consolidated financial statements. Changes in fair value in each reporting period are recognized as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. The estimated fair value as of December 31, 2025 and 2024 was determined to be $73.2 million and $17.9 million, respectively. We have not recorded any net sales and, as a result, have not paid any amounts under this obligation.

Accrued research and development expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of services performed and the associated cost incurred for the services when we have not yet been invoiced or otherwise notified of actual costs. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of the estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include activities with vendors in connection with preclinical and clinical development activities, CROs in connection with preclinical and clinical studies and testing, and CMOs in connection with the process development and scale up activities and the production of materials.

We base the expense recorded related to contract research, manufacturing, or other vendors on our estimates of the services received and efforts expended pursuant to the terms of the individual agreements with the CROs, CMOs, or other vendors that conduct services and supply materials. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses. While the majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met, some require advance payments. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. We record these as prepaid expenses and other current assets and other assets on our consolidated balance sheets.

Stock-based compensation

We account for our stock-based compensation awards in accordance with FASB ASC Topic 718, *Compensation — Stock Compensation* (ASC 718). We have granted stock options and restricted stock units (RSUs), both of which are subject to service-based vesting conditions, and RSUs with performance-based vesting conditions (PSUs). In accordance with ASC 718, we recognize stock-based compensation expense in the consolidated statements of operations and comprehensive loss based on a stock-based award's grant-date fair value.

We use the Black-Scholes option-pricing model to determine the fair value of stock options granted. For RSUs and PSUs, the fair value is equal to the market price of a share of our Class A common stock on the grant date. We recognize forfeitures as they occur. Stock-based compensation expense for stock awards with service-based vesting conditions is recognized on a straight-line basis based on the grant-date fair value over the associated service period of the award, which is generally the vesting period. Stock awards with service-based vesting conditions generally vest over three- or four-year service periods and stock options expire after ten years. Stock-based compensation expense for stock awards with performance-based vesting conditions is recognized on a straight-line basis over the requisite service period for each separately vesting portion of the underlying stock award when the performance-based vesting condition is deemed probable to occur. We reassess the probability of vesting at each reporting period and adjust stock-based compensation expense, if applicable, based on our probability assessment.

We record stock-based compensation expense to research and development expense or general and administrative expense based on the underlying function of the individual that was granted the stock-based compensation award. Shares issued upon stock option exercise and RSU and PSU vesting are newly-issued shares.

The assumptions used in our Black-Scholes option-pricing model for stock options are as follows:

Expected Term — As we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term, we utilize the "simplified" method, as prescribed in the SEC's Staff Accounting Bulletin No. 107, whereby the expected term equals the arithmetical average of the vesting term and the original contractual term of the stock option.

Expected Volatility — The expected volatility is based on our historical volatility and that of similar entities within our industry for periods corresponding with the expected term of the grant.

Risk-Free Interest Rate — The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant for a period that corresponds with the expected term of the grant.

Expected Dividends — The expected dividend yield is 0% as we have not historically paid, and do not expect for the foreseeable future to pay, a dividend on our common stock.

The assumptions used in our Black-Scholes option-pricing model are inherently subjective and represent management's best estimates. These assumptions involve a number of variables, uncertainties and the application of management's judgment. If any assumptions change, our stock-based compensation expense could be materially different in the future.

Stock-based compensation expense for stock awards with service-based vesting conditions was $86.5 million, $60.6 million and $25.6 million for the years ended December 31, 2025, 2024 and 2023, respectively. The performance-based vesting conditions under the PSUs have not been deemed probable to occur, and accordingly, no stock-based compensation expense has been recognized.

As of December 31, 2025, total unrecognized compensation cost, excluding unrecognized compensation costs related to PSUs, was $170.4 million, which is expected to be recognized over a weighted-average period of 2.3 years. As of December 31, 2025, total unrecognized compensation cost related to PSUs was $11.1 million, which will be recognized when the performance-based vesting conditions are deemed probable to occur.

Recently Issued Accounting Pronouncements

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

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 related to our cash, cash equivalents and marketable securities. As of December 31, 2025, we had $261.7 million in cash and cash equivalents and $1.1 billion in marketable securities classified as available-for-sale securities. We invest our excess cash in money market funds, commercial paper, corporate bonds, government and agency securities and U.S. treasury bills. We mitigate credit risk by maintaining a diversified portfolio, placing our cash with high credit quality financial institutions and limiting the amount of investment exposure as to maturity and investment type according to our investment policy. We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure.

Interest income is sensitive to changes in the general level of interest rates; however, due to the short-term maturities and low risk profiles of our investments, we do not anticipate a significant exposure to interest rate risk. A 10% change in market interest rates would not be expected to have a material impact on our financial condition or results of operations.

Item 8. Financial Statements and Supplementary Data.

NUVALENT, INC.

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Nuvalent, Inc.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Nuvalent, Inc. and subsidiary (the Company) as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2025, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2025, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2025, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2025 based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are

material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Valuation of the related party revenue share liability

As discussed in Note 4 to the consolidated financial statements, the Company's related party revenue share liability balance as of December 31, 2025 was $73.2 million. As discussed in Note 2, the revenue share liability is remeasured at the end of each reporting period using a discounted cash flow model to calculate the estimated payments that could become due following commercialization. Assumptions in the model include but are not limited to probability and timing of product approval, future product revenues and discount rate.

We identified the assessment of the valuation of the related party revenue share liability as a critical audit matter. Subjective and challenging auditor judgment and specialized skills and knowledge were required to evaluate certain assumptions used to determine the fair value of the liability. These assumptions included probability and timing of product approval, future product revenues, and discount rate. The assessment of these assumptions was challenging because they were derived from unobservable inputs. Additionally, changes to probability and timing of product approval or future product revenues could have had a significant impact on the determination of the fair value.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls related to the Company's valuation process for the related party revenue share liability, including certain controls related to management's determination of the probability and timing of product approval, future product revenues and discount rate. We evaluated the Company's probability and timing of product approval and future product revenues by comparing these assumptions to externally available publications and scientific studies for comparable products. We involved valuation professionals with specialized skills and knowledge, who assisted in evaluating the discount rate used by the Company by comparing the Company's inputs to the discount rate to publicly available data for comparable entities and assessing the resulting discount rate.

/s/ KPMG LLP

We have served as the Company's auditor since 2020.

