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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 001-42504

SIONNA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**84-2801521**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
21 Hickory Drive, Suite 500, Waltham, MA	**02451**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(617) 819-2020**

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value per share	SION	The Nasdaq Global 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 ☒
As of June 30, 2025, the last business day of the registrant's most recently completed second quarter, the aggregate market value of the registrant's common stock held by nonaffiliates of the registrant, based on the closing price of the shares of common stock on the Nasdaq Global Market on June 30, 2025, was approximately $342,014,009.

The number of shares of registrant's common stock outstanding as of February 20, 2026 was 44,998,073.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A relating to the 2026 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2025. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (the "Annual Report") contains forward-looking statements about us and our industry that involve substantial risks and uncertainties, and which are made pursuant to the safe harbor provisions of 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"). All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, product candidates, preclinical studies and clinical trials, results of preclinical studies and clinical trials, research and development costs, regulatory approvals, commercial strategy, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements involve known and unknown risks, uncertainties and other important factors that are in some cases beyond our control and may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. Forward-looking statements contained in this Annual Report include, but are not limited to, statements about:

- the initiation, timing, progress and results of our research and development programs, preclinical studies and clinical trials;
- the ability of clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results, and the ability of our earlier clinical trials and preclinical studies to predict later clinical trial results;
- the timing, scope and likelihood of regulatory filings and approvals of our product candidates;
- the implementation of our business model, and strategic plans for our business, programs, and current and future product candidates;
- our ability to obtain additional cash and the sufficiency of our existing cash, cash equivalents and investments in marketable securities to fund our future operating expenses and capital expenditure requirements;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our potential and ability to successfully manufacture and supply our current and future product candidates for clinical trials and for commercial use, if approved;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- developments relating to our competitors and our industry, including competing product candidates and therapies;
- existing regulations and regulatory developments in the U.S. and other jurisdictions, including changes in U.S. federal policy, such as trade policies or tariffs;
- expectations regarding future events under collaboration and licensing agreements, including potential future payments, as well as our plans and strategies for entering into further collaboration and licensing agreements;
- general economic, industry and market conditions, including elevated interest rates and inflation;

- our ability to attract and retain the continued service of our key personnel and to identify, hire and then retain additional qualified personnel;

- our expectations regarding the period during which we will qualify as an emerging growth company under the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"); and

- our anticipated use of our existing cash, cash equivalents and investments in marketable securities.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions described in the section entitled “Risk Factors” and elsewhere in this Annual Report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely upon these statements.

You should read this Annual Report and the documents that we reference herein or incorporated by reference as exhibits hereto with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

NOTE REGARDING TRADEMARKS

Sionna Therapeutics, Inc. is the owner of the trademarks SIONNA and SIONNA THERAPEUTICS, as well as certain other trademarks, including design versions of some of these trademarks. The symbols ™ and ® are not used in connection with the presentation of these trademarks in this Annual Report and their absence does not indicate a lack of trademark rights. Certain other trademarks used in this Annual Report are the property of third-party trademark owners and may be presented with or without trademark references.

All brand names or trademarks appearing in this Annual Report are the property of their respective owners. Unless the context requires otherwise, references in this report to “Sionna,” the “Company,” “we,” “us” and “our” refer to Sionna Therapeutics, Inc. and its subsidiary.

SUMMARY OF MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

We are subject to numerous risks and uncertainties, including those further described below in the section entitled “Risk Factors” in this Annual Report, as well as in other documents that we file with the U.S. Securities and Exchange Commission (“SEC”). The following considerations, among others, may offset our competitive strengths or have a negative effect on our business strategy, which could materially adversely affect our business, financial conditions, results of operations and future growth prospects:

- We are a clinical-stage biopharmaceutical company and have incurred significant operating losses since inception and anticipate that we will continue to incur significant operating losses for the foreseeable future.
- We will need to raise substantial additional funding. We may be unable to raise capital on acceptable terms, if at all, and, as a result, we may be required to delay, reduce or eliminate our product development programs or future commercialization efforts.
- We are substantially dependent on the success of at least one of our nucleotide binding domain 1 ("NBD1") stabilizers. If we are unable to advance an NBD1 stabilizer product candidate into later-stage clinical development or unable to obtain regulatory approval and commercialize a product candidate, or experience significant delays in doing so, our business will be materially harmed.
- Targeting the NBD1 domain of the cystic fibrosis transmembrane conductance regulator protein is novel, and the time, cost of development and likelihood of successful product development is difficult to predict.
- We intend to develop a proprietary dual combination of an NBD1 stabilizer with a complementary modulator, and/or an NBD1 stabilizer as an add-on to the standard of care. Developing combination treatments increases complexity and risk, including risks of drug-drug interactions, unforeseen side effects or failures in our clinical trials that could delay or prevent their regulatory approval or limit the commercial profile of an approved label.
- We may incur additional costs and experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- Positive results from our preclinical studies or prior clinical trials are not necessarily predictive of the results of later clinical trials of our current or future product candidates. If we cannot replicate the positive results from our earlier preclinical studies or clinical trials of our current or potential future product candidates, or if we suffer any other significant setbacks in our later clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our current or potential future product candidates.
- Our preclinical studies and clinical trials may fail to demonstrate the safety and efficacy of our product candidates, or serious or unacceptable adverse side effects or unexpected toxicology findings may be identified during the development of our product candidates, which could prevent or delay further clinical development, regulatory approvals and commercialization, impact the product’s labeling, if approved, increase our costs or necessitate the abandonment or limitation of the development of some of our product candidates.
- We rely, and in the future expect to rely, on third parties to conduct our ongoing and planned clinical trials for our current and future product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, or if we experience delays or difficulties in the initiation of, or enrollment of patients in, clinical trials, obtaining necessary regulatory approvals could be delayed or prevented.
- The regulatory approval processes of the U.S. Food and Drug Administration and comparable foreign authorities are lengthy, time-consuming and inherently unpredictable. If we are not able to obtain the required regulatory approval for any product candidate, our business will be substantially harmed.
- We may not be successful in our efforts to identify or discover additional product candidates, or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

- We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing our product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.

- We contract with third parties for the manufacture of our product candidates for clinical drug supply and expect to continue to do so for commercialization, if our product candidates are approved. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

- If we or our licensors are unable to obtain, maintain and enforce intellectual property rights relating to any of our product candidates, or if the scope of the protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, our ability to successfully commercialize our product candidates may be adversely affected and we may not be able to compete effectively in our markets.

- We face substantial competition. Our main competitor in the CF market holds substantial market share and has substantially greater resources than we do. We may not be able to compete successfully in this environment and, in particular, against a much larger competitor.

- The trading price of the shares of our common stock may be volatile, and investors could lose all or part of their investment.

The summary risk factors described above should be read together with the text of the full risk factors in the section titled “Risk Factors” and the other information set forth in this Annual Report, including our audited consolidated financial statements and the related notes, as well as in other documents that we file with the SEC. The risks summarized above or described in full elsewhere in this Annual Report are not the only risks that we face. Additional risks and uncertainties not presently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

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PART I

ITEM 1. BUSINESS

Overview

We are a clinical-stage biopharmaceutical company on a mission to revolutionize the current treatment paradigm for cystic fibrosis ("CF") by developing novel medicines that normalize the function of the cystic fibrosis transmembrane conductance regulator ("CFTR") protein to deliver clinically meaningful benefit to people with CF. CF is a progressive and life-threatening genetic disease caused by inherited mutations in the CFTR gene, which lead to insufficient CFTR function. While advances in the discovery and development of CFTR modulators have significantly improved the lives of people with CF, at least two-thirds of patients on the current standard of care do not have normal CFTR function, defined as sweat chloride levels below 30 mmol/L. Patients with reduced CFTR function can experience debilitating multi-system complications that lead to significantly impaired quality of life and shorter life expectancy. Our goal is to deliver differentiated medicines for people with CF that can restore their CFTR function to as close to normal as possible by directly stabilizing CFTR's nucleotide binding domain 1 ("NBD1"). Despite having long been identified as a critical component for proper CFTR function, NBD1 has been considered "undruggable," and none of the currently approved CF therapies directly stabilizes NBD1. Leveraging more than a decade of our co-founders' research on NBD1, we are advancing a pipeline of small molecules engineered to correct the defects caused by the F508del genetic mutation, the most common CFTR mutation, which occurs in the NBD1 domain. Approximately 90% of people with CF carry at least one copy of the F508del genetic mutation.

We believe stabilizing NBD1 is central to unlocking dramatic improvements in clinical outcomes and quality of life for people with CF. The NBD1 domain of the CFTR protein, as illustrated in Figure 1 below, plays a key role in the folding, assembly, stability and trafficking of CFTR to a cell's surface, where it normally functions as an ion channel to regulate chloride and water transport. Within the NBD1 domain, F508del severely destabilizes CFTR, disrupting its proper assembly, impairing half-life and decreasing chloride channel function. We have employed biophysical, cell-based and virtual screening campaigns and extensive use of structural biology to guide the optimization of our novel small molecule NBD1 stabilizers. We are also advancing a portfolio of complementary CFTR modulator candidates designed to work synergistically with our NBD1 stabilizers to improve CFTR function, as seen in preclinical models.

We believe our robust pipeline provides multiple potential pathways to achieve our mission, either through development of an NBD1 stabilizer and a complementary modulator in combination with each other to produce a proprietary dual combination, or an NBD1 stabilizer administered in combination with the standard of care for CF. While we have prioritized development of a proprietary dual combination, we believe both development pathways offer attractive commercial opportunities.

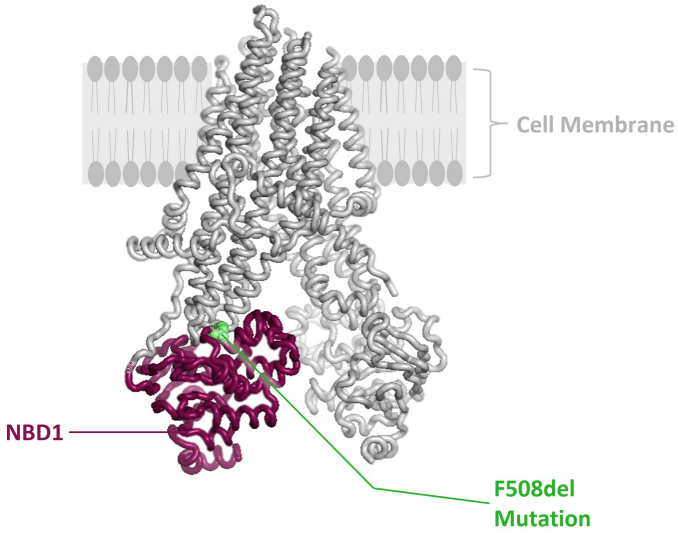


Figure 1

Our Pipeline

The following table summarizes our clinical stage pipeline:

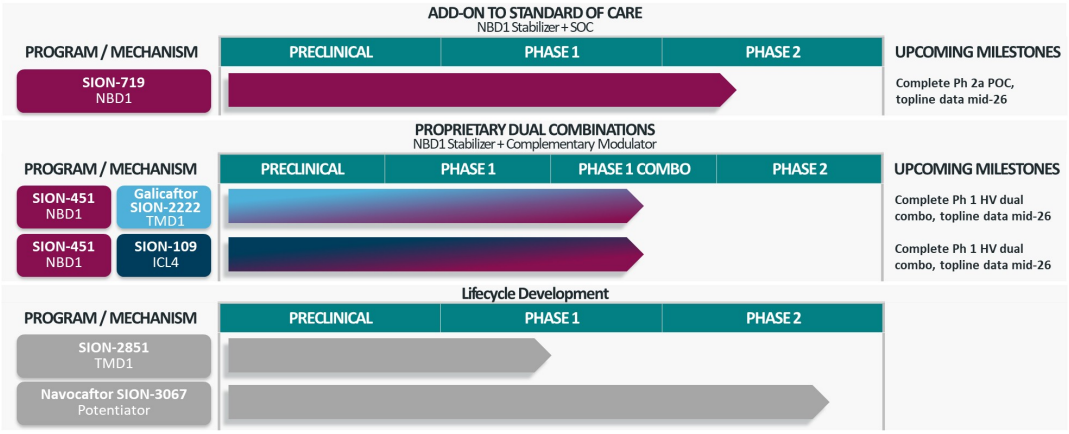


Figure 2

Our proprietary portfolio is anchored by our NBD1 stabilizers and our complementary modulators. Our portfolio includes:

- **SION-719, which is being evaluated as an add-on to the standard of care**: SION-719, a highly potent NBD1 stabilizer, is currently in a Phase 2a proof-of-concept trial in CF patients, called PreciSION CF. The trial is evaluating SION-719 when administered with the standard of care for CF, Vertex Pharmaceuticals, Inc.'s ("Vertex") Trikafta. Topline data from this trial is anticipated in mid-2026. In June 2025, we announced positive topline data from a Phase 1 trial of SION-719, which evaluated its pharmacokinetic ("PK") profile, safety and tolerability in healthy volunteers.

- **SION-451, which is being evaluated in combinations with SION-2222 and SION-109**: SION-451, a highly potent NBD1 stabilizer, is currently being evaluated in dual combinations with each of galicaftor (SION-2222) and SION-109, two of our complementary modulators, in a Phase 1 trial in healthy

volunteers. Topline data from this trial is anticipated in mid-2026. In June 2025, we announced positive topline data from the single agent portion of the Phase 1 trial, which evaluated SION-451's PK profile, safety and tolerability in healthy volunteers.

- **SION-2222**, a corrector that targets CFTR's transmembrane domain 1 ("TMD 1"), was generally well tolerated in Phase 1 and Phase 2 trials previously conducted by AbbVie Global Enterprises Ltd. ("AbbVie"). Improvement in sweat chloride as a monotherapy and improvements in sweat chloride and lung function as a combination therapy with navocaftor (SION-3067), a potentiator, were observed.

- **SION-109**, a corrector that targets CFTR's intracellular loop 4 ("ICL4") region, has been evaluated in a Phase 1 clinical trial in healthy volunteers, which was completed in 2024.

- **Additional complementary modulators**: We have additional CFTR modulators in our portfolio. SION-2851, a TMD1-directed CFTR corrector, has completed a Phase 1 single-ascending dose ("SAD") trial in healthy volunteers. SION-3067, a potentiator, has been evaluated in Phase 2 trials, where it demonstrated potential as a combination therapy.