Boston, Massachusetts
February 26, 2026

NUVALENT, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31, 2025	December 31, 2024
Assets		
Current assets		
Cash and cash equivalents	$ 261,745	$ 145,691
Marketable securities	1,110,207	972,611
Prepaid expenses and other current assets	20,474	14,146
Total current assets	1,392,426	1,132,448
Other assets	20,279	9,304
Total assets	$ 1,412,705	$ 1,141,752
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 30,158	$ 5,225
Accrued expenses and other current liabilities	61,013	48,795
Total current liabilities	91,171	54,020
Related party revenue share liability	73,160	17,940
Other liabilities	35	—
Total liabilities	164,366	71,960
Commitments and contingencies (Note 10)		
Stockholders' equity		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized; no shares issued or outstanding	—	—
Class A common stock, $0.0001 par value; 140,000,000 shares authorized; 72,804,111 shares and 65,909,564 shares issued and outstanding at December 31, 2025 and 2024, respectively	7	7
Class B convertible common stock, $0.0001 par value; 10,000,000 shares authorized; 5,435,254 shares issued and outstanding at December 31, 2025 and 2024	1	1
Additional paid-in capital	2,218,407	1,616,895
Accumulated other comprehensive income (loss)	2,353	(59)
Accumulated deficit	(972,429)	(547,052)
Total stockholders' equity	1,248,339	1,069,792
Total liabilities and stockholders' equity	$ 1,412,705	$ 1,141,752

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

NUVALENT, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2025	2024	2023
Operating expenses			
Research and development	$ 306,970	$ 217,774	$ 113,243
General and administrative	107,337	62,594	36,249
Total operating expenses	414,307	280,368	149,492
Loss from operations	(414,307)	(280,368)	(149,492)
Other income (expense)			
Change in fair value of related party revenue share liability	(55,220)	(17,940)	—
Interest income and other income (expense), net	44,735	38,316	23,273
Total other income (expense), net	(10,485)	20,376	23,273
Loss before income taxes	(424,792)	(259,992)	(126,219)
Income tax provision	585	764	—
Net loss	$ (425,377)	$ (260,756)	$ (126,219)
Net loss per share attributable to Class A and Class B common stockholders, basic and diluted	$ (5.85)	$ (3.93)	$ (2.17)
Weighted average shares of Class A and Class B common stock outstanding, basic and diluted	72,686,749	66,408,807	58,223,339
Comprehensive loss			
Net loss	$ (425,377)	$ (260,756)	$ (126,219)
Other comprehensive income (loss)			
Unrealized gains (losses) on marketable securities	2,412	(90)	525
Comprehensive loss	$ (422,965)	$ (260,846)	$ (125,694)

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

NUVALENT, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands, except share amounts)

	Class A Common Stock		Class B Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balances at December 31, 2022	51,233,701	$ 5	5,435,254	$ 1	$ 623,543	$ (494)	$ (160,077)	$ 462,978
Issuance of common stock upon public offering, net	6,160,714	1	—	—	323,533	—	—	323,534
Issuance of common stock upon exercise of stock options	1,222,294	—	—	—	13,793	—	—	13,793
Issuance of common stock under employee stock purchase plan	13,187	—	—	—	387	—	—	387
Unrealized gains on marketable securities	—	—	—	—	—	525	—	525
Stock-based compensation expense	—	—	—	—	25,563	—	—	25,563
Net loss	—	—	—	—	—	—	(126,219)	(126,219)
Balances at December 31, 2023	58,629,896	$ 6	5,435,254	$ 1	$ 986,819	$ 31	$ (286,296)	$ 700,561
Issuance of common stock upon public offering, net	5,750,000	1	—	—	540,011	—	—	540,012
Issuance of common stock upon exercise of stock options	1,518,096	—	—	—	28,834	—	—	28,834
Issuance of common stock under employee stock purchase plan	11,572	—	—	—	652	—	—	652
Unrealized losses on marketable securities	—	—	—	—	—	(90)	—	(90)
Stock-based compensation expense	—	—	—	—	60,579	—	—	60,579
Net loss	—	—	—	—	—	—	(260,756)	(260,756)
Balances at December 31, 2024	65,909,564	$ 7	5,435,254	$ 1	$ 1,616,895	$ (59)	$ (547,052)	$ 1,069,792
Issuance of common stock upon public offering, net	4,950,496	—	—	—	471,787	—	—	471,787
Issuance of common stock upon exercise of stock options and restricted stock unit vesting	1,925,600	—	—	—	42,037	—	—	42,037
Issuance of common stock under employee stock purchase plan	18,451	—	—	—	1,186	—	—	1,186
Unrealized gains on marketable securities	—	—	—	—	—	2,412	—	2,412
Stock-based compensation expense	—	—	—	—	86,502	—	—	86,502
Net loss	—	—	—	—	—	—	(425,377)	(425,377)
Balances at December 31, 2025	72,804,111	$ 7	5,435,254	$ 1	$ 2,218,407	$ 2,353	$ (972,429)	$ 1,248,339

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

NUVALENT, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2025	2024	2023
Cash flows from operating activities			
Net loss	$ (425,377)	$ (260,756)	$ (126,219)
Adjustments to reconcile net loss to net cash used in operating activities			
Stock-based compensation expense	86,502	60,579	25,563
Net accretion on marketable securities	(11,107)	(14,669)	(10,109)
Change in fair value of related party revenue share liability	55,220	17,940	—
Other non-cash	345	—	—
Changes in operating assets and liabilities			
Prepaid expenses and other current assets	(6,342)	(7,563)	644
Other assets	(10,508)	(3,408)	(1,428)
Accounts payable	24,599	(4,049)	2,169
Accrued expenses and other liabilities	11,459	26,862	9,641
Net cash used in operating activities	(275,209)	(185,064)	(99,739)
Cash flows from investing activities			
Purchases of marketable securities	(1,057,766)	(1,024,963)	(459,486)
Proceeds from maturities and sales of marketable securities	933,689	451,449	315,959
Net cash used in investing activities	(124,077)	(573,514)	(143,527)
Cash flows from financing activities			
Proceeds from issuance of common stock, net	515,722	569,987	338,480
Payments of equity issuance costs	(382)	(483)	(856)
Payments of insurance costs financed by a third-party	—	(622)	(777)
Net cash provided by financing activities	515,340	568,882	336,847
Net increase (decrease) in cash and cash equivalents	116,054	(189,696)	93,581
Cash and cash equivalents at beginning of period	145,691	335,387	241,806
Cash and cash equivalents at end of period	$ 261,745	$ 145,691	$ 335,387
Supplemental disclosure of noncash investing and financing information:			
Operating lease right-of-use asset	$ 798	$ —	$ —
Equity issuance costs	$ 336	$ 6	$ —
Insurance premium financed by a third-party	$ —	$ —	$ 1,399

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

1. Nature of Business

Nuvalent, Inc. (the "Company") is a clinical-stage biopharmaceutical company focused on creating precisely targeted therapies for patients with cancer. The Company was founded in January 2017 as a Delaware corporation. The Company is headquartered in Cambridge, Massachusetts.

The Company is subject to risks similar to those of other pre-commercial stage companies in the biopharmaceutical industry, including dependence on key individuals, the need to develop commercially viable products, competition from other companies, many of which are larger and better capitalized, the need for adequate financing to fund the development of its product candidates, the need to obtain and maintain adequate protection for the Company's intellectual property, and the impact of geopolitical events on the Company's business. There can be no assurance that the Company's research and development will be successful, that adequate protection for the Company's intellectual property will be obtained and maintained, that any product candidates will receive required regulatory approval, or that approved products, if any, will be commercially viable. Even if the Company's development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from the sale of its products.

The Company has incurred recurring losses since inception, including net losses of $425.4 million, $260.8 million and $126.2 million for the years ended December 31, 2025, 2024 and 2023, respectively. As of December 31, 2025, the Company had an accumulated deficit of $972.4 million. The Company expects to continue to generate net losses for the foreseeable future. The Company believes that its existing cash, cash equivalents and marketable securities will be sufficient to fund its operating expenses and capital expenditure requirements for at least 12 months from the date of issuance of these consolidated financial statements.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of presentation and consolidation

The Company's consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP") and under the rules and regulations of the United States Securities and Exchange Commission ("SEC"). The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Nuvalent Securities Corporation. All intercompany balances and transactions have been eliminated in consolidation. Certain prior period amounts have been reclassified to conform with current period presentation.

Use of estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of expenses during the reporting period. Due to the inherent uncertainty involved in making estimates, actual results reported in future periods may be affected by changes in these estimates. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the fair value of the related party revenue share liability, the accounting for research and development contracts, including clinical trial accruals, and valuation of equity instruments. The Company bases its estimates, assumptions, and judgments on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates as there are changes in circumstances, facts and experience. Actual results may differ from those estimates or assumptions.

Concentrations of credit risk and of significant suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. The Company's cash, cash equivalents and marketable securities may be held in accounts at financial institutions that may exceed federally insured limits. However, the Company mitigates credit risk by maintaining a diversified portfolio, placing its cash with high credit quality financial institutions and limiting the amount of investment exposure as to maturity and investment type according to its investment policy. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to significant credit risk beyond the standard credit risk associated with commercial banking relationships.

The Company is dependent on third-party vendors for the manufacturing of its product candidates. In particular, the Company relies, and expects to continue to rely, on a small number of vendors to manufacture materials and components required for the production of its product candidates. These programs could be adversely affected by a significant interruption in the manufacturing process.

Cash and cash equivalents

The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. Cash equivalents may include money market funds and marketable securities. The Company records interest income received on cash, cash equivalents, and marketable securities to other income (expense) in the consolidated statements of operations

and comprehensive loss. The Company invests its excess cash in money market funds, commercial paper, corporate bonds, government and agency securities and U.S. treasury bills.

Fair value measurements

The Company follows the provision of Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 820, *Fair Value Measurements* ("ASC 820"), which defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. ASC 820 also establishes a fair value hierarchy, which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. ASC 820 describes three levels of inputs that may be used to measure fair value:

Level 1 — quoted prices for identical assets or liabilities in active markets.

Level 2 — quoted prices for similar assets or liabilities in active markets or inputs that are observable.

Level 3 — inputs that are unobservable (for example, cash flow modeling inputs based on assumptions).

The Company's cash equivalents, marketable securities, and related party revenue share liability are carried at fair value, determined according to the fair value hierarchy described above (see Note 4).

Marketable securities

The Company accounts for marketable securities in accordance with FASB ASC Topic 320, *Investments - Debt and Equity Securities*. The Company's marketable securities are classified as available-for-sale debt securities and recorded at fair value based on inputs that are observable, either directly or indirectly, such as quoted prices for identical securities in active markets (Level 1) or quoted prices for similar securities in active markets or inputs that are observable (Level 2). At the time of purchase, the Company classifies marketable securities with maturities of three months or less as cash equivalents on the consolidated balance sheets. The Company's available-for-sale securities are classified as current assets as they are readily available to be converted to cash and for use in the Company's current operations.

Unrealized gains and losses are included as a component of accumulated other comprehensive income (loss) in the consolidated statements of stockholders' equity. Realized gains and losses are recorded to other income (expense) in the consolidated statements of operations and comprehensive loss.

When the fair value is below the amortized cost of an available-for-sale security, the Company must determine if the decline in fair value below the amortized cost basis has resulted from a credit loss or other factors. If the Company determines that the decline in fair value below the amortized cost basis is due to credit-related factors, the Company measures the credit loss and recognizes an allowance for credit losses in the consolidated balance sheet and the credit-related impairment in the consolidated statements of operations and comprehensive loss. The allowance for credit losses is measured as the amount by which the amortized cost basis exceeds the present value of expected cash flows, limited to the difference between the amortized cost basis and the security's fair value. The Company subsequently assesses whether the measurement of credit losses has increased or decreased and adjusts the allowance for credit losses with corresponding gains or losses recognized in the consolidated statements of operations and comprehensive loss. Impairments not relating to credit losses are recorded to other comprehensive income (loss).

If the Company intends to sell the available for sale security or it is more likely than not that the Company will be required to sell the security prior to the recovery of its amortized cost basis, then the allowance for the credit losses is written off and the excess of the amortized cost basis of the asset over its fair value is recorded in the consolidated statements of operations and comprehensive loss.

Fair value option for related party revenue share liability

The Company has a revenue sharing agreement with Deerfield Healthcare Innovations Fund, L.P. and Deerfield Private Design Fund IV, L.P. (collectively, "Deerfield"), each an investor in the Company, to pay a fixed low single-digit percentage rate of net sales of certain commercial products, which represents a freestanding financial instrument. In accordance with FASB ASC Topic 825, *Financial Instruments*, the Company elected the fair value option. Accordingly, the related party revenue share liability was measured at fair value upon issuance and is remeasured at the end of each reporting period with changes in fair value recognized as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. The fair value of the related party revenue share liability is estimated using a discounted cash flow model to calculate the estimated payments that could become due following commercialization. Assumptions in the model include but are not limited to the following: probability and timing of product approval, future product revenues and discount rate. The fair value measurement is based on significant inputs that are not observable in the market and thus represents a Level 3 measurement.