Our pipeline of product candidates target distinct binding sites across the CFTR structure, as depicted in Figure 3 below:

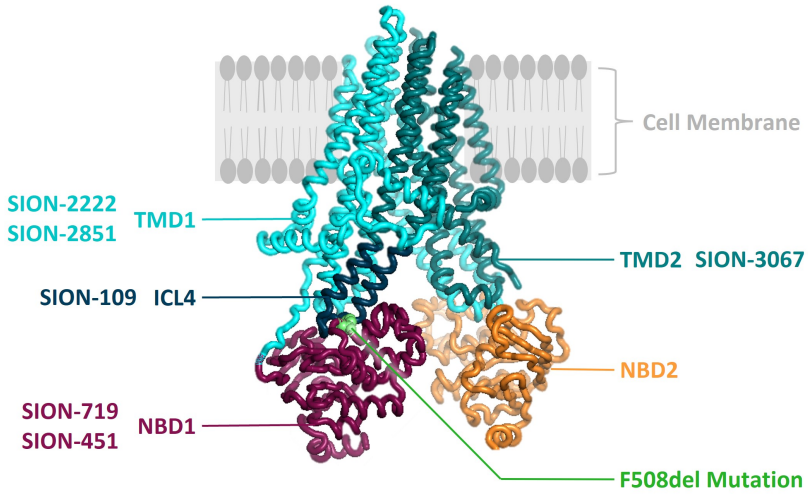


Figure 3

Our Strategy

Our mission is to revolutionize the current treatment paradigm for CF by developing novel medicines that normalize the function of the CFTR protein to deliver clinically meaningful benefit to people with CF. The key pillars of our strategy are:

- **Advance our novel NBD1 stabilizers leveraging a data-driven approach**. Leveraging the differentiated profiles of SION-719 and SION-451, we have advanced both product candidates to the next phase of development. Figure 4 below presents our strategy for the advancement of SION-719 and SION-451, focusing on distinct development pathways.

- **Develop and advance our pipeline of complementary modulators for proprietary combination product development**. We are developing a proprietary pipeline of complementary CFTR modulators designed to work synergistically with our NBD1 stabilizers to improve CFTR function, as seen in preclinical models.

- **Fortify our CF franchise through continued research efforts and utilization of the translational CFHBE model**. Central to our development strategy is our use of the industry standard, clinically predictive preclinical cystic fibrosis human bronchial epithelial ("CFHBE") model to measure CFTR function. The CFHBE model has been highly predictive of clinical outcomes for approved CFTR modulators, and our application of the model provides a key translational roadmap for us to prioritize compounds for further evaluation. We believe the model allows us to determine the target exposure needed to achieve a desired level of clinical activity, such as the level of improvement in a patient's forced expiratory volume in one second ("FEV_{1}"), a measure of lung function, and sweat chloride level, the clinical biomarker of CFTR function. We intend to invest in research activities and leverage insights from the model in our pursuit of delivering additional differentiated product candidates that meaningfully impact the lives of people with CF and facilitate our company's long-term growth. We also intend to opportunistically consider strategic in-licensing opportunities to maximize the value of our pipeline.

- **Expand and protect our intellectual property estate**. We have developed a broad patent estate and expect to expand and protect our proprietary know-how and intellectual property.

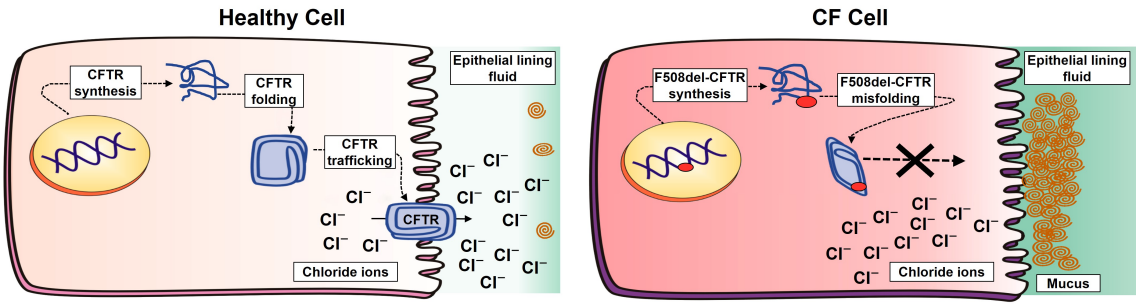
Figure 4

Overview of Cystic Fibrosis, CFTR Function and the F508del Mutation

An estimated 106,000 people have been diagnosed with CF across 94 countries, which includes approximately 40,000 adults and children living with this disease in the U.S., according to the Cystic Fibrosis Foundation ("CFF"). About 1,000 new CF cases are diagnosed every year in the U.S. While life expectancy for people with CF has improved significantly over the years since the first CFTR modulator was approved, the median predicted survival age for individuals with CF born in the U.S. between 2020 and 2024 is still just 65 years, according to the 2024 CFF patient registry. The majority of people who have been diagnosed with CF live in the U.S., the United Kingdom and Europe. CF is the most common fatal inherited disease in the U.S., and it can affect people of every racial and ethnic group.

CF is caused by mutations to the CFTR gene that result in reduced or no function of the CFTR protein. The disease is autosomal recessive, meaning that two copies of a CFTR mutation are required to cause the disease: either two copies of the same mutation ("homozygous") or two different mutations ("heterozygous"). The most common CFTR mutation is F508del, which is a deletion of the amino acid phenylalanine at position 508, which is in NBD1; approximately 90% of people with CF carry at least one copy of the F508del mutation, and approximately 44% of people with CF are homozygous for F508del. The F508del mutation is considered a severe CF mutation, and individuals with this mutation tend to fall at the worst end of the CF severity spectrum because they have little or no CFTR function in epithelial cells.

The CFTR protein is found on the apical membrane, or surface, of epithelial cells throughout the body, including in the lungs, pancreas, sweat glands, biliary tract and intestines. The CFTR protein is critical for proper salt and water balance in the cell, which drives production of freely flowing mucus for tissue hydration in the airways, digestive system and other organs. In people with CF, mutations in the CFTR gene cause the CFTR protein to become dysfunctional. When the CFTR protein is not working properly, chloride—a component of salt—gets trapped in cells, as illustrated in Figure 5. Without chloride to attract water to the cell surface, thick mucus accumulates in vital organs such as the lungs, pancreas and gastrointestinal tract and causes multisystem complications, including respiratory infections, chronic lung inflammation, poor nutrient absorption and often progressive respiratory failure, which is the primary cause of death in people with CF.



*(Figure 5. **Source:** Favia, 2019)*

As illustrated in Figure 6, the CFTR protein includes two nucleotide binding domains (NBD1 and NBD2) and two transmembrane domains (TMD1 and TMD2). The transmembrane domains form the ion channel across an epithelial cell's membrane. The nucleotide binding domains facilitate the ion channel's opening and closing by binding and hydrolyzing adenosine triphosphate. There are also four intracellular loops that link the nucleotide binding domains to the transmembrane domains and are important to regulating ion channel gating.

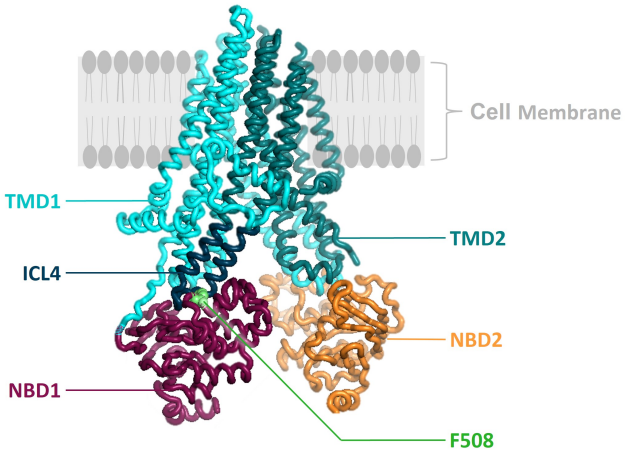


Figure 6

The F508del mutation occurs in the NBD1 domain near an interface with the fourth intracellular loop, ICL4, which is particularly critical to the folding of CFTR. When the ICL4 interface is disrupted, as it is by the F508del mutation, CFTR can neither fold nor function properly. The F508del mutation severely destabilizes CFTR's NBD1 domain, preventing normal folding and trafficking of CFTR to a cell's surface and impairing chloride channel function. Support for NBD1 as a key target is based in part on in vitro studies that introduced mutations at other sites on NBD1 that suppressed the effect of the F508del mutation.

Current Unmet Need and Market Opportunity

While advances in the treatment of CF have improved the lives of people with the disease and resulted in a large commercial market, we believe significant opportunity remains to provide clinically meaningful benefit to people with CF through the development of NBD1-anchored treatments. NBD1 has long been considered an important target to normalize CFTR function because it is the site where the F508del mutation—the most common mutation that causes CF—occurs. However, attempts by others to stabilize NBD1 have fallen short, leading to the view that NBD1 is "undruggable." The current standard of care for CF, Trikafta, and Alyftrek, which

was approved in December 2024, are each made up of three components that target certain domains of CFTR, but not NBD1.

At least two-thirds of patients on Trikafta do not have normal CFTR function, defined as sweat chloride levels below 30 mmol/L. Even treated CF patients can continue to experience the ongoing effects of reduced CFTR function over time, including respiratory infections, pulmonary exacerbations, or “lung attacks,” and continued lung function decline. More than 6,000 patients have discontinued use of approved CFTR modulators, none of which target NBD1. Additionally, some patients on Trikafta reduce dosages due to tolerability issues, including elevated liver function tests and mental health effects such as mood disturbances, depression, and mental fogginess. In December 2024, the Trikafta label was updated to include a boxed warning for the risks of drug-induced liver injury and liver failure, and the Alyftrek label includes the same boxed warning. Seven to eight percent of patients on Trikafta have experienced significant mental health effects, and depression, including suicidal ideation and attempt, is listed in the warnings and precautions section of the summary of product characteristics for Kaftrio, the brand name for Trikafta in Europe. Patients who discontinue use of Trikafta or experience tolerability challenges have limited or no alternative treatments available to improve their clinical outcomes or quality of life.

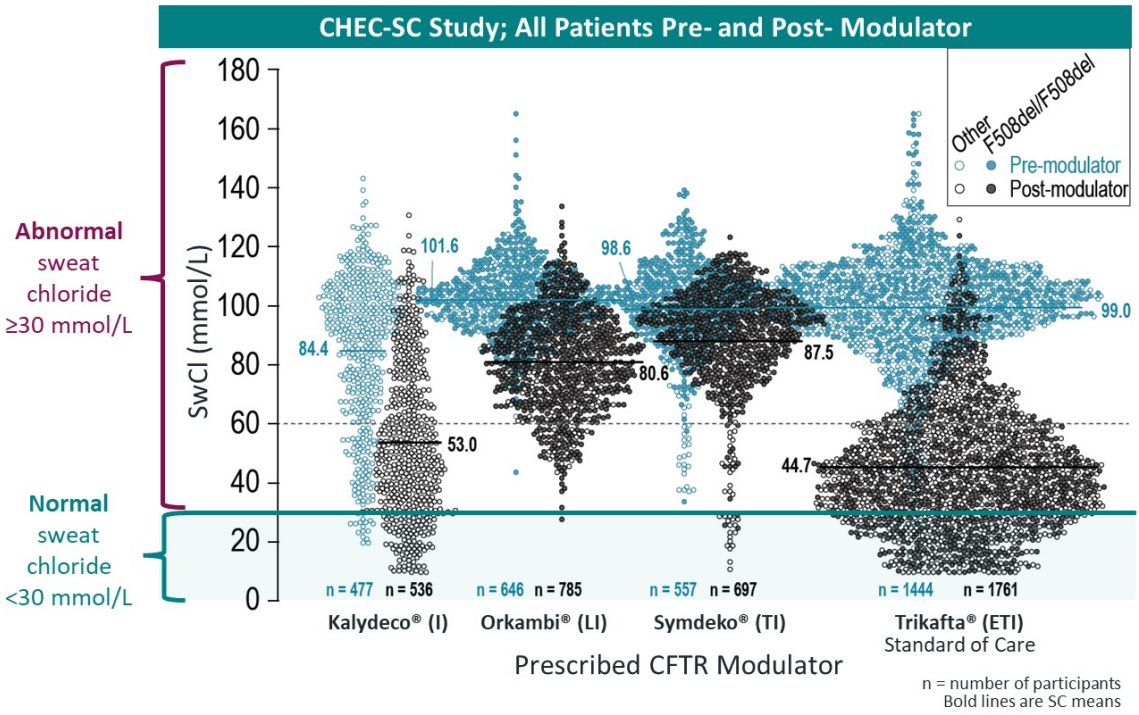
Current treatment alternatives for these patients are limited to less efficacious combination products that include one or more components of Trikafta, or Alyftrek. In two Phase 3 clinical trials, Alyftrek demonstrated non-inferiority to Trikafta in the primary endpoint, providing participants with similar FEV_1 to Trikafta and sweat chloride level improvements of approximately 3 to 8 mmol/L. In participants who were homozygous for the F508del mutation, the sweat chloride improvement observed was approximately 3 mmol/L. Across both trials, approximately 69% of Alyftrek patients did not achieve normal CFTR function. Our research with key opinion leaders has indicated the desire for more treatment options for people with CF, particularly in support of a new mechanism of action that could provide clinically meaningful benefit or an alternative for those patients who experience tolerability issues on Trikafta.

Worldwide revenue for approved CFTR modulators was approximately $12 billion in 2025, and it is expected to grow to over $15 billion by 2030. CF screening of newborn infants has served to identify CF patients as early as possible in their lives. For example, newborn screening for CF has been required in the U.S. since 2010, and in 2024, 55.8% of newly diagnosed people with CF in the U.S. were identified by newborn screening, based on CFF registry data. The availability of CFTR modulators has also increased the use of genetic testing to determine eligibility for treatment.

Current Standard of Care and its Limitations

The approved CFTR modulators are oral small molecule therapies that improve CFTR function either by potentiating channel gating or by improving cellular processing and trafficking of the CFTR protein. The current standard of care for people with the F508del mutation is a triple combination product marketed by Vertex as Trikafta (elexacaftor, tezacaftor, ivacaftor and ivacaftor). In addition, in December 2024, Vertex received approval from the U.S. Food and Drug Administration (“FDA”) for a second-generation, triple modulator combination, Alyftrek, for the treatment of CF in patients who have at least one F508del mutation or another responsive mutation in the CFTR gene. Vertex also markets three other approved CFTR modulators. None of the approved modulators directly stabilize NBD1.

Despite the clinical benefits Trikafta provides CF patients, including improved lung function and quality of life, at least two-thirds of people with CF being treated on Trikafta or another approved CFTR modulator do not have normal CFTR function. CF progression is most commonly assessed through a patient’s mean lung function, as measured by FEV_1 improvement. In addition, sweat chloride level, the clinical biomarker of CFTR function, has been used for decades as a diagnostic test for CF and has served as a highly useful tool in the development of approved CFTR modulators. A sweat chloride level greater than or equal to 60mmol/L indicates that CF is likely, while a sweat chloride level under 30 mmol/L is normal and indicates that CF is unlikely. Sweat chloride levels between 30 mmol/L and 59 mmol/L are considered abnormal, indicating partial CFTR dysfunction or “residual function” in diagnostic settings. An observational study of 3,131 individuals with CF from the CFF Registry found that, while treatment with Trikafta resulted in improvements in sweat chloride level to below 60 mmol/L in most patients, two-thirds of patients still had sweat chloride levels above normal levels (Figure 7).