Research and development and clinical trial accruals

Research and development costs are expensed as incurred. These consist primarily of salaries and related costs, including stock-based compensation, for personnel engaged in research and development functions; costs incurred in connection with the advancement of the Company's discovery programs and product candidates in preclinical and clinical studies, including under agreements with contract

research organizations ("CROs"); and the cost of developing and scaling the Company's manufacturing process, including under agreements with contract manufacturing organizations, to manufacture drug substance and drug product for use in the Company's research and preclinical and clinical studies and manufacture commercial-scale validation batches in preparation for the commercial launch of the Company's product candidates that obtain regulatory approval.

Payments for such activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and may be reflected in the consolidated balance sheets as prepaid or accrued expenses. Determining the prepaid and accrued expenses balances at the end of any reporting period incorporates certain judgments and estimates by management that are based on information available to the Company including information provided by employees and vendors regarding the progress to completion of specific tasks or costs incurred.

Patent costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Stock-based compensation

The Company accounts for its stock-based compensation awards in accordance with FASB ASC Topic 718, *Compensation — Stock Compensation* ("ASC 718"). The Company has granted stock options and restricted stock units ("RSUs"), both of which are subject to service-based vesting conditions, and RSUs with performance-based vesting conditions ("PSUs"). In accordance with ASC 718, the Company recognizes stock-based compensation expense in the consolidated statements of operations and comprehensive loss based on a stock award's grant-date fair value.

The Company uses the Black-Scholes option-pricing model to determine the fair value of stock options granted. For RSUs and PSUs, the fair value is equal to the market price of a share of the Company's Class A common stock on the grant date. The Company recognizes forfeitures as they occur. Stock-based compensation expense for stock awards with service-based vesting conditions is recognized on a straight-line basis based on the grant-date fair value over the associated service period of the award, which is generally the vesting period. Stock awards with service-based vesting conditions generally vest over three- or four-year service periods and stock options expire after ten years. Stock-based compensation expense for stock awards with performance-based vesting conditions is recognized on a straight-line basis over the requisite service period for each separately vesting portion of the underlying stock award when the performance-based vesting condition is deemed probable to occur. The Company reassesses the probability of vesting at each reporting period and adjusts stock-based compensation expense, if applicable, based on its probability assessment.

The Company records stock-based compensation expense to research and development expense or general and administrative expense based on the underlying function of the individual that was granted the award. Shares issued upon stock option exercise and RSU and PSU vesting are newly-issued shares.

The assumptions used in the Company's Black-Scholes option-pricing model for stock options are as follows:

Expected Term — As the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate expected term, the Company utilizes the "simplified" method, as prescribed in the SEC's Staff Accounting Bulletin No. 107, whereby the expected term equals the arithmetical average of the vesting term and the original contractual term of the stock option.

Expected Volatility — The expected volatility is based on the historical volatility of the Company and that of similar entities within the Company's industry for periods corresponding with the expected term of the grant.

Risk-Free Interest Rate — The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant for a period that corresponds with the expected term of the grant.

Expected Dividends — The expected dividend yield is 0% as the Company has not historically paid, and does not expect for the foreseeable future to pay, a dividend on its common stock.

The assumptions used in the Company's Black-Scholes option-pricing model are inherently subjective and represent management's best estimates. These assumptions involve a number of variables, uncertainties and the application of management's judgment. If any assumptions change, the Company's stock-based compensation expense could be materially different in the future.

Net income (loss) per share

Basic net income (loss) per common share is computed by dividing net income (loss) by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) per common share is computed by dividing net income (loss) by the weighted average number of common shares outstanding for the period, including potentially dilutive common shares. For periods in which the Company reported a net loss, diluted net loss per common share is the same as basic net loss per common share, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Income taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to the provision for income taxes.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. Any resulting unrecognized tax benefits are recorded within the provision for income taxes.

Recently adopted accounting pronouncements

Effective January 1, 2025, the Company prospectively adopted Accounting Standards Update ("ASU") 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09") on an annual basis, which requires public entities to provide disclosure of specific categories in their income tax rate reconciliations, as well as disclosure of income taxes paid disaggregated by jurisdiction.

Recently issued accounting pronouncements

In November 2024, the FASB issued ASU 2024-03, *Income Statement — Reporting Comprehensive Income — Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses* ("ASU 2024-03"), which requires public entities, at annual and interim reporting periods, to disclose in a tabular format additional information about specific expense categories in the notes to the consolidated financial statements. ASU 2024-03 is effective for annual reporting periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027, with early adoption permitted. The Company does not expect the impact of the adoption of this standard to be material to its consolidated financial statements or disclosures.

In September 2025, the FASB issued ASU 2025-06, *Intangibles — Goodwill and Other — Internal-Use Software (Subtopic 350-40): Targeted Improvements to the Accounting for Internal-Use Software* ("ASU 2025-06"), which modernizes the accounting for internal use software. The standard removes references to project stages and clarifies the criteria for capitalizing software costs. ASU 2025-06 is effective for annual reporting periods beginning after December 15, 2027, and interim reporting periods within those annual reporting periods, with early adoption permitted. The Company does not expect the impact of the adoption of this standard to be material to its consolidated financial statements or disclosures.

3. Marketable Securities

The following tables provide the amortized cost and fair value of the Company's available-for-sale securities by security type (in thousands):

	December 31, 2025			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 107,889	$ 17	$ (22)	$ 107,884
Corporate bonds	772,457	2,233	(184)	774,506
Government and agency securities	207,684	340	(34)	207,990
U.S. treasury bills	19,824	3	—	19,827
	$ 1,107,854	$ 2,593	$ (240)	$ 1,110,207

	December 31, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 251,473	$ 12	$ (176)	$ 251,309
Corporate bonds	468,673	532	(588)	468,617
Government and agency securities	162,783	132	(29)	162,886
U.S. treasury bills	89,741	60	(2)	89,799
	$ 972,670	$ 736	$ (795)	$ 972,611

The following table summarizes the amortized cost and fair value of the Company's available-for-sale securities by contractual maturity (in thousands):

	December 31, 2025	
	Amortized Cost	Fair Value
Due within one year	$ 523,630	$ 524,421
Due after one year through three years	584,224	585,786
	$ 1,107,854	$ 1,110,207

There were no credit losses recorded during the years ended December 31, 2025, 2024 and 2023. Interest income for the years ended December 31, 2025, 2024 and 2023 was $44.8 million, $38.4 million and $23.3 million, respectively.

4. Fair Value Measurements

The following tables present the Company's fair value hierarchy for its assets and liabilities, which are measured at fair value on a recurring basis (in thousands):

	Fair Value Measurements at December 31, 2025			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents	$ 251,567	$ —	$ —	$ 251,567
Marketable securities:				
Commercial paper	—	107,884	—	107,884
Corporate bonds	—	774,506	—	774,506
Government and agency securities	—	207,990	—	207,990
U.S. treasury bills	—	19,827	—	19,827
	$ 251,567	$ 1,110,207	$ —	$ 1,361,774
Liabilities:				
Related party revenue share liability	$ —	$ —	$ 73,160	$ 73,160

	Fair Value Measurements at December 31, 2024			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents	$ 135,902	$ —	$ —	$ 135,902
Marketable securities:				
Commercial paper	—	251,309	—	251,309
Corporate bonds	—	468,617	—	468,617
Government and agency securities	—	162,886	—	162,886
U.S. treasury bills	—	89,799	—	89,799
	$ 135,902	$ 972,611	$ —	$ 1,108,513
Liabilities:				
Related party revenue share liability	$ —	$ —	$ 17,940	$ 17,940

Cash equivalents were valued by the Company based on quoted market prices for identical securities, which represent a Level 1 measurement within the fair value hierarchy. Commercial paper, corporate bonds, government and agency securities, and U.S. treasury bills were valued by the Company using quoted prices in active markets for similar securities, which represent a Level 2 measurement within the fair value hierarchy. During the periods presented, there were no transfers in or out of Level 3. The carrying values of the Company's accounts payable and accrued expenses and other current liabilities approximate their fair values due to the short-term nature of these liabilities.

The following table sets forth the changes in estimated fair value of the Company's related party revenue share liability for the year ended December 31, 2025, which represents a Level 3 measurement within the fair value hierarchy (in thousands):

Estimated fair value as of December 31, 2024	$ 17,940
Change in fair value	55,220
Estimated fair value as of December 31, 2025	$ 73,160

The fair value of the related party revenue share liability was estimated using a discounted cash flow model to calculate the estimated payments that could become due following commercialization. Assumptions in the model include but are not limited to the following: probability and timing of product approval, future product revenues and discount rate. Changes in fair value each reporting period are recognized as a component of other income (expense) in the consolidated statements of operations and comprehensive loss. See Note 10 for additional information regarding the revenue sharing agreement with Deerfield.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2025	2024
Accrued clinical and other research and development	$ 30,235	$ 25,555
Accrued manufacturing	10,976	11,511
Accrued employee compensation and benefits	16,935	10,452
Accrued other and other current liabilities	2,867	1,277
	$ 61,013	$ 48,795

6. Equity

In November 2025, the Company issued and sold 4,950,496 shares of its Class A common stock in an underwritten public offering at a public offering price of $101.00 per share (the "2025 Public Offering"). Upon the closing of the 2025 Public Offering, the Company received net proceeds of $471.8 million, after deducting equity issuance costs of $0.7 million in addition to underwriting discounts and commissions. In addition, the underwriters exercised their option in full to purchase an additional 742,574 shares of the Company's Class A common stock (the "Additional Shares") from Deerfield. The Company did not receive any proceeds from the sale of the Additional Shares by Deerfield.

In September 2024, the Company issued and sold 5,750,000 shares of its Class A common stock in an underwritten public offering, including the exercise in full by the underwriters of their option to purchase an additional 750,000 shares of the Company's Class A common stock, at a public offering price of $100.00 per share (the "2024 Public Offering"). Upon the closing of the 2024 Public Offering, the Company received net proceeds of $540.0 million, after deducting equity issuance costs of $0.5 million in addition to underwriting discounts and commissions.

In October 2023, the Company issued and sold 6,160,714 shares of its Class A common stock in an underwritten public offering, including the exercise in full by the underwriters of their option to purchase an additional 803,571 shares of the Company's Class A common stock, at a public offering price of $56.00 per share (the "2023 Public Offering"). Upon the closing of the 2023 Public Offering, the Company received net proceeds of $323.5 million, after deducting equity issuance costs of $0.8 million in addition to underwriting discounts and commissions.

7. Stock-Based Compensation

The Company recorded stock-based compensation expense within its consolidated statements of operations and comprehensive loss as follows (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Research and development expenses	$ 48,097	$ 31,369	$ 11,600
General and administrative expenses	38,405	29,210	13,963
	$ 86,502	$ 60,579	$ 25,563

Under the 2021 Plan (as defined below), the Company has granted stock options, RSUs and PSUs. As of December 31, 2025, total unrecognized compensation cost, excluding unrecognized compensation cost related to PSUs, was $170.4 million, which is expected to be recognized over a weighted-average period of 2.3 years. Stock-based compensation expense for PSUs is recognized on a straight-line basis over the requisite service period for each separately vesting portion of the PSUs when the performance-based vesting condition is deemed probable to occur. The performance-based vesting conditions under the PSUs have not been deemed probable to occur, and accordingly, no stock-based compensation expense has been recognized. As of December 31, 2025, total unrecognized compensation cost related to PSUs was $11.1 million, which will be recognized when the performance-based vesting conditions are deemed probable to occur.

2021 equity incentive plan

In July 2021, the Company adopted the 2021 Stock Option and Incentive Plan (the "2021 Plan"). The 2021 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, RSUs (including PSUs), unrestricted stock awards, cash-based awards and dividend equivalent rights. The number of shares of Class A common stock reserved for issuance under the 2021 Plan is subject to increase on each January 1 thereafter by 5.0% of the number of shares of the Company's Class A and Class B common stock outstanding on the immediately preceding December 31 or such lesser number of shares determined by the Company's board of directors or compensation committee of the board of directors. The shares of Class A common stock underlying any awards that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of stock, expired or are otherwise

terminated (other than by exercise) under the 2021 Plan will be added back to the shares of Class A common stock available under the 2021 Plan. As of December 31, 2025, 8,244,716 shares of Class A common stock remained available for future issuance under the 2021 Plan.

2021 employee stock purchase plan

In July 2021, the Company adopted the 2021 Employee Stock Purchase Plan (as amended and restated, the "ESPP"). The ESPP permits eligible employees to purchase shares of Class A common stock at a discount in accordance with the terms of the offering and consists of consecutive, overlapping 12-month offering periods, each consisting of two six-month purchase periods. As of December 31, 2025, 2,322,110 shares remained available for issuance and sale under the ESPP.