(Figure 7. Sweat chloride levels less than or equal to 29 mmol/L indicate that CF is unlikely; levels of 30 - 59 mmol/L indicate that CF is possible and additional testing is needed; and levels greater than or equal to 60 mmol/L indicate that CF is likely.)

Two-year interim data from a five-year post-marketing real-world observational trial of patients taking Trikafta showed that mean rates of pulmonary exacerbations and the presence of bacterial pathogens improved but were not normalized after initiating treatment on Trikafta. The three-year interim data, presented at the European CF Society meeting in Glasgow in 2024, showed numerical increases in mean rates of pulmonary exacerbations and decreases in mean lung function compared to the two-year interim data, supporting the opportunity for clinical improvements over the standard of care. In addition to continued pulmonary complications, patients also experienced negative mental health side effects, including numerical increases in rates of depression, anxiety disorder and hypertension after initiating treatment on Trikafta. Another side effect associated with ivacaftor (a component of Trikafta) is cataracts, which can complicate use and requires monitoring, especially in children. In addition, both the Trikafta and Alyftrek labels include a boxed warning for the risks of drug-induced liver injury and liver failure.

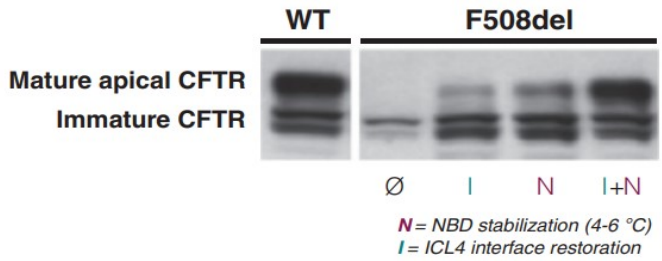
Alyftrek demonstrated non-inferiority to Trikafta in the primary endpoint of two Phase 3 clinical trials, providing patients with similar FEV_1 as Trikafta and sweat chloride level improvements of approximately 3 to 8 mmol/L. In participants who were homozygous for the F508del mutation, the sweat chloride improvement observed was approximately 3 mmol/L. Across both trials, approximately 69% of Alyftrek patients did not achieve normal CFTR function. These results support our beliefs that NBD1 stabilization is required to meaningfully improve upon the standard of care and that a high unmet need remains for an alternative therapy that can provide clinically meaningful benefit to CF patients.

Research Findings Support NBD1 as a Key Target for Stabilizing F508del-CFTR

Multiple studies by third parties have concluded that NBD1 is a key drug target for correcting the F508del mutation, including in vitro studies that introduced mutations at other sites on NBD1 that suppressed the effect of the F508del mutation. For example, researchers at Utrecht University and University of Texas

Southwestern Medical Center identified a second site NBD1 mutation ("I539T") that rescued the misfolding and instability of F508del-CFTR. They concluded the "co-translational rescue of F508del NBD1 misfolding in CFTR by I539T advocates this domain as the most important drug target for cystic fibrosis."

At University of Texas Southwestern Medical Center, University of Alabama Birmingham, and McGill University, a second group of researchers identified additional mutations that suppressed the effect of F508del and which, in in vitro studies, stabilized NBD1 and the NBD1-ICL4 interface and fully restored F508del-CFTR maturation and function to wild-type levels, as shown in the western blot in Figure 8. A western blot is an assay that uses gel electrophoresis to separate a mixture of proteins, which are then transferred to a solid membrane, and then an antibody is used to detect a specific protein in the sample. The mature apical CFTR band is seen with wild-type CFTR. Partial restoration is observed with NBD1 stabilization and ICL4 interface restoration individually; full restoration of CFTR function occurred in the presence of both NBD1 and ICL4 suppressor mutations. Without a suppressor mutation, no F508del-CFTR is produced (Ø).



(Figure 8. **Source:** Thibodeau, 2010)

Research Findings Link Further Improvements in CFTR Function to Improved Clinical Outcomes

Clinical evidence obtained by third parties has illustrated that further reductions in sweat chloride, the clinical biomarker of CFTR function, towards wild-type levels, are associated with improved clinical outcomes, even for patients who have already experienced some benefits from an approved modulator therapy. According to a trial published in the New England Journal of Medicine, when CF patients heterozygous for F508del and a "gating" mutation were switched from Kalydeco, which does not target F508del, to Trikafta, which targets F508del, they experienced significant improvements in CFTR function, as measured by improvements in the mean sweat chloride levels, and in mean lung function, as measured by FEV_1. Patients with a gating mutation represent approximately 6% of the CF patient population. Their mean sweat chloride level at baseline was 50.9 mmol/L. After eight weeks of treatment with Trikafta, the patients' mean sweat chloride level was 32.7 mmol/L, representing an improvement of approximately 20 mmol/L, and their mean lung function level, as measured by FEV_1, improved by 5.8 percentage points.

Our Approach and Leveraging the CFHBE Model

Our programs leverage an industry standard, clinically predictive CFHBE model to measure CFTR protein function in vitro. The CFHBE model uses lung cells from people with CF and has been highly predictive of clinical outcomes for approved CFTR modulators. Activity in the CFHBE model has been shown to be correlated to chloride transport activity, which in turn, has been shown to be correlated to improved lung function in clinical trials designed to evaluate product candidates in CF patients. We have used, and plan to continue to use, insights from the CFHBE model to identify active compounds, predict potential clinical exposures, and inform critical pipeline prioritization and development decisions. For example, we selected SION-719 and SION-451 to advance based on their preclinical profiles, including potency in the CFHBE model. In preclinical studies using the CFHBE model, we evaluated our NBD1 stabilizers in several combinations (including SION-719 with the components of Trikafta (elexacaftor/tezacaftor/ivacaftor, or "ETI"), and SION-451 with each of SION-2222 and SION-109) in direct comparison to ETI alone, with all compounds at their respective highest effective dose ("E_{max}"), and observed a marked improvement in CFTR protein activity of more than 1.5-fold relative to ETI alone. We believe that we can leverage the reproducible correlation between chloride transport at different drug exposure levels in the CFHBE model and clinical outcomes to predict the target level of exposure to achieve clinically meaningful benefit in CF patients.

The CFHBE model uses electrophysiology to evaluate CFTR function by measuring CFTR protein activity in an Ussing Chamber, which is commonly used in CF drug discovery efforts. In this model, human bronchial cells derived from the lungs of CF patients are cultured in a manner to resemble the lung epithelium and to increase their numbers. These cultured cells are then placed in the Ussing Chamber, which uses electrodes to measure ion movement across the membranes of the cultured epithelial cells grown into a monolayer with tight junctions. Cultured CFHBE cells exhibit many of the structural and functional attributes believed to be associated with CF airway disease.

Vertex has successfully applied a variation of the CFHBE model with 20% human serum for multiple CFTR modulators advanced to clinical trials, including their five approved modulators, and has demonstrated that increased chloride transport in the CFHBE model is strongly correlated with improved CFTR function in CF patients. Importantly, the CFHBE model provided key preclinical data on CFTR function to support the clinical evaluation of elexacaftor as part of Trikafta. Based on publications detailing Vertex's use of the CFHBE model, we believe we conducted our CFHBE model using similar methods and under similar experimental conditions to those Vertex employed. Similar to Vertex, in our model, cell culture media is supplemented with human serum to 20% by volume to estimate the amount of free drug available to engage CFTR in CFHBE cells. This adjustment is designed to simulate the in vivo environment, where much of a drug is bound to serum proteins and not available to enter epithelial cells.

We conduct detailed dose-response studies in our CFHBE model to estimate the level of clinical improvement we believe we can achieve with our modulators at specific levels of drug exposure in clinical trials. The addition of human serum helps correct for the high levels of protein binding that are characteristic of our modulators, similar to approved modulators, which we believe enables our model to more accurately predict the clinical exposure required for efficacy. Our CFHBE model accurately predicted the required total plasma concentration of lumacaftor (a component of Orkambi) at its efficacious clinical exposures, as shown in Figure 9 below. We compared lumacaftor's CFTR-dependent chloride transport activity in two CFHBE model variants—with 20% human serum (like our model) and without 20% human serum—and benchmarked these against published Phase 2 clinical results regarding sweat chloride levels for lumacaftor. Figure 9 shows that the predicted lumacaftor dose response, as depicted by the red line, closely matched lumacaftor's clinical dose response, as depicted by the black line. The CFHBE model without 20% human serum, depicted by the blue line, failed to accurately predict the clinical exposure of lumacaftor required for efficacy, even if adjusted for lumacaftor's measured free fraction in human plasma, depicted by the dotted green line.

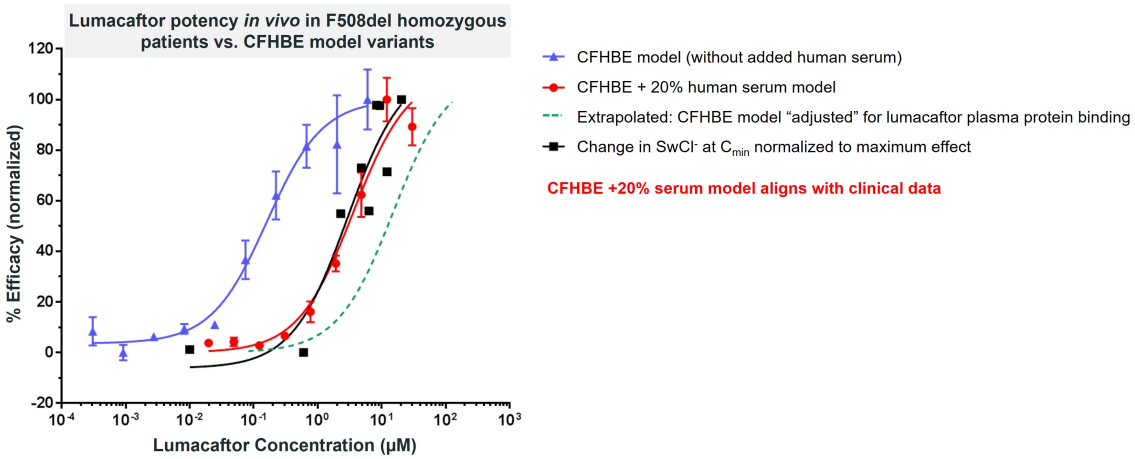


Figure 9

Using published data from the clinical trials of Vertex's approved CFTR modulators, we have validated internally our CFHBE model by assessing the relationship between in vitro CFTR protein function, as measured by chloride transport in our CFHBE model, and the mean sweat chloride levels seen in Vertex's clinical trials of these approved modulators.

As shown in Figure 10 below, improvements in CFTR function we observed in our CFHBE model for approved and investigational CFTR modulators have been highly correlated with improvements in sweat chloride measurements from clinical trials for these therapies. Notably, we have used the CFHBE model to predict negative clinical trial outcomes, too. For example, we modeled other third-party modulators previously in development and independently determined that these compounds had insufficient activity to demonstrate target clinical efficacy, which was supported by published clinical trial data.

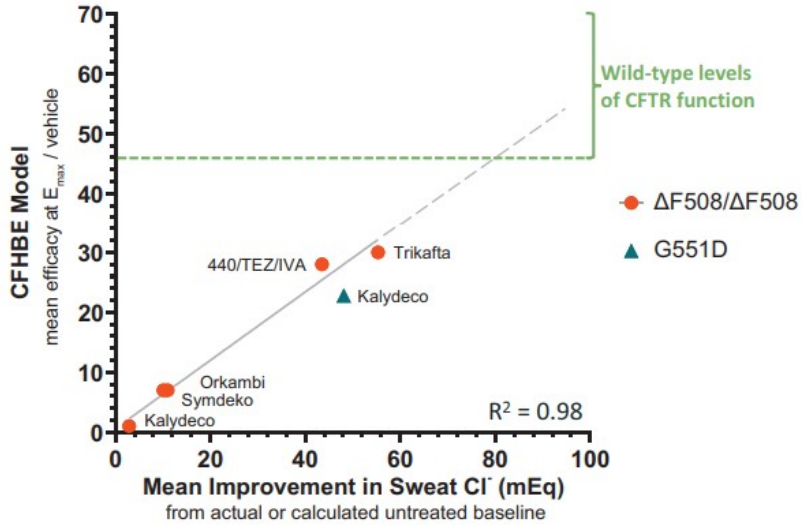


Figure 10

Mean improvements in sweat chloride levels in clinical trials have been shown to be correlated with mean improvements in lung function as measured by FEV_1, as shown in Figure 11 below.

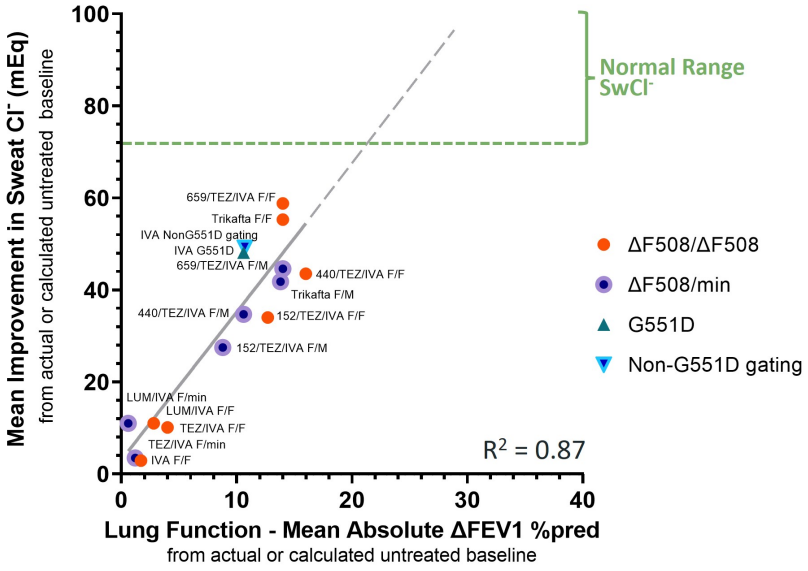


Figure 11

We consider our CFHBE model a translational roadmap because of its ability to correlate with sweat chloride improvement in clinical trials, as seen in Figure 10 above, which in turn has been shown to correlate to improved lung function in clinical trials, as shown in Figure 11 above. We have observed this correlation with our CFHBE data and clinical lung function data for approved and investigational CFTR modulators that demonstrated activity in clinical trials, including SION-2222 and SION-3067, as shown in Figure 12 below.