Stock options

The following table presents the range of assumptions used in the Black-Scholes option-pricing model to determine the grant-date fair value of stock options granted:

	Year Ended December 31,		
	2025	2024	2023
Weighted average expected option term (years)	6.0	6.0	6.0
Range of expected stock price volatility	70% — 71%	72% — 76%	76% — 82%
Weighted average expected stock price volatility	71%	75%	80%
Range of risk-free interest rate	3.7% — 4.4%	3.5% — 4.6%	3.4% — 4.7%
Expected dividend rate	0%	0%	0%

The following table summarizes the Company's stock option activity since December 31, 2024:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2024	7,980,047	$ 28.93	7.45	$ 398,407
Granted	1,544,070	$ 78.51		
Exercised	(1,672,786)	$ 25.13		
Cancelled or forfeited	(133,690)	$ 73.63		
Outstanding as of December 31, 2025	7,717,641	$ 38.90	6.90	$ 476,355
Exercisable as of December 31, 2025	4,701,612	$ 22.06	5.95	$ 369,254

The aggregate intrinsic value of stock options exercised during the years ended December 31, 2025, 2024 and 2023 was $107.6 million, $102.3 million and $52.3 million, respectively. The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock on the date of exercise.

The weighted average grant-date fair value of stock options granted during the years ended December 31, 2025, 2024 and 2023 was $51.94 per share, $53.07 per share and $23.01 per share, respectively.

RSUs

The following table summarizes the Company's RSU activity since December 31, 2024:

	Number of Shares	Weighted Average Grant-Date Fair Value
Outstanding as of December 31, 2024	716,921	$ 75.13
Granted	657,148	$ 78.05
Vested	(252,814)	$ 75.29
Forfeited	(30,139)	$ 77.97
Outstanding as of December 31, 2025	1,091,116	$ 76.77

The RSU activity above includes 141,935 of outstanding PSUs. The total fair value of RSUs vested during the year ended December 31, 2025 was $19.0 million. No RSUs vested during the years ended December 31, 2024 and 2023.

8. Net Loss Per Share

The Company has two classes of common stock outstanding: Class A common stock and Class B common stock. The rights of the holders of Class A common stock and Class B common stock are substantially identical, except with respect to voting and conversion.

Each share of Class A common stock is entitled to one vote. Class B common stock is nonvoting, and each share of Class B common stock is convertible into one share of Class A common stock at the option of the holder at any time, subject to the ownership limitations provided for in the Company's amended and restated certificate of incorporation. The Company allocates undistributed earnings attributable to common stock between the common stock classes on a one-to-one basis when computing net loss per share. As a result, basic and diluted net loss per share of Class A common stock and per share of Class B common stock are equivalent.

The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	As of December 31,		
	2025	2024	2023
Options to purchase common stock	7,717,641	7,980,047	8,034,755
RSUs	1,091,116	716,921	—
ESPP	18,400	—	—
	8,827,157	8,696,968	8,034,755

9. Income Taxes

All of the Company's net losses have been generated in the United States. The Company recognized income tax provisions of $0.6 million and $0.8 million during the years ended December 31, 2025 and 2024, respectively, as a result of investment income earned in Nuvalent Securities Corporation. The Company recognized no income tax provision during the year ended December 31, 2023.

Reconciliation of federal statutory income tax rate to effective income tax rate

The Company has elected to prospectively adopt the guidance in ASU 2023-09. The following tables present reconciliations of the U.S. federal statutory income tax rate of 21% to the Company's effective income tax rate for the years ended December 31, 2025, 2024 and 2023 (dollar values in thousands):

	Year Ended December 31, 2025	
U.S. federal statutory income tax rate	$ (89,206)	21.0%
State and local income tax, net of federal (national) income tax effect	585	(0.1)%
Foreign tax effects	—	—%
Effect of changes in tax laws or rates enacted in the current period	—	—%
Effect of cross-border tax laws	—	—%
Tax credits		
Orphan drug credit	(27,137)	6.4%
R&D credit	1,061	(0.3)%
Changes in valuation allowances	114,819	(27.0)%
Nontaxable or nondeductible items		
Section 162(m) limitation	12,316	(2.9)%
Stock-based compensation	(12,413)	2.9%
Permanent adjustments	113	—%
Changes in unrecognized tax benefits	—	—%
Other adjustments	447	(0.1)%
Effective income tax rate	$ 585	(0.1)%

	Year Ended December 31,	
	2024	2023
U.S. federal statutory income tax rate	21.0%	21.0%
State income taxes, net of federal benefit	6.7%	8.3%
Tax credits generated	14.3%	5.7%
Change in deferred tax asset valuation allowance	(45.8)%	(38.7)%
Stock-based compensation	3.6%	3.5%
Other	(0.1)%	0.2%
Effective income tax rate	(0.3)%	—%

During the years ended December 31, 2025, 2024 and 2023, the Company recorded no income tax benefits for the net operating losses incurred or for the research and development tax credits generated in each year, due to its uncertainty of realizing a benefit from those items.

Net deferred tax assets

Net deferred tax assets consisted of the following (in thousands):

	December 31,	
	2025	2024
Deferred tax assets:		
Net operating loss carryforwards	$ 139,120	$ 56,677
Capitalized research and development	103,127	94,002
Research and development tax credit carryforwards	82,361	52,117
Change in fair value of related party revenue share liability	19,284	4,785
Stock-based compensation	14,225	9,705
Other, net	4,648	2,714
Total gross deferred tax assets	362,765	220,000
Valuation allowance	(362,495)	(220,000)
Total net deferred tax assets	270	—
Deferred tax liabilities:		
Other	(270)	—
Total gross deferred tax liabilities	(270)	—
Net deferred tax assets	$ —	$ —

As of December 31, 2025, the Company had U.S. federal and state net operating loss carryforwards of $503.2 million and $531.1 million, respectively, which may be available to offset future taxable income. The federal net operating losses include $1.2 million which expire in 2037 and $502.0 million which carryforward indefinitely, but may only be used to offset 80% of annual taxable income. The state net operating losses expire at various dates beginning in 2037. As of December 31, 2025, the Company also had federal and state research and development tax credit carryforwards of $14.6 million and $14.1 million, respectively, and federal orphan drug credits of $56.5 million, which may be available to offset future tax liabilities. The federal and state research and development tax credit carryforwards and the federal orphan drug credits expire at various dates beginning in 2033.

Utilization of the U.S. federal and state net operating loss carryforwards, as well as the research and development tax credit carryforwards and federal orphan drug credits may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986 ("IRC"), and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income or tax liabilities. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards, research and development tax credit carryforwards or the federal orphan drug credits would be subject to an annual limitation under Section 382. Any limitation may result in expiration of a portion of the net operating loss carryforwards, research and development tax credit carryforwards or the federal orphan drug credits before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

Valuation allowance

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the net deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and that the Company has yet to commercialize any of its product candidates to generate revenue from product sales and has concluded that it is more likely than not that the Company will not realize the benefits of the net deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2025 and 2024. Management reevaluates the positive and negative evidence at each reporting period.

The valuation allowance increased by $142.5 million, $119.1 million and $48.8 million during the years ended December 31, 2025, 2024 and 2023, respectively, primarily as a result of increases in net operating loss carryforwards, research and development tax credit carryforwards, the change in fair value of related party revenue share liability and research and development costs capitalized under Section 174 of the IRC.

Unrecognized tax benefits and tax examinations

As of December 31, 2025 and 2024, the Company had not recorded any amounts for unrecognized tax benefits. The Company files income tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company is open to future tax examination under statute from 2022 to the present.

10. Commitments and Contingencies

Revenue sharing agreements

The Company has a revenue sharing agreement with Deerfield pursuant to which the Company is obligated to pay Deerfield a fixed low single-digit percentage rate of net sales of certain commercial products (the "Deerfield Revenue Sharing Agreement"). The Company is also party to a revenue sharing agreement with its scientific founder pursuant to which the Company was obligated to pay the scientific founder 1.5% of net sales of certain commercial products (the "Scientific Founder Revenue Sharing Agreement" and together with the Deerfield Revenue Sharing Agreement, the "Revenue Sharing Agreements"). In December 2025, the scientific founder assigned the Scientific Founder Revenue Sharing Agreement to Royalty Pharma plc ("Royalty Pharma") and, as a result, any payments the Company is obligated to make under the Scientific Founder Revenue Sharing Agreement will be made to Royalty Pharma.

Under the Revenue Sharing Agreements, the payment obligation in respect of such products expires on the later of 12 years from the first commercial sale in a country or the expiration of the last-to-expire patent in that country. The Company accounts for the liability with Deerfield at fair value with changes recognized in the consolidated statements of operations and comprehensive loss (see Note 4). The Company accounts for the obligation to Royalty Pharma as a contingent liability and has not accrued any liability as of December 31, 2025 or 2024. The Company has not recorded any net sales and, as a result, has not paid any amounts under the Revenue Sharing Agreements.

Indemnification agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, CROs, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and its executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. The Company has not incurred any material costs as a result of such indemnifications and is not currently aware of any indemnification claims.

11. Segment Information

The Company is a clinical-stage biopharmaceutical company and has not generated any revenue since commencing significant operations in 2018. The Company's operations are organized and reported as one reportable segment, which includes all activities related to the discovery, development, and commercialization of precisely targeted therapies for patients with cancer. This presentation is consistent with how the Company's chief operating decision maker ("CODM"), its Chief Executive Officer, assesses the performance of the Company and makes operating decisions on a consolidated basis. The accounting policies of the consolidated segment are the same as those described in the summary of significant accounting policies (see Note 2). The CODM assesses performance and decides how to allocate resources based on consolidated net loss as reported on the consolidated statements of operations and comprehensive loss. The CODM uses consolidated net loss to monitor budget versus actual results, assess cash runway, and benchmark against the Company's competitors. The measure of segment assets is reported on the consolidated balance sheets as total assets. The Company's assets are held in the United States.

The following table sets forth the Company's segment information (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Direct external expenses by program:			
Zidesamtinib	$ 59,519	$ 62,110	$ 27,878
Neladalkib	105,446	67,778	31,894
NVL-330	21,819	8,293	10,634
Discovery programs	11,875	9,178	8,586
Personnel-related expenses	73,163	44,121	29,225
Stock-based compensation expense	86,502	60,579	25,563
General and administrative professional and consultant fees	15,033	10,854	6,423
Change in fair value of related party revenue share liability	55,220	17,940	—
Interest income	(44,794)	(38,372)	(23,277)
Other segment items[(1)]	41,009	17,511	9,293
Income tax provision	585	764	—
Consolidated net loss	$ (425,377)	$ (260,756)	$ (126,219)

[1] Other segment items included in consolidated net loss include expenses for commercialization preparation activities, research and development consulting services, information technology, insurance, employee recruitment and other miscellaneous activities.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our President and Chief Executive Officer and our Chief Financial Officer (our principal executive officer and principal financial and accounting officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2025. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of December 31, 2025, our President and Chief Executive Officer and our Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control-Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, management concluded that, as of December 31, 2025, our internal control over financial reporting was effective.

Our independent registered public accounting firm, KPMG LLP, which audited the consolidated financial statements included in this Annual Report, has issued an attestation report on our internal control over financial reporting, which is included herein.

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) during the three months ended December 31, 2025, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Director and Officer Trading Arrangements

The following table describes for the quarterly period ended December 31, 2025, each trading arrangement for the sale or purchase of Company securities adopted or terminated by our directors and officers that is either (1) a contract, instruction or written plan intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) (a Rule 10b5-1 trading arrangement) or (2) a "non-Rule 10b5-1 trading arrangement" (as defined in Item 408(c) of Regulation S-K):

Name (Title)	Action Taken (Date of Action)	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
Alexandra Balcom *(Chief Financial Officer)*	Adoption *(December 23, 2025)*	Rule 10b5-1 trading arrangement	Sale	Until December 11, 2026, or such earlier date upon which all transactions are completed or expire without execution	Up to 128,000 shares of Class A common stock
Henry Pelish *(Chief Scientific Officer)*	Adoption *(December 11, 2025)*	Rule 10b5-1 trading arrangement	Sale	Until November 30, 2027, or such earlier date upon which all transactions are completed or expire without execution	Up to 116,306 shares of Class A common stock
James Porter *(Chief Executive Officer)*	Adoption *(December 4, 2025)*	Rule 10b5-1 trading arrangement	Sale	Until March 10, 2027, or such earlier date upon which all transactions are completed or expire without execution	Up to 390,000 shares of Class A common stock
Anna Protopapas *(Director)*	Adoption *(December 7, 2025)*	Rule 10b5-1 trading arrangement	Sale	Until March 31, 2027, or such earlier date upon which all transactions are completed or expire without execution	Up to 20,000 shares of Class A common stock

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

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information concerning our executive officers is set forth under the heading "Information about our Executive Officers" in Item 1 of this Annual Report on Form 10-K. The remaining information required by this Item 10 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders, which, for the avoidance of doubt, does not include the information required by Item 402(v) of Regulation S-K, and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2026 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) The financial statements, financial statement schedules, and exhibits filed as part of this Annual Report are as follows:

1. Financial Statements

See "Index to Consolidated Financial Statements" beginning on page 106 of this Annual Report.

2. Financial Statement Schedules

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

3. Exhibits

The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report are listed in the Exhibit Index immediately preceding the signature page of this Annual Report. The exhibits listed in the Exhibit Index are incorporated by reference herein.

Item 16. Form 10-K Summary.

Not applicable.

Exhibit Index.