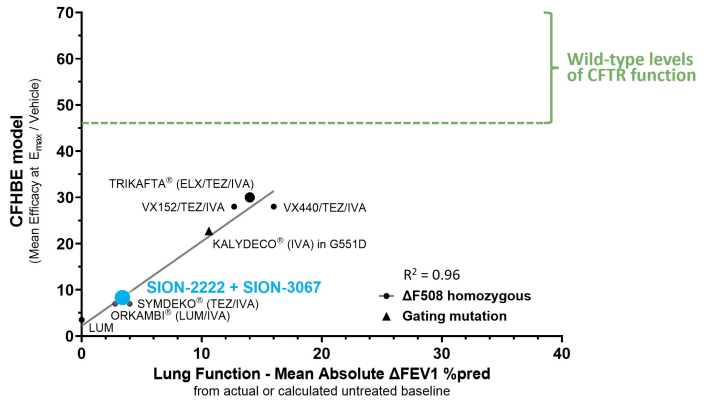


Figure 12

We believe our CFHBE model allows us to predict the target exposure needed for our product candidates to achieve a desired level of clinical activity, such as the level of improvement in patients' lung function, as measured by FEV_1 improvement, and sweat chloride levels. We have tested our product candidates in the CFHBE model at E_{max} and generated a prediction of sweat chloride and FEV_1 changes, based on the documented correlation, observed in clinical trials of approved and investigational modulators, between improvements in sweat chloride levels and improvements in lung function. We believe that the CFTR function improvement observed in our CFHBE model of our product candidates has the potential to translate clinically to deliver clinically meaningful benefit to CF patients.

Our CF Programs

We have a portfolio of NBD1 stabilizers and complementary modulators that target other regions of the CFTR protein, with the goal of advancing a combination therapy that has the potential to deliver clinically meaningful benefit to CF patients. We believe our robust pipeline provides multiple potential pathways to achieve our goal, either through development of an NBD1 stabilizer and a complementary modulator in combination with each other to produce a proprietary dual combination, or an NBD1 stabilizer administered in combination with the standard of care for CF. Leveraging the differentiated profiles of our two lead NBD1 stabilizer product candidates observed in their respective Phase 1 trials, we have advanced both SION-451 and SION-719 to the next phase of development.

NBD1 Stabilizer Program

NBD1 is recognized as a key target in treating CF patients with the F508del mutation, as the mutation drives NBD1 instability and defects in its interface assembly. However, NBD1 has presented significant challenges as a drug target due to the attributes of the region's binding sites. Our NBD1 program builds on more than a decade of our cofounders' research, which has combined biophysical, cell-based and virtual screening campaigns, along with extensive use of structural biology. We believe the technical challenge associated with NBD1-targeted drug discovery, along with our intellectual property rights, represent a substantial competitive barrier.

SION-719 — Clinical Data

Phase 2a PreciSION CF Trial

In October 2025, we announced the initiation of our ongoing Phase 2a proof-of-concept trial in CF patients, called PreciSION CF, which is evaluating SION-719 when added to the current standard of care. The

trial is designed to evaluate the safety, tolerability, and PK of SION-719 when administered with Trikafta, and to assess change in CFTR function as measured by sweat chloride levels. The trial is a two-way crossover trial anticipated to enroll approximately 16 participants with CF who are stable on physician-prescribed Trikafta. All participants will be randomly allocated to one of two trial arms and will continue taking Trikafta throughout the trial. Participants in "Arm A" will first receive Trikafta in combination with SION-719 for 14 days, and, after a 28-day washout period, will then receive Trikafta in combination with placebo for 14 days. Participants in "Arm B" receive the same treatments in reverse order, followed by a 28-day safety follow-up period. We expect topline data from the PreciSION CF trial in mid-2026.

Phase 1 Single Agent Trial of SION-719

In June 2025, we announced positive topline data from a randomized, double blind, placebo-controlled Phase 1 clinical trial of SION-719 in healthy participants. The trial was designed to evaluate the safety, tolerability and PK profile of single and multiple ascending doses ("MAD") of SION-719, administered as an oral suspension. In a Part C of the Phase 1 trial, we evaluated the effect of food on PK and the bioequivalence of a tablet formation compared to the oral suspension used in the Phase 1 SAD and MAD trials.

A total of 100 healthy adult participants were dosed in this Phase 1 trial. The trial was designed to enroll eight participants, randomized 3:1 active:placebo, to each dosing cohort. SAD cohorts evaluated single doses ranging from 20 mg to 160 mg in a fasted state; 20 mg taken with food was also evaluated in a SAD cohort to provide a preliminary assessment of the effect of food on PK. Five MAD cohorts evaluated doses ranging from 20mg to 160mg dosed twice daily ("BID") over ten dosing days. Twenty participants were dosed in the open-label food effect and tablet bioequivalence part evaluating 30 mg and 120 mg single doses each of suspension (fasted), tablet (fasted), and tablet (fed).

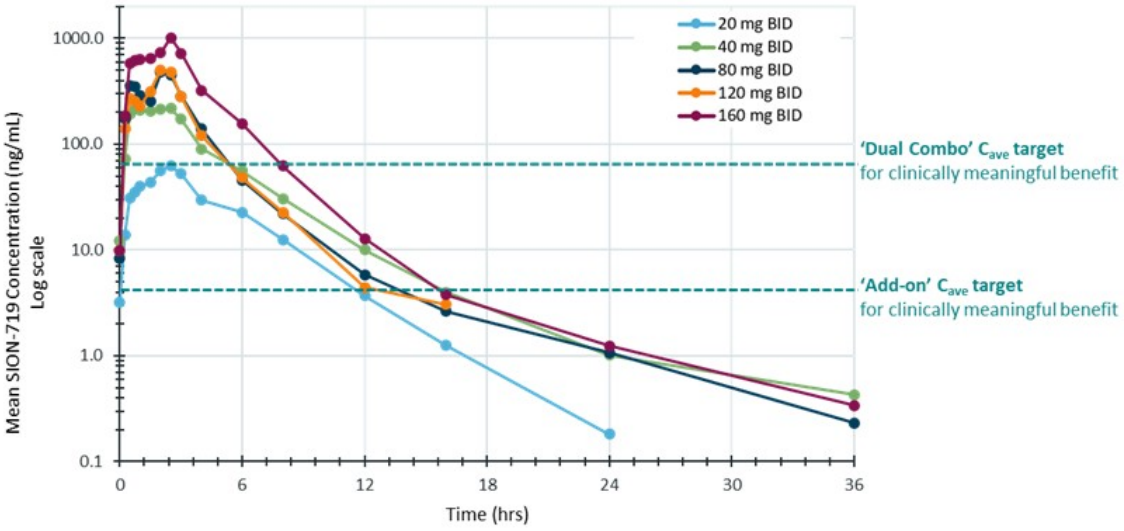
SION-719 was generally well tolerated at all dose levels administered in all parts of this Phase 1 trial. A summary table of reported treatment emergent adverse events ("TEAEs") is shown in Figure 13 below. There were no serious adverse events ("SAEs"), and most TEAEs were mild to moderate (Grade 1 or Grade 2). No TEAEs led to the discontinuation of trial drug, and no dose-limiting TEAEs were observed. The most common TEAEs, occurring in >2 participants, were headache, diarrhea, and nausea. There were no TEAEs related to liver function tests in SION-719 treated patients. There were no clinically meaningful, treatment-emergent trends in other safety parameters, vital signs or electrocardiograms. The data from Part C support the use of a tablet formulation in future trials and indicate that SION-719 can be dosed in a fed or fasted state.

Study Participants (n)*	Placebo BID *(n=10)*	20 mg BID *(n=6)*	40 mg BID *(n=6)*	80 mg BID *(n=6)*	120 mg BID *(n=6)*	160 mg BID *(n=6)*	MAD Total *(n=40)*
Any TEAE, n (%)	**4 (40)**	**2 (33)**	**4 (67)**	**6 (100)**	**5 (83)**	**3 (50)**	**24 (60)**
Mild (Grade 1)	3 (30)	2 (33)	3 (50)	5 (83)	2 (33)	3 (50)	18 (45)
Moderate (Grade 2)	1 (10)	-	2 (33)	1 (17)	3 (50)	1 (17)	8 (20)
Severe (Grade 3)	-	-	-	-	-	-	-
Life-threatening (Grade 4)	-	-	-	-	-	-	-
Leading to treatment discontinuation	-	-	-	-	-	-	-
Serious TEAEs, n (%)	-	-	-	-	-	-	-
Most frequent TEAEs (≥2 subjects), n (%)							
Headache	-	-	4 (67)	1 (17)	2 (33)	2 (33)	9 (23)
Diarrhea	1 (10)	1 (17)	-	-	-	2 (33)	4 (10)
Nausea	1 (10)	-	1 (17)	-	-	1 (17)	3 (8)
Catheter site phlebitis	-	-	-	-	2 (33)	-	2 (5)
Pruritus	1 (10)	-	-	-	-	1 (17)	2 (5)

(Figure 13. Safety observations in the SAD and Part C portions of the trial were generally consistent with the MAD findings shown.)

Increasing exposure was observed with increasing single and multiple doses. The concentration targets for SION-719 as an add-on to the standard of care and as part of a dual combination with SION-2222 or SION-109 were achieved with single and multiple doses.

The PK of SION-719 observed in the Phase 1 trial was consistent with BID dosing, and is summarized in Figure 14 below.



(Figure 14. Each solid line shows mean concentration data from a dosing cohort on Day 10. Dotted lines represent average PK concentration exposure targets that have the potential, based on our preclinical CFHBE model, to provide clinically meaningful benefit, if SION-719 is administered in a proprietary dual combination with either SION-2222 or SION-109, or as an add-on to the standard of care. PK observations in the SAD and Part C portions of the trial were generally consistent with the MAD findings shown.)

Following completion of this Phase 1 trial, we evaluated the achieved clinical exposures of SION-719 in our CFHBE model with a fixed concentration of ETI, to assess SION-719's potential as an add-on to ETI. As shown in the CFHBE model, and depicted in Figure 15, at the clinical exposures achieved in the lower dose range of SION-719, SION-719 in combination with ETI has the potential to improve CFTR channel activity above our minimum target for clinically meaningful benefit, including up to wild-type levels. In Figure 15, CFTR activity in the model is expressed as a ratio relative to ETI at E_{max}, which is set at a reference value of 1.00. Based on these findings, we believe that SION-719, when added to standard of care, has the potential to provide clinically meaningful benefit to CF patients.

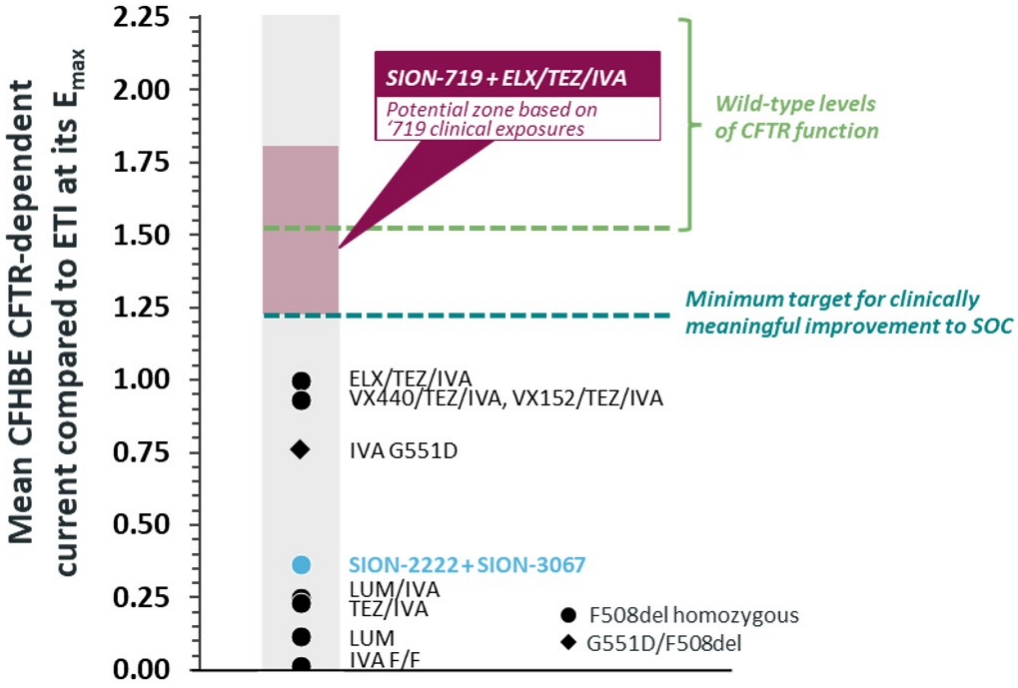


Figure 15

SION-451 — Clinical Data

Phase 1 Dual Combination Trial

In August 2025, we announced the initiation of a Phase 1 dual combination trial in healthy volunteers evaluating SION-451 in dual combinations with each of SION-2222 and SION-109, two of our complementary CFTR modulators. The trial is designed to evaluate the safety, tolerability, and PK of varying doses of the dual combinations and will inform selection of a dual combination for further development. We expect topline data from the trial in mid-2026.

Phase 1 Single Agent Trial

In June 2025, we announced positive topline data from the single-agent portion of a randomized, double blind, placebo-controlled Phase 1 clinical trial of SION-451 in healthy participants. The trial was designed to evaluate the safety, tolerability and PK profile of single and multiple ascending doses of SION-451, administered as an oral suspension. In Part C of the Phase 1 trial, we evaluated the effect of food on PK and the bioequivalence of a tablet formation compared to the oral suspension used in the Phase 1 SAD and MAD trials.

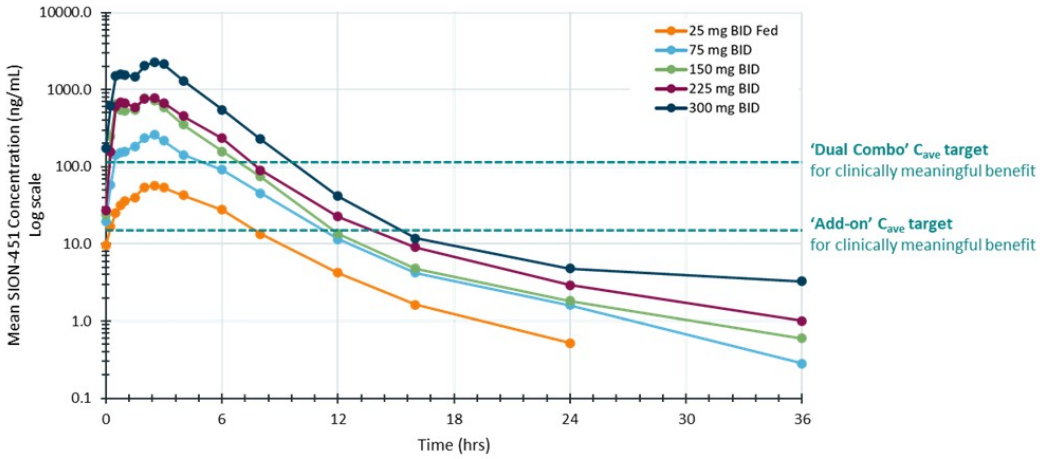
One hundred and ten total healthy adult participants were dosed in the single-agent portion of this Phase 1 trial. The trial was designed to enroll eight participants, randomized 3:1 active:placebo, to each dosing cohort. SAD cohorts evaluated single doses of 75 mg to 450 mg while fasted, as well as single doses of 25 mg and 75 mg with food to provide a preliminary assessment of the effect of food on PK. Five MAD cohorts evaluated doses between 75mg and 300mg BID over ten dosing days, and 25 mg taken with food to provide a preliminary assessment of the effect of food on PK. Twenty-four participants were dosed in the open-label food effect and tablet bioequivalence part, with separate cohorts evaluating 25 mg and 300 mg as single doses of suspension (fasted), tablet (fasted), and tablet (fed).

SION-451 was generally well tolerated at all dose levels administered. A summary table of reported TEAEs is shown in Figure 16 below. There were no SAEs, and most TEAEs were mild to moderate (Grade 1 or Grade 2). No TEAEs led to the discontinuation of trial drug, and no dose-limiting TEAEs were observed. Most TEAEs occurring in >2 participants were Grade 1 or Grade 2, and several were in an isolated dose cohort that was impacted by an outbreak of respiratory infection in the Phase 1 unit. One Grade 1 TEAE of increased transaminases was observed in a participant with influenza A infection; the same participant had transient Grade 3 neutropenia concurrent with influenza A infection. There were no other TEAEs related to liver function tests. There were no clinically meaningful, treatment-emergent trends in other safety parameters, vital signs or electrocardiograms. The data from Part C supported the use of a tablet formulation in future studies and indicate that SION-451 can be dosed in a fed or fasted state.

Study Participants (n)*	Placebo BID *(n=9)*	25 mg BID *(n=6)*	75 mg BID *(n=5)*	150 mg BID *(n=6)*	225 mg BID *(n=6)*	300 mg BID *(n=6)*	MAD Total *(n=38)*
Any TEAE, n (%)	**5 (56)**	**2 (33)**	**3 (60)**	**3 (50)**	**4 (67)**	**2 (33)**	**19 (50)**
Mild (Grade 1)	4 (44)	2 (33)	2 (40)	1 (17)	4 (67)	-	13 (34)
Moderate (Grade 2)	1 (11)	-	1 (20)	1 (17)	-	2 (33)	5 (13)
Severe (Grade 3)	-	-	-	1 (17)	-	-	1 (3)
Life-threatening (Grade 4)	-	-	-	-	-	-	-
Leading to treatment discontinuation	-	-	-	-	-	-	-
Serious TEAEs, n (%)	-	-	-	-	-	-	-
Most frequent TEAEs (≥2 subjects), n (%)							
Headache	3 (33)	1 (17)	-	-	2 (33)	1 (17)	7 (18)
Influenza	-	-	-	2 (33)	-	-	2 (5)
Upper Respiratory Tract Infection	1 (11)	-	-	1 (17)	-	-	2 (5)

(Figure 16. Safety observations in the SAD and Part C portions of the trial were generally consistent with the MAD findings shown.)

Increasing exposure was observed with increasing single and multiple doses. The concentration targets for SION-451 as both an add-on to the standard of care and as part of a dual combination with SION-2222 or SION-109 were achieved with single and multiple doses. A PK summary of SION-451 in the MAD portion of the trial is shown in Figure 17 below. The observed PK was consistent with BID dosing.



(Figure 17. Each solid line shows mean concentration data from a dosing cohort on Day 10. Dotted lines represent average PK concentration exposure targets that have the potential, based on our preclinical CFHBE model, to provide clinically meaningful benefit, if SION-451 is administered in a proprietary dual combination with either SION-2222 or SION-109, or as an add-on to the standard of care. PK observations in the SAD and Part C portions of the trial were generally consistent with the MAD findings shown.)

Following completion of the single agent portion of this Phase 1 trial, we evaluated the achieved clinical exposures of SION-451 in our CFHBE model with a fixed concentration of SION-109 and SION-2222, to assess their potential in dual combinations. As shown in the CFHBE model, and depicted in Figure 18, at these clinical exposures achieved, SION-451 in combination with each of SION-2222 or SION-109 has the potential to improve CFTR channel activity above our minimum target for clinically meaningful benefit, including up to wild-type levels. In Figure 18, CFTR activity in the model is expressed as a ratio relative to ETI at E_{max}, which is set at a reference value of 1.00. Based on these findings, we believe that SION-451 in a dual combination with a complementary modulator has the potential to provide clinically meaningful benefit to CF patients, and we advanced SION-451 into our ongoing dual combination trial with each of SION-2222 and SION-109.

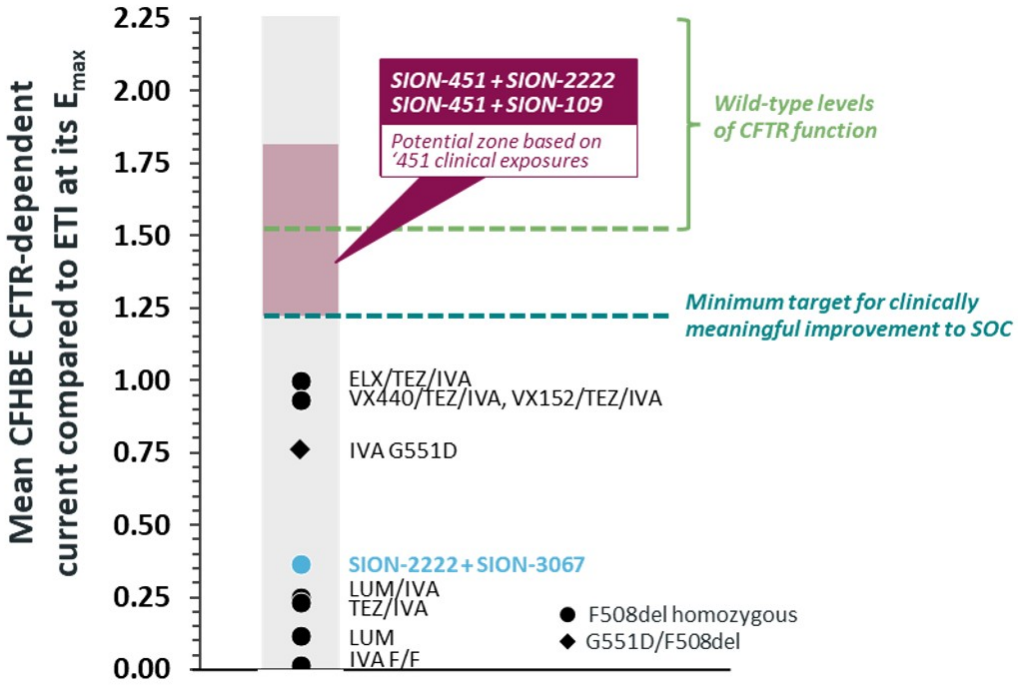

Mean CFHBE CFTR-dependent current compared to ETI at its E_{max}
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
SION-451 + SION-2222
SION-451 + SION-109
Potential zone based on '451 clinical exposures
Wild-type levels of CFTR function
Minimum target for clinically meaningful improvement to SOC
ELX/TEZ/IVA
VX440/TEZ/IVA, VX152/TEZ/IVA
IVA G551D
SION-2222 + SION-3067
LUM/IVA
TEZ/IVA
LUM
IVA F/F
F508del homozygous
G551D/F508del

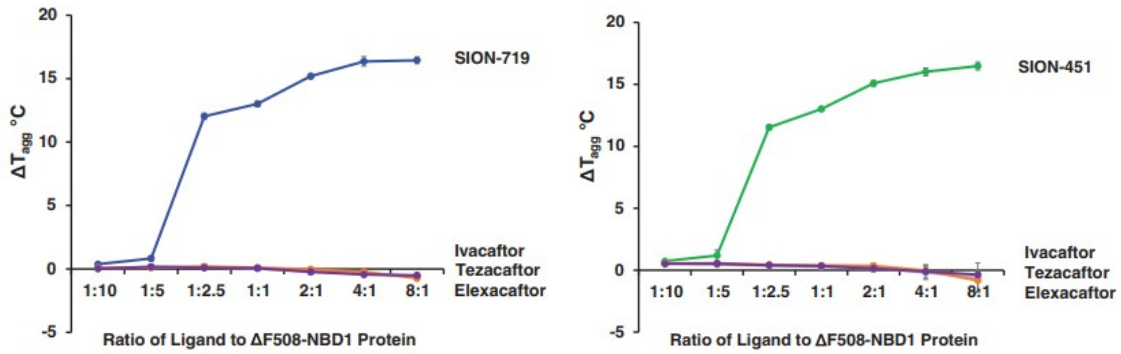
Figure 18

Preclinical Studies of SION-719 and SION-451

We have used numerous complementary methods to validate and characterize the activity of our compounds. In addition to the CFHBE model, we have utilized differential static light scattering ("DSLS") experiments to measure the thermal stability of the NBD1 protein, surface plasmon resonance ("SPR") studies to evaluate the interaction of SION-719 and SION-451 with the NBD1 domain, CFTR western blot analysis to assess the impact of NBD1 stabilizers on the folding, maturation and stability of F508del-CFTR, and metabolic pulse-chase analysis studies to assess the impact of SION-719 and SION-451 on F508del-CFTR half-life. Given the results of these preclinical studies, we believe that we have identified highly potent NBD1 stabilizers.

SION-719 and SION-451 Increased NBD1 Thermal Stability

In preclinical studies, SION-719 and SION-451 increased the stability of the NBD1 domain as measured using DSLS experiments. Light scattering provides a measure of the temperature at which a protein unfolds. As the temperature rises, the CFTR protein unfolds and creates aggregates that interfere with the passage of light. These preclinical studies evaluated the change in temperature that the protein aggregated as the ratio of the compound to CFTR protein increased, which is an indicator of stability. We also evaluated ETI in these preclinical studies, and we found that they had no effect on NBD1 thermal stability, as measured by light scattering techniques. Restoration of NBD1 thermal stability has been highlighted as being both necessary and sufficient to correct F508del CFTR folding and assembly. Both SION-719 (Figure 19, left) and SION-451 (Figure 19, right) increased F508del-NBD1 stability by approximately 16°C. These preclinical models show the ability of SION-719 and SION-451 to improve the stability of NBD1 as compared to ETI, as measured by light scattering techniques.



***ΔTagg °C** = Change in the temperature at which F508del-NBD1 protein unfolds and aggregates*
***N=4,** error bars represent standard deviation*

Figure 19

SION-719 and SION-451 Bound to NBD1 with High Affinity

To evaluate the binding ability of our stabilizer candidates, we employed SPR studies to evaluate the interaction of SION-719 and SION-451 with the NBD1 domain. SPR studies measure changes in the mass of biomolecules immobilized on a metal film. When a small molecule ligand binds to the immobilized target protein, the refractive index of the metal film changes, resulting in a changed reflection angle of light. In these studies, we found that the strength of the binding interaction was high; the binding affinity of SION-719 to F508del-NBD1 was approximately 4.3 nM and the binding affinity of SION-451 to F508del-NBD1 was approximately 2.4 nM, each expressed as a K_D value.

SION-719 and SION-451 Restored F508del Folding and Maturation

In preclinical studies, we evaluated SION-719 and SION-451 in various combinations, including with ETI, SION-2222, and SION-109 to assess these combinations' ability to improve CFTR folding, maturation and stability and thereby correct F508del-CFTR. Preclinical studies with both SION-719 and SION-451-based combinations resulted in F508del-CFTR maturation to levels that are similar to wild-type CFTR. We believe

these results demonstrated potential synergy between an NBD1 stabilizer and these complementary modulators.

The results of studies of CFTR maturation in human CF submucosal gland epithelial ("CFSMEo") cells by western blot with SION-719 are shown in Figure 20 (top), and the results with SION-451 combinations are shown in Figure 20 (bottom). Together, the western blots illustrate F508del-CFTR protein in a submucosal-gland epithelial cell line that expresses CFTR, treated with various combinations of CFTR modulators. The top molecular weight bands, labeled C-band, indicate the presence of the active, mature apical glycoform of CFTR (dark bands), which is responsible for CFTR channel function. The compounds were evaluated at their E_{max}.

In Figure 20, the far-left column in the C-band is F508del in dimethylsulfoxide ("DMSO") alone, showing no mature protein, and the far-right column is wild-type CFTR in DMSO with a dark band indicating the presence of mature CFTR protein. As seen in Figure 20 (top), dual combinations of SION-719 with SION-2222 or SION-109, or the addition of SION-719 to ETI, resulted in wild-type levels of corrected F508del-CFTR protein. Treatment with SION-719 as a single agent demonstrated a greater effect on F508del maturation than ETI at E_{max}. On the other hand, there was little improvement in the maturation of F508del-CFTR protein with SION-2222 alone, SION-109 alone or ETI at their respective E_{max} concentrations, as indicated by the light gray bands. The results with SION-451 presented in Figure 20 (bottom) are similar. The western blots below demonstrate the importance of NBD1 stabilization to the correction of F508del maturation.

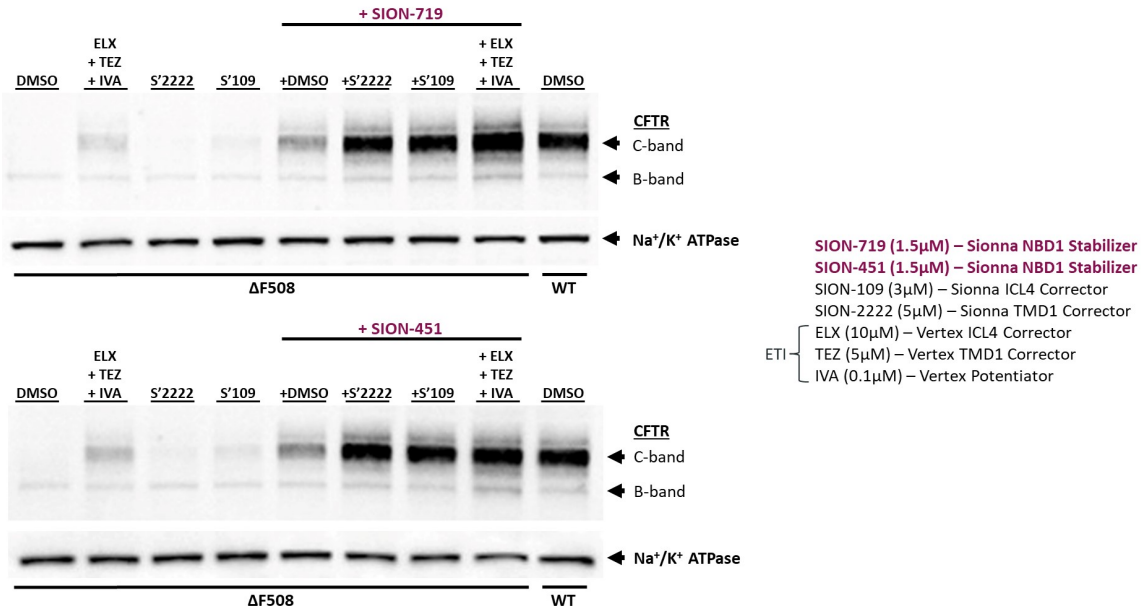
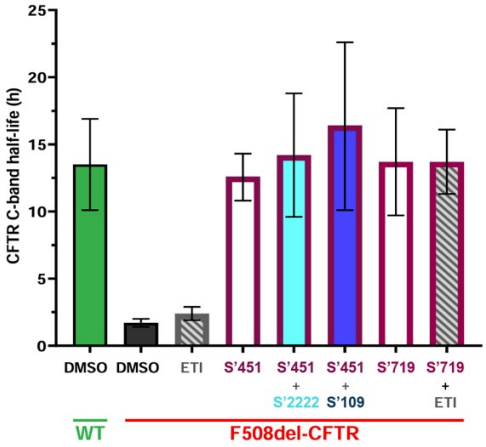


Figure 20

SION-719 and SION-451 Improved the Half-life of F508del-CFTR

In preclinical studies, we used metabolic pulse-chase labeling analysis to evaluate the impact of NBD1 stabilizers SION-451 and SION-719 on F508del-CFTR half-life at the apical cell surface. In these studies, cells expressing F508del-CFTR were labeled to track newly synthesized CFTR protein, and the rate at which the labeled protein declined over time was measured to assess whether treatment with SION-719 or SION-451 increased the half-life of the mature CFTR protein relative to controls. We evaluated SION-451 in the presence or absence of SION-2222 or SION-109, and SION-719 in the presence or absence of ETI. As shown in Figure 21, treatment with either NBD1 stabilizer, as single agents or in combination with other complementary modulators, increased F508del-CFTR half-life to that of wild-type CFTR. In comparison, treatment with ETI alone had a minimal effect on F508del-CFTR half-life.



Treatment	CFTR Half-life 95% CI (low to high h)	p-value treatment vs WT	p-value treatment vs F508del
WT-CFTR	13.5h (10.1 to 16.9)	nd	1E-11
F508del-CFTR	1.7h (1.4 to 2.0)	1E-11	nd
F508del + ETI	2.4h (1.9 to 2.9)	3E-10	0.02
F508del + S'451	12.6h (10.8 to 14.3)	0.65	3E-34
F508del + S'2222 + S'451	14.2h (9.6 to 18.8)	0.79	9E-08
F508del + S'109 + S'451	16.4h (10.1 to 22.6)	0.43	5E-06
F508del + S'719	13.7h (9.7 to 17.7)	0.93	4E-09
F508del + ETI + S'719	13.7h (11.3 to 16.1)	0.92	6E-22

Figure 21

SION-719 and SION-451 Normalized CFTR Function in CFHBE Model at E_{max}

In our CFHBE model, SION-719 and SION-451 as single agents at E_{max} improved F508del-CFTR activity to levels observed near those with triple combination ETI at E_{max}. The results of the SION-719 and SION-451 studies are shown in Figure 22. In Figure 22, CFTR activity is expressed as a ratio relative to ETI at Emax. The vertical bars represent the mean CFTR channel activity (+/- standard error of eight replicates) from a representative study in homozygous F508del CFHBE cells in response to the treatments indicated. The dashed line represents the average response to ETI in each study.

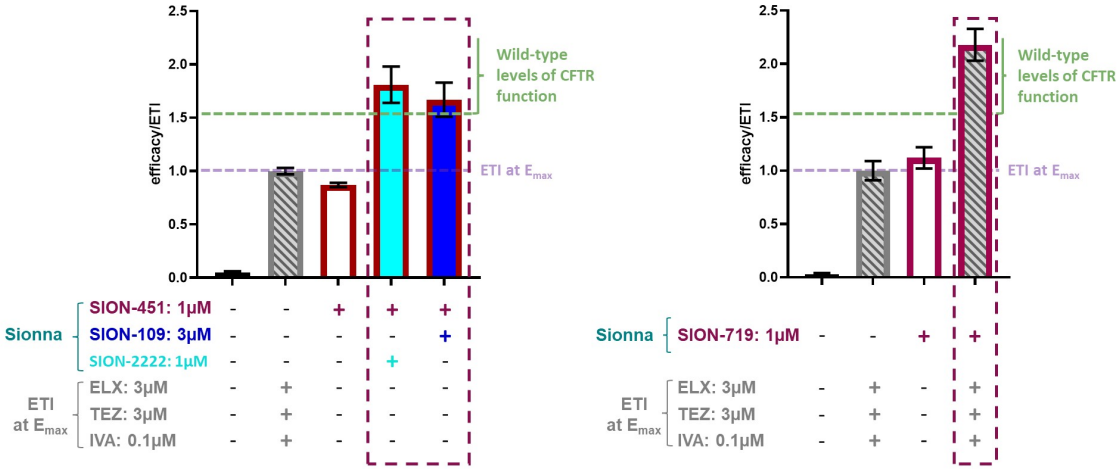


Figure 22

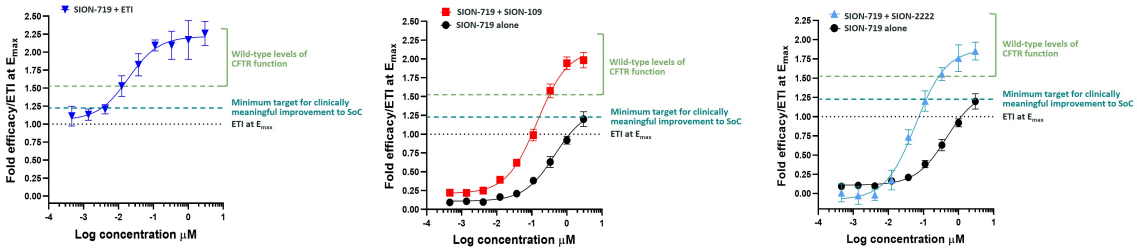
In our CFHBE model, SION-719 when added to ETI and SION-451 in dual combinations with SION-2222 or SION-109, improved in vitro F508del-CFTR activity to wild-type levels, when administered at E_{max}. As noted above, improvements in CFTR function we observed in our CFHBE model have been highly correlated with mean improvements in sweat chloride levels and mean improvements in lung function.

Based on our findings in these preclinical studies and the strong correlation between chloride conductance and improved clinical activity, we believe that SION-719 in combination with ETI and SION-451 in combination with a complementary CFTR modulator, have the potential to achieve significant improvement in

CFTR function, as measured by sweat chloride levels and lung function, and thereby have the potential to lead to clinically meaningful benefit for CF patients.

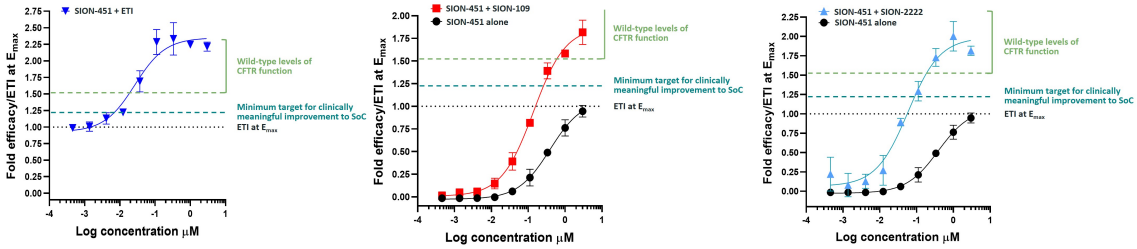
Setting Initial Clinical Exposure Targets Based on CFHBE Model

To set total plasma concentration targets in our Phase 1 clinical trials with SION-719 and SION-451 in healthy volunteers, we conducted multiple dose response studies of both compounds in our CFHBE model that assessed F508del-CFTR activity as a function of each compound's concentration in cell culture media supplemented with human serum to 20% by volume. We selected a target exposure for our Phase 1 trials based on an average of these preclinical dose response studies along with studies to define an adequate safety margin. Figure 23 below presents illustrative dose responses of SION-719, as a single agent and in combination with ETI, SION-109 or SION-2222, as a function of the fold efficacy (CFTR activity) of ETI at increasing dose concentrations, in CFHBE cells from single donors. The black dotted horizontal line indicates ETI's improvement in F508del-CFTR activity at E_{max}, the teal horizontal line indicates our minimum target for clinically meaningful improvement in F508del-CFTR activity based on our CFHBE assay, and the green horizontal line represents the lower bound of the CFTR activity range observed across a panel of eight CFTR wild-type CFHBE donors. The X-axis shows increasing drug concentrations on a logarithmic scale. A roughly two-fold increase over ETI, as seen with SION-719 treatment at its E_{max} in each of the three combinations, is in the range of wild-type channel activity.



(Figure 23. ETI = 3 μM Elexacaftor + 45 μM Tezacaftor + 0.3 μM Ivacaftor. SION-109 and SION-2222 were used at 3 μM.)

Figure 24 below presents illustrative dose responses of SION-451, as a single agent and in combination with ETI, SION-109 or SION-2222, as a function of the fold efficacy (CFTR activity) of ETI at increasing dose concentrations, in CFHBE cells from single donors. A roughly two-fold increase over ETI, as seen with SION-451 treatment at its E_{max} in each of the three combinations, is in the range of wild-type channel activity.



(Figure 24. ETI = 3 μM Elexacaftor + 45 μM Tezacaftor + 0.3 μM Ivacaftor. SION-109 and SION-2222 were used at 3 μM.)

These dose response curves illustrate that our NBD1 stabilizers work synergistically with complementary modulators, and with the standard of care, to significantly improve CFTR function in preclinical models. Given the correlation seen in our preclinical studies between CFTR function and clinical activity, we believe that achieving target exposure levels for our product candidates in our ongoing and future clinical trials has the potential to translate to significant improvements in sweat chloride and lung function, as measured by FEV_1, in CF patients.

Preclinical Safety/Pharmacology and Toxicology to Support Clinical Trials

For both SION-719 and SION-451, we conducted standard in vitro and in vivo toxicology and safety pharmacology studies necessary to support first in human studies. The preclinical study results supported early clinical testing above exposure levels that we have predicted can be effective.

Additional NBD1 Stabilizer Candidates

Our portfolio includes additional NBD1 stabilizer candidates with differentiated profiles from SION-719 and SION-451. We have nominated two additional NBD1 stabilizers as development candidates.

Complementary Modulator Programs

There are two types of complementary modulators: correctors, which partially improve CFTR protein folding to aid its trafficking to the cell surface, and potentiators, which increase CFTR channel function by enabling chloride flow through the cell membrane. We have established a pipeline of proprietary complementary modulators, representing three different mechanisms of action: TMD1-directed correctors, an ICL4-directed corrector, and a potentiator. Our two prioritized clinical-stage complementary modulators are SION-2222 and SION-109. We are currently evaluating each of SION-2222 and SION-109 in dual combinations with SION-451 in a Phase 1 trial in healthy volunteers.

Clinical Data — Complementary Modulators

TMD1 Programs—SION-2222 and SION-2851

SION-2222 is currently being evaluated in a dual combination with SION-451 in a Phase 1 healthy volunteer trial. In a Phase 2 clinical trial conducted by AbbVie prior to our in-licensing transaction, SION-2222 demonstrated clinical activity in improving sweat chloride and lung function as part of a combination trial with SION-3067. SION-2222 has been evaluated in Phase 1, Phase 1b and Phase 2 clinical trials involving healthy participants and CF patients. Across these studies, SION-2222 was generally well-tolerated at all doses administered. The majority of adverse events (“AEs”) were mild to moderate in severity. No SAEs were reported in healthy volunteers, and among CF patients, SAEs were reported infrequently and consisted of common manifestations of the underlying CF disease. The PK profile of SION-2222 in CF patients was similar to that observed in healthy volunteers. The activity of SION-2222 in patients with CF has been evaluated in three randomized, double-blind, placebo-controlled Phase 2 trials: trial M19-530, conducted by AbbVie, and trials GLPG-2222-CL-201 and GLPG-2222-CL-202, conducted by Galapagos NV (“Galapagos”).

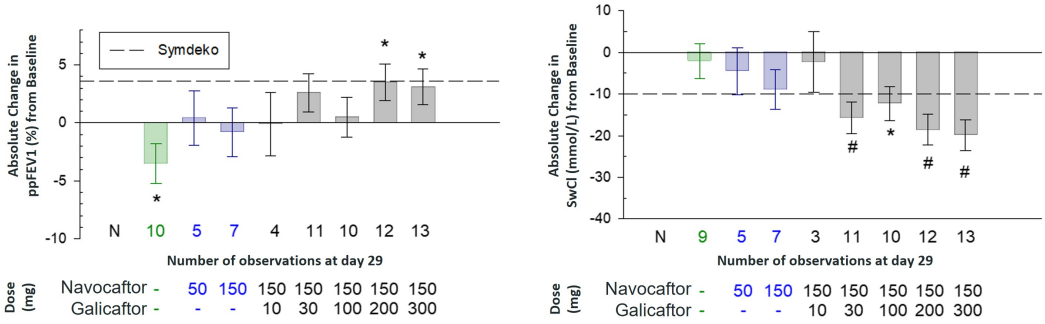
Trial M19-530 was a Phase 2 dose-ranging trial that evaluated the safety, tolerability and efficacy of SION-3067 alone and in combination with SION-2222 in CF patients that were homozygous for F508del mutation. The primary efficacy endpoint of this trial was absolute change in lung function (ppFEV1), and the secondary efficacy endpoint was improvement in sweat chloride. In this trial, treatment with SION-2222 in combination with SION-3067 was associated with improvements from baseline ppFEV1 and sweat chloride, both compared to placebo, as shown in Figure 25. SION-2222 was generally well tolerated in combination with SION-3067. Most AEs were mild to moderate. Two SAEs were reported in two participants receiving SION-2222 in combination with SION-3067, which investigators considered unrelated to study drug.

Trial GLPG-2222-CL-202 was a Phase 2 dose-ranging trial that evaluated the safety and tolerability and the effect of SION-2222 on CFTR function (as assessed by sweat chloride), lung function (as assessed by $ppFEV_1$) and the Cystic Fibrosis Questionnaire— Revised (“CFQ-R”), which measures health-related quality of life, in CF patients that were homozygous for F508del mutation. In this trial, mean sweat chloride concentrations decreased dose-dependently with increasing doses of SION-2222; the decrease was statistically significant in the 200 mg dose group. ppFEV1 and CFQ-R did not significantly improve in any group. SION-2222 was generally well-tolerated in this trial. The majority of reported TEAEs were mild or moderate in severity. SAEs reported were considered not related to study drug.

Trial GLPG-2222-CL-201 was a Phase 2 trial that evaluated the safety and tolerability and the effect of two dose levels of SION-2222 in CF patients that were heterozygous for the F508del mutation and a gating mutation, receiving ivacaftor, on CFTR function (as assessed by sweat chloride), lung function (as assessed by $ppFEV_1$) and CFQ-R. In this trial, one SION-2222 treatment group (300 mg once daily) was associated with an improvement in sweat chloride compared to placebo, while other dose treatment groups did not show

statistically significant changes in sweat chloride. ppFEV1 and CFQ-R did not significantly improve in any group. SION-2222 was generally well-tolerated in this trial. Most TEAEs were mild in severity, and there were no SAEs.

These Phase 2 results demonstrated that SION-2222 as a single agent increased CFTR activity in patients with the F508del mutation. The activity of SION-2222 in combination with SION-3067 in Trial M19-530 was similar to the activity of approved dual combination modulators, as seen via indirect, cross-trial comparisons and as predicted based on our CFHBE model (Figure 25).



Data presented as LS mean ± standard error. * p < 0.05; # p < 0.001

Figure 25

In addition to SION-2222, we licensed SION-2851 from AbbVie in July 2024. SION-2851 is a potent TMD1-directed corrector that has completed a Phase 1 SAD trial in healthy volunteers. The trial was conducted by AbbVie and Galapagos in Belgium in 2018. The primary endpoint was safety and tolerability, assessed by the number of participants with adverse events. Based on its mechanism of action and preclinical studies, we believe it may be potentially synergistic with NBD1 stabilizers.

ICL4 Program—SION-109

We are also advancing SION-109, which targets the ICL4 interface, for development in combination with an NBD1 stabilizer. SION-109 is currently being evaluated in combination with SION-451 in our ongoing Phase 1 dual combination trial.

In December 2024, we completed a randomized, double blind, placebo-controlled Phase 1 clinical trial of SION-109 in healthy participants, following clearance of its Investigational New Drug application ("IND") by the FDA in June 2023. The trial was designed to evaluate the safety, tolerability and PK profile of single and multiple ascending doses of SION-109, administered as an oral suspension. In a Part C of the Phase 1 trial, we evaluated the effect of food on PK and the bioequivalence of a tablet formation compared to the oral suspension used in the Phase 1 SAD and MAD cohorts.

Over 100 healthy adult participants received SION-109 in this Phase 1 trial. The trial was designed to enroll eight participants, randomized 3:1 active:placebo, to each dosing cohort. Six SAD cohorts evaluated single doses from 50 mg to 400 mg. Five MAD cohorts evaluated from 50 mg to 150 mg BID over ten dosing days. Fifteen participants enrolled in the open-label food effect and tablet bioequivalence part evaluating 100 mg single doses each of suspension fasted, tablet fasted, and tablet fed.

SION-109 was generally well tolerated at all dose levels administered in all parts of this Phase 1 trial. A summary table of reported TEAEs is shown in Figure 26 below. There were no SAEs, and most TEAEs were mild to moderate (Grade 1 or Grade 2). No TEAEs led to the discontinuation of trial drug, and no dose-limiting TEAEs were observed. Sporadic increases in potassium were observed that were determined to be related to sample collection and/or processing. A 150 mg MAD cohort was repeated with revised sampling guidance, and no increased potassium values were observed. Isolated and transient increases in transaminases were observed associated with four AEs in three participants in the MAD and Part C (one Grade 1 AE, two Grade 2 AEs and one Grade 3 AE) whose values returned to the normal range in follow-up. Other liver function tests,

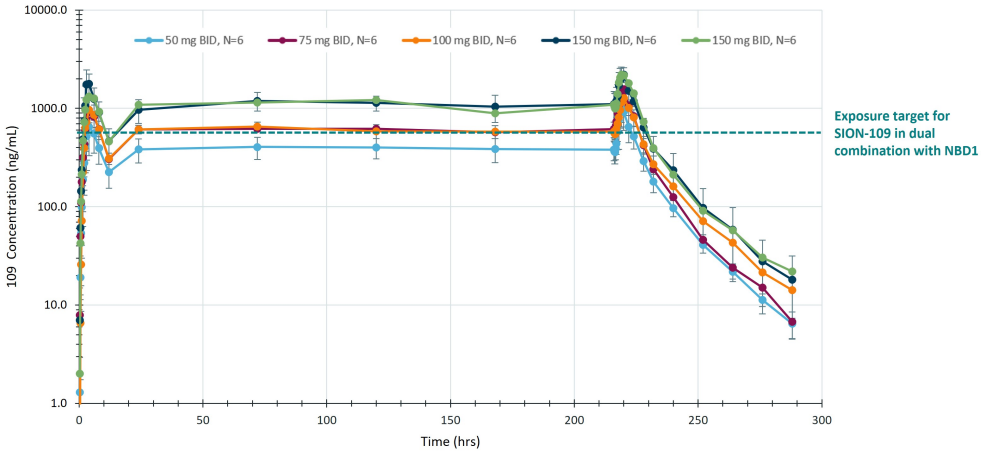
including bilirubin, were unremarkable. There were no clinically meaningful, treatment-emergent trends in other safety parameters, vital signs or electrocardiograms.

	Placebo (n=9)	Cohort 1 50 mg (n=6)	Cohort 2 100 mg (n=6)	Cohort 3 150 mg (n=6)	Cohort 4 75 mg (n=7)	Cohort 5 150 mg (n=6)	MAD Total (n=40)
Any TEAE, n (%)	**4 (44)**	**4 (67)**	**3 (50)**	**3 (50)**	**0**	**1 (17)**	**15 (38)**
Mild (Grade 1)	2 (22)	-	-	1 (17)	-	-	3 (8)
Moderate (Grade 2)	2 (22)	4 (67)	2 (33)	1 (17)	-	1 (17)	10 (25)
Severe (Grade 3)	-	-	1 (17)	1 (17)	-	-	2 (5)
Life-threatening (Grade 4)	-	-	-	-	-	-	-
Leading to treatment discontinuation	-	-	-	-	-	-	-
Serious TEAEs, n (%)	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Most frequent TEAEs (>1 subject), n (%)							
Headache	2 (22)	2 (33)	-	-	-	1 (17)	5 (13)
Abdominal pain	-	-	1 (17)	1 (17)	-	-	2 (5)
Alanine aminotransferase increased	-	-	1 (17)	1 (17)	-	-	2 (5)
Constipation	-	1 (17)	1 (17)	-	-	-	2 (5)
Diarrhea	-	-	1 (17)	1 (17)	-	-	2 (5)
Myalgia	1 (11)	-	1 (17)	-	-	-	2 (5)

(Figure 26. Safety observations in the SAD and Part C portions of the trial were generally consistent with the MAD findings shown.)

Increasing exposure was observed with increasing single and multiple doses. The target exposure for SION-109 as part of a dual combination with SION-451 or SION-719 was achieved with multiple doses of 75 mg BID and higher doses.

A PK summary of SION-109 is shown in Figure 27 below. The PK observed was consistent with BID dosing.



(Figure 27. Each solid line shows mean concentration data for a dosing cohort over ten days of dosing. Data points for Day 2 through Day 9 are trough (pre-dose) concentrations. The dotted line represents the Cminimum (trough) PK exposure target for SION-109, with the aim to achieve targeted exposure to deliver clinically meaningful benefit when administered in a proprietary dual combination, based on CFHBE assay data. PK observations in the SAD and Part C portions of the trial were generally consistent with the MAD findings shown.)

Potentiator Program—SION-3067

SION-3067 is a clinical-stage potentiator of CFTR gating activity that we have licensed from AbbVie. SION-3067 provides our pipeline with a third mechanism of action complementary to NBD1 stabilizers and future opportunities to develop additional combination products to potentially expand our CF franchise. SION-3067 has completed Phase 1, Phase 1b and Phase 2 trials and was generally well-tolerated in CF patients and healthy volunteers, with improvements observed in sweat chloride levels in combination with SION-2222. When SION-3067 was given as a monotherapy or in combination with SION-2222, all AEs were mild to moderate. The PK profile in CF patients was similar in healthy volunteers.

The activity of SION-3067 in patients with CF was evaluated in a randomized, double-blind, placebo-controlled Phase 2 trial in combination with SION-2222, as summarized above. Combination treatment of SION-3067 150 mg QD with SION-2222 resulted in improvements in FEV_1 and sweat chloride levels in the homozygous F508del population. As expected, treatment with 50 mg QD or 150 mg QD SION-3067 monotherapy for 28 days did not result in improvements in FEV_1 or sweat chloride levels.

Manufacturing

We have leveraged multiple third-party manufacturers to support the manufacturing of our product candidates for clinical trials and, if we receive regulatory approval, we intend to rely on third parties for commercial manufacture. We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We expect this strategy will enable us to maintain a more efficient infrastructure, outsourcing instead of building manufacturing and supply chain capabilities, while simultaneously enabling us to focus our expertise on the clinical development of our product candidates. We expect to enter into commercial supply agreements with such manufacturers prior to any potential approval of our product candidates.

Commercialization

We have exclusive worldwide commercial rights to our product candidates. Given our stage of development, we have not yet established a commercial organization or distribution capabilities. The CF patient populations are well-characterized and clearly identified in the U.S., Canada, Europe, Australia, and several other regions around the world, with highly active and informed CF patient advocacy groups. Most CF patients are treated at a limited number of centralized CF patient care centers by teams of healthcare professionals who are experts in and dedicated to treating CF.

We plan to independently commercialize our products, if approved, in the U.S. and in other regions where we determine it makes commercial sense to do so. Given the established CF patient care centers and the concentrated group of prescribing healthcare professionals, we believe we could commercialize our product(s) for CF with a relatively small specialty sales force focused on CF treatment centers and prescribers. At the appropriate time, and subject to regulatory approval and the scope of any approved indication, we plan to recruit a sales force and expand our medical affairs team and take other steps to establish the necessary commercial infrastructure. As our product candidates advance through our pipeline, our plans may change with respect to the timing, scope and manner of commercialization.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe we have competitive advantages, we face substantial competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic research institutions and governmental agencies, and public and private research institutions. This may include other small-molecule drug discovery companies using similar approaches or other types of therapies, such as small molecule, gene therapy, gene editing and/or mRNA therapies.

In particular, we expect to compete with Vertex, which has multiple approved products, as well as additional product candidates in development, for the treatment of CF that would compete with our product candidates, if approved. Vertex is the manufacturer of the five approved CFTR modulators, including the standard of care, Trikafta, and the triple modulator combination, Alyftrek, approved in December 2024. Any product candidates that we successfully develop and commercialize will compete with these existing therapies, as well as any new therapies that may become available in the future that are approved to treat the same diseases for which we may obtain approval for our product candidates.

We may also face competition from other companies attempting to develop therapeutics targeting CF. For example, in October 2025, Fair Therapeutics, Inc. announced final results from a Phase 2b trial evaluating its CFTR modulators. Multiple companies are developing CF-utilizing nucleic acid therapies, which are compounds that allow expression of a functional CFTR protein and are relevant for the more than 5,000 people with CF who cannot make full-length CFTR protein and are not eligible for CFTR modulators. In addition, multiple companies are developing candidates for gene therapy approaches to treat CF.

Some of our competitors have significantly greater financial resources than we do and an established presence in the market. Our competitors may have greater expertise in research and development, manufacturing, obtaining regulatory approvals and marketing approved products and may obtain regulatory approvals for their products more rapidly than we can, if at all. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. We also compete with these companies in recruiting, hiring and retaining qualified scientific and management talent, establishing clinical trial sites and patient registration for clinical trials and obtaining manufacturing slots at contract manufacturing organizations.

If our product candidates do not offer advantages over available products, we may not be able to successfully compete against current and future competitors. The key factors affecting the success of our products, if approved, are likely to be their potential efficacy, safety, tolerability, convenience and availability of reimbursement.

Intellectual Property

We strive to protect and enhance the intellectual property and proprietary technology that we consider important to our business, including by pursuing patent applications that cover our product candidates and methods of using the same, as well as any other relevant inventions and improvements that we believe to be commercially important to the development of our business. We also rely on trade secrets relating to our proprietary know-how, continuing innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary and intellectual property position. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions, where available.

Our commercial success may depend in part on our ability to: obtain, maintain, enforce and protect our intellectual property and other proprietary rights for commercially important technology, inventions and know-how related to our business; defend and enforce any patents we may own or in-license in the future; prevent others from infringing any patents we may own or in-license in the future; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to limit third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents or trade secrets that cover these activities. In some cases, enforcement of these rights may depend on third party licensors. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

Patent expiration dates noted in the following paragraphs refer to statutory expiration dates and do not take into account any potential patent term adjustment or extension that may be available.

NBD1 Stabilizers

We co-own with Sanofi a patent family that discloses and covers each of SION-719 and SION-451 and methods of using SION-719 and SION-451 for the treatment of CF. The patent family has entered the national phase and is pending in the United States, Argentina, Australia, Brazil, Canada, Chile, China, Colombia, Ecuador, Egypt, Eurasian Patent Organization, European Patent Office, Hong Kong, India, Israel, Jordan, Japan, Mexico, New Zealand, Oman, Peru, Qatar, Saudi Arabia, Singapore, South Africa, South Korea, Taiwan, and the United Arab Emirates. The statutory expiration for this family is September 2043. We own a non-provisional patent application that discloses and claims the use of our NBD1 stabilizer product candidates in combination with other agents for the treatment of CF, which has a statutory expiration of March 2045.

Complementary Modulators

We exclusively license from Sanofi one patent family that discloses and covers SION-109 and methods of using SION-109 for the treatment of CF. The patent family has entered national phase and is pending in the U.S., the European Patent Office, African Regional Industrial Property Organization, African Intellectual Property Organization, Algeria, Australia, Bahrain, Brazil, Canada, Chile, China, Colombia, Eurasian Patent Office, Ecuador, Egypt, Guatemala, Hong Kong, Honduras, Israel, India, Jordan, Japan, Kuwait, Mexico, Malaysia, New Zealand, Nigeria, Oman, Panama, Peru, Philippines, Saudi Arabia, Singapore, South Africa, South Korea, Sri Lanka, Thailand and the United Arab Emirates. The statutory expiration for this family is November 2040.

We exclusively license from AbbVie one patent family that discloses and covers SION-2222 and methods of using SION-2222 for the treatment of CF. The patent family includes granted patents in the United States, Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, Chile, China, Colombia, Costa Rica, Croatia, Czech Republic, Denmark, Dominican Republic, Estonia, Finland, France, Germany, Greece, Hong Kong, Hungary, India, Ireland, Israel, Italy, Japan, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Mexico, Monaco, Netherlands, Norway, Panama, Peru, Philippines, Poland, Portugal, Romania, Russia, Singapore, Slovakia, Slovenia, South Africa, South Korea, Spain, Sweden, Switzerland, Taiwan, Turkey, Ukraine, United Kingdom, Uruguay, and Vietnam, and has a statutory expiration date of October 2035. We exclusively license from AbbVie one patent family that discloses and covers SION-2851 and methods of using SION-2851 for the treatment of CF. The patent family includes granted patents in the United States, Argentina, Australia, Brazil, Canada, Chile, China, Colombia, Costa Rica, Dominican Republic, France, Germany, India, Israel, Italy, Japan,

Malaysia, Mexico, New Zealand, Pakistan, Panama, Peru, Philippines, Russia, Singapore, South Africa, South Korea, Spain, Taiwan, Ukraine, United Kingdom, Uruguay, and Vietnam, and has a statutory expiration date of July 2036.

We exclusively license from AbbVie one patent family that discloses and covers SION-3067 and methods of using SION-3067 for the treatment of CF. The patent family includes granted patents in the United States, Albania, Australia, Austria, Belgium, Brazil, Bulgaria, Chile, China, Colombia, Costa Rica, Croatia, Cyprus, Czech Republic, Denmark, Dominican Republic, Estonia, Finland, France, Germany, Greece, Hong Kong, Hungary, Iceland, India, Ireland, Israel, Italy, Japan, Latvia, Liechtenstein, Lithuania, Luxembourg, Macau, Malta, Mexico, Monaco, Netherlands, New Zealand, North Macedonia, Norway, Panama, Peru, Philippines, Poland, Portugal, Romania, Russia, San Marino, Serbia, Singapore, Slovakia, Slovenia, South Africa, South Korea, Spain, Sweden, Switzerland, Turkey, United Kingdom, and Vietnam, a pending application in Canada and Ecuador, and has a statutory expiration date of May 2037. Additionally, the patent family includes granted patents in Argentina and Taiwan, each of which has a statutory expiration date of June 2037.

We own two patent applications that each disclose and contain claims that recite the use of our NBD1 stabilizer product candidates in combination with SION-109, SION-2222, SION-3067, Trikafta and/or other modulators for the treatment of CF. The first is a Patent Cooperation Treaty international application and has a statutory expiration of October 2043, and the second is a non-provisional patent application (discussed above), which has a statutory expiration of March 2045.

Licensing and Collaboration Agreements

Sanofi License Agreement

On December 20, 2019, we entered into a license agreement, as amended by Amendment No. 1 dated May 14, 2020, Amendment No. 2 dated June 8, 2020, Amendment No. 3 dated December 14, 2021, Amendment No. 4 dated January 28, 2022, Amendment No. 5 dated February 21, 2023 and Amendment No. 6 dated October 28, 2024 (as amended, the "Sanofi License Agreement"), with Sanofi, pursuant to which we have been granted an exclusive, worldwide license to develop, commercialize, manufacture, use, hold, keep, register or dispose of certain compounds, patents and proprietary information and inventions, in each case for therapeutic, prophylactic, prognostic and diagnostic purposes in or for humans, subject to retained rights. The licensed and derived rights are directed, among other things, to CFTR modulator therapies which are being utilized in SION-719, SION-109 and SION-451.

Pursuant to the terms of the Sanofi License Agreement, we must use commercially reasonable efforts to develop, pursue regulatory approval for and commercialize a licensed product. Sanofi and its affiliates retain the right to practice under the licensed patents and use the licensed know-how solely to conduct non-clinical research for all therapeutic, prophylactic, prognostic and diagnostic uses in or for humans, other than for CF; provided, however, that Sanofi will not file any patents that claim a licensed compound.

As initial consideration for the license, we paid a non-refundable, upfront payment of $1.5 million, as well as a reimbursement of $0.3 million for Sanofi's research and development expenses. In addition, we are required to pay Sanofi a total of up to $40.0 million upon achievement of certain late-stage developmental and commercial milestones. None of such milestones have been achieved to date. We are also required to pay royalties to Sanofi in the low single-digit percentage range based on net sales of licensed products, subject to customary reductions and offsets. Such royalty payments shall be reduced for products covered by derived patents. The royalty term will terminate on a product-by-product and country-by-country basis upon the later of (i) the expiration of the last-to-expire valid claim within the relevant licensed patent rights, (ii) the expiration of regulatory exclusivity in such country for such licensed product and (iii) the tenth anniversary of the first commercial sale of a licensed product in such country.

We are entitled to sublicense the rights granted to us under the Sanofi License Agreement under certain circumstances, provided that any such sublicense must be consistent with the terms of the Sanofi License Agreement. If we receive sublicense income from any such sublicense, we are required to pay Sanofi a low double digit percentage of such sublicense income.

We have also granted Sanofi an exclusive option to purchase, at a defined price, any priority review voucher ("PRV") granted to us as a result of the development of the licensed compounds or products. In the event that Sanofi does not exercise its option with respect to any PRV, we may (x) use the PRV, in which case we must pay Sanofi a high seven-digit amount or (y) sell the PRV to a third party, in which case we must share a sub-teen double-digit percentage of the sale consideration with Sanofi.

We have the right, but not the obligation, to prepare, file, prosecute and maintain the licensed patents and product trademarks at our own cost. We have the first right to enforce and defend any licensed patents, with Sanofi having back-up enforcement and defense rights. We also have the sole right to enforce and defend any product trademarks at our sole cost and expense.

We have the right to terminate the Sanofi License Agreement for convenience, subject to a 90-day notice period. Sanofi has customary termination rights under the Sanofi License Agreement, including for our material breach, payment default, bankruptcy or challenge of the validity of any patent right, subject to specified notice and cure periods. Unless earlier terminated, the Sanofi License Agreement will expire in each country upon the expiration of the last-to-expire royalty term in such country and, with respect to the Sanofi License Agreement in its entirety, upon the expiration of the royalty term for the last licensed product for which there has been a first commercial sale. Upon expiration of the Sanofi License Agreement, the license granted to us will become non-exclusive, royalty-free, fully paid-up and perpetual.

CFF Payment Agreement

On December 20, 2019, we entered into a payment agreement (the "CFF Payment Agreement") with CFF, pursuant to which we agreed to provide CFF with compensation in exchange for the grant of, and forbearance from exercising, certain of CFF's rights existing under the Research, Development and Commercialization Agreement, dated October 1, 2011, by and between CFF (through an assignment by Cystic Fibrosis Foundation Therapeutics, Inc.) and Genzyme Corporation, an affiliate of Sanofi (the "CFFT-Genzyme Agreement"). As described above, we have been granted a license to certain compounds, patents and know-how pursuant to the Sanofi License Agreement, some of which were generated as a result of a research plan under the CFFT-Genzyme Agreement. Under the CFF Payment Agreement, we are obligated to compensate CFF in connection with our development and commercialization of licensed products under the Sanofi License Agreement. Concurrent with the execution of the CFF Payment Agreement, Sanofi and CFF terminated the CFFT-Genzyme Agreement.

As initial consideration for CFF's grant of, and forbearance from exercising, its rights under the CFFT-Genzyme Agreement, we issued CFF 300,300 shares of our Series Seed preferred stock. In addition, we agreed to pay CFF a sub-teen double-digit percentage of any amounts paid by us to Sanofi under the Sanofi License Agreement, other than milestone, royalty or reimbursement payments. As of December 31, 2025, we have paid CFF a total of approximately $0.2 million in accordance with the terms of the CFF Payment Agreement. In addition, we are required to pay CFF a total of up to $40.0 million upon achievement of certain late-stage developmental and commercial milestones. None of such milestones have been achieved to date. We are also required to pay revenue-shares of royalty payments to CFF in the low single-digit percentage range based on net sales of licensed products, subject to customary reductions and offsets. Such milestone and royalty payments shall be reduced for products covered by derived patents. The royalty term will terminate on a product-by-product and country-by-country basis upon the later of (i) the expiration of the last-to-expire valid claim within the relevant patent rights that claims such product or its exploitation in such country, (ii) the tenth anniversary of the first commercial sale of a product in such country and (iii) expiration of regulatory exclusivity of a product in such country. Further, a side letter was executed between us and Sanofi, which clarifies the relationship between us, Sanofi and CFF, under which we are obligated to pay Sanofi 20% of the milestones it would have been obligated to pay CFF, net of the milestone amounts it is obligated to pay under the Sanofi License Agreement.

If at any time prior to the first commercial sale of a product developed as a result of the CFF Payment Agreement, we cease to use commercially reasonable efforts to develop, and obtain and maintain regulatory approvals for, at least one of our products for therapeutic, prophylactic, prognostic or diagnostic uses in or for humans in specified major markets for a continuous period of 365 days, CFF has the option to exercise rights to an exclusive, irrevocable, worldwide interruption license under our patents, the licensed patents and the

licensed know-how, to develop, manufacture, use, sell, offer to sell and import any of our products containing a licensed compound or any compound covered by a licensed patent or incorporating licensed know-how.

Either party may terminate the CFF Payment Agreement for a material breach by the other party, subject to a specified notice and cure period. Unless earlier terminated, the CFF Payment Agreement will expire (a) with respect to each product in each country, upon the expiration of the last-to-expire royalty term in such country, and (b) with respect to the CFF Payment Agreement in its entirety, upon the later of (i) the expiration of the royalty term for the last licensed product for which there has been a first commercial sale or (ii) the expiration or termination of our obligation to pay consideration to Sanofi under the Sanofi License Agreement.

AbbVie License Agreement

On July 11, 2024, we entered into a license agreement (the "AbbVie License Agreement") with AbbVie, pursuant to which we have been granted an exclusive worldwide, royalty-bearing, sublicensable license to certain patent and other intellectual property rights to research, develop, commercialize, make, manufacture, use, import and sell products for prophylactic or therapeutic use in humans for all indications, subject to certain limitations and retained rights. The licensed rights are directed, among other things, to three clinical-stage CFTR modulator therapies: SION-2222, a TMD1-directed CFTR corrector, SION-3067, a CFTR potentiator, and SION-2851, a TMD1-directed corrector. Under the AbbVie License Agreement, we have assumed all global development and commercialization responsibilities for such therapies. Pursuant to the terms of the AbbVie License Agreement, we must use commercially reasonable efforts to develop, pursue regulatory approval for and commercialize a licensed product. We are also required to achieve certain development milestones within specified time periods for products incorporating intellectual property covered by the AbbVie License Agreement.

The license granted to us under the AbbVie License Agreement is subject to certain preexisting rights held by AbbVie and Galapagos. In particular, certain of the licensed patents and other intellectual property rights were developed by or on behalf of Galapagos and are sublicensed to us subject to the terms of the second amended and restated collaboration agreement between Galapagos and AbbVie dated as of October 24, 2018 (the "Galapagos License Agreement"), as amended by a side letter between Galapagos and AbbVie dated as of July 11, 2024. We are also entitled to sublicense the rights granted to us under the AbbVie License Agreement under certain circumstances, provided that any such sublicense must be consistent with the terms of the AbbVie License Agreement and the Galapagos License Agreement.

As initial consideration for the license, we paid a non-refundable, upfront payment of $5.0 million and issued 1,414,445 shares of our common stock to AbbVie. In addition, we are required to pay AbbVie a total of up to $360.0 million upon achievement of certain development and commercial milestones, consisting of up to $70.0 million in late-stage development milestones and up to $290.0 million in commercial milestones. None of such milestones have been achieved to date. We are also required to pay royalties to AbbVie in the low to mid single-digit percentage range based on net sales of licensed products, subject to customary reductions and offsets, with the percentage range depending in part on the compounds used. The royalty term will terminate on a product-by-product and country-by-country basis upon the later of (i) the expiration of the last-to-expire valid claim within the relevant patent rights that covers the manufacture, use, sale or other exploitation of a product in such country, (ii) the tenth anniversary of the first commercial sale of a product in such country and (iii) expiration of regulatory exclusivity of a product in such country. In addition, we are required to pay AbbVie up to $130.0 million in commercial and sales-based milestone payments, mid to high single-digit royalties on the licensed products or other payments due to Galapagos pursuant to the Galapagos License Agreement, to the extent such payments are triggered by our use of the licensed rights under the AbbVie License Agreement. To date, no payments have been triggered.

We have also granted AbbVie a right of first negotiation (the "ROFN") if we decide to pursue a license or sublicense to commercialize a licensed product (a "Commercial License Transaction") prior to initiating Phase 3 clinical trials. If AbbVie timely exercises the ROFN, then it will have an exclusive period to negotiate in good faith the terms of a Commercial License Transaction. In the event (x) AbbVie does not timely exercise the ROFN or notifies us that it does not intend to pursue a Commercial License Transaction (including after timely exercising the ROFN) or (y) the parties fail to reach agreement or enter into a definitive agreement for the Commercial License Transaction within the exclusive negotiation period, then the ROFN regarding all licensed products will terminate.

We are responsible for the prosecution and maintenance of the licensed patents at our own cost. We have the first right to enforce and defend any licensed patent at our own cost, with AbbVie having back-up enforcement and defense rights.

We have the right to terminate the AbbVie License Agreement for convenience, subject to a prescribed notice period. AbbVie has customary termination rights under the AbbVie License Agreement, including for our material breach, payment default, bankruptcy, challenge of the validity of any patent right or shelving of a product for a specified time period, subject to specified notice and cure periods. Unless earlier terminated, the AbbVie License Agreement will expire upon the expiration of the last-to-expire royalty term. Upon expiration of the AbbVie License Agreement, the license granted to us will become non-exclusive, royalty-free, fully paid-up and perpetual.

In the event the AbbVie License Agreement is terminated, we and AbbVie shall agree upon a transition plan to revert the licensed compounds or licensed products containing such licensed compounds to AbbVie. Within a prescribed time period of such termination, we are obligated to (i) assign and transfer all of our rights and interests in the documentation and data related to the reverting compounds or products to AbbVie, (ii) grant to AbbVie a non-exclusive, royalty-free license right of reference for AbbVie to develop or commercialize any of the reverting compounds or products, (iii) grant to AbbVie an exclusive, royalty-bearing worldwide license to exploit any of the reverting compounds or products and (iv) transfer to AbbVie control of all clinical studies being conducted for any of the reverting compounds or products.

Government Regulation

The FDA and comparable regulatory authorities in federal, state and local jurisdictions and in other foreign countries impose extensive requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities extensively regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, packaging, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of drugs. The process of obtaining regulatory approvals in the U.S. and in foreign countries and jurisdictions, along with subsequent compliance with applicable federal, state, local and foreign statutes and regulations, requires the expenditure of substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process, approval process or after approval, may subject an applicant and/or sponsor to a variety of sanctions. For example, failure to comply with the applicable U.S. requirements may result in administrative or judicial sanctions