Exhibit Number	Description of Exhibit	Form	File No.	Exhibit	Filing Date	Filed Herewith
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant	8-K	001-40671	3.1	6/16/2023	
3.2	Amended and Restated Bylaws of the Registrant	10-K	001-40671	3.2	3/16/2023	
4.1	Specimen Class A Common Stock Certificate	S-1	333-257730	4.1	7/7/2021	
4.2	Specimen Class B Common Stock Certificate	S-1	333-257730	4.2	7/7/2021	
4.3	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, effective as of April 30, 2021	S-1	333-257730	4.3	7/7/2021	
4.4	Description of Securities Registered Under Section 12 of the Exchange Act	10-K	001-40671	4.4	3/29/2022	
10.1#	2021 Stock Option and Incentive Plan and forms of award agreements thereunder	S-1/A	333-257730	10.2	7/26/2021	
10.2#	Revised Form of Restricted Stock Unit Award Agreement under 2021 Stock Option and Incentive Plan	10-K	001-40671	10.2	2/27/2024	
10.3#	Form of Restricted Stock Unit Award Agreement (Performance-Vesting) under 2021 Stock Option and Incentive Plan	8-K	001-40671	99.1	12/9/2024	
10.4#	Amended and Restated 2021 Employee Stock Purchase Plan	10-Q	001-40671	10.1	8/10/2022	
10.5#	Form of Indemnification Agreement between the Registrant and each of its directors	S-1	333-257730	10.4	7/7/2021	
10.6#	Form of Indemnification Agreement between the Registrant and each of its executive officers	S-1	333-257730	10.5	7/7/2021	
10.7#	Senior Executive Cash Incentive Bonus Plan	S-1	333-257730	10.6	7/7/2021	
10.8#α	Form of Executive Employment Agreement, as amended	10-Q	001-40671	10.2	11/12/2024	
10.9#	Non-Employee Director Compensation Policy	10-Q	001-40671	10.1	5/9/2024	
10.10#	Employment Agreement, by and between the Registrant and James R. Porter, effective August 2, 2021	S-1	333-257730	10.9	7/7/2021	
10.11#	Amendment to Employment Agreement by and between the Registrant and James R. Porter, dated as of November 5, 2024	10-Q	001-40671	10.1	11/12/2024	
10.12†	Amended and Restated Revenue Sharing Agreement, by and between the Registrant and Matthew Shair, effective as of February 2, 2017	S-1	333-257730	10.11	7/7/2021	
10.13†	Amended and Restated Revenue Sharing Agreement, by and between the Registrant, Deerfield Healthcare Innovations Fund, L.P. and Deerfield Private Design Fund, IV, L.P., effective as of February 2, 2017	S-1	333-257730	10.12	7/7/2021	
10.14	Sales Agreement, by and between the Registrant and Cowen and Company, LLC, effective as of August 10, 2022	S-3	333-266731	1.2	8/10/2022	
10.15	Amendment No. 1 to the Sales Agreement with Cowen and Company, LLC, effective as of October 31, 2022	8-K	001-40671	1.2	11/1/2022	

Exhibit Number	Description of Exhibit	Form	File No.	Exhibit	Filing Date	Filed Herewith
19.1	Amended and Restated Insider Trading Policy					X
21.1	Subsidiaries of the Registrant	10-K	001-40671	21.1	3/29/2022	
23.1	Consent of KPMG LLP, independent registered public accounting firm					X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1+	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2+	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
97.1	Nuvalent Inc. Dodd-Frank Compensation Recovery Policy	10-K	001-40671	97.1	2/27/2024	
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document					
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Document					
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)					

# Indicates a management contract or any compensatory plan, contract or arrangement.

α Nuvalent, Inc. has entered into an Executive Employment Agreement, as amended, with each of Alexandra Balcom, Deborah Miller, Darlene Noci, Henry E. Pelish and Christopher D. Turner.

† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with Item 601(b)(10) of Regulation S-K.

+ The certifications furnished in Exhibits 32.1 and 32.2 hereto are deemed to be furnished with this Annual Report on Form 10-K and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

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.

NUVALENT, INC.

Date: February 26, 2026

By: /s/ James R. Porter
James R. Porter, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ James R. Porter James R. Porter, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	February 26, 2026
/s/ Alexandra Balcom Alexandra Balcom	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 26, 2026
/s/ Grant Bogle Grant Bogle	Director	February 26, 2026
/s/ Michael L. Meyers Michael L. Meyers, M.D., Ph.D.	Director	February 26, 2026
/s/ Christy Oliger Christy Oliger	Director	February 26, 2026
/s/ Joseph Pearlberg Joseph Pearlberg, M.D., Ph.D.	Director	February 26, 2026
/s/ Anna Protopapas Anna Protopapas	Director	February 26, 2026
/s/ Ron Squarer Ron Squarer	Director	February 26, 2026
/s/ Sapna Srivastava Sapna Srivastava, Ph.D.	Director	February 26, 2026
/s/ Cameron A. Wheeler Cameron A. Wheeler, Ph.D.	Director	February 26, 2026

BOARD OF DIRECTORS

Grant C. Bogle
Former President and CEO,
Epizyme

Michael L. Meyers, MD, PhD
Former CMO,
Flare Therapeutics

Christy Oliger
Former SVP, Oncology,
Genentech

Joseph Pearlberg, MD, PhD
VP of Scientific Affairs,
Deerfield Management

James R. Porter, PhD
President and CEO,
Nuvalent

Anna Protopapas
Former President and CEO,
Mersana Therapeutics

Ron Squarer
Former CEO,
Array Biopharma

Sapna Srivastava, PhD
Former Interim CFO,
eGenesis Bio

Cameron A. Wheeler, PhD
Partner,
Deerfield Management

Annual Meeting of Stockholders

The 2026 annual meeting of stockholders will be held on Tuesday, June 16, 2026 at 2:00 p.m. Eastern Time online at: www.virtualshareholdermeeting.com/NUVL2026

Stock Listing

Nasdaq: NUVL

Independent Auditors

KPMG LLP

SEC Form 10-K

A copy of Nuvalent's Form 10-K filed with the Securities and Exchange Commission is available free of charge from Nuvalent's Investor Relations Department by calling (857) 357-7000, emailing ir@nuvalent.com or sending a written request to:

Investor Relations, Nuvalent
One Broadway 14th Floor
Cambridge, MA 02142

Transfer Agent

The transfer agent is responsible, among other things, for handling stockholder questions regarding stock ownership, address changes, including duplicate mailings, and changes in ownership or name in which shares are held. These requests may be directed to the transfer agent at the following address:

Computershare Trust Company, N.A.
150 Royall Street, Suite 101
Canton, MA 02021

www-us.computershare.com/Investor/#Contact

Nuvalent

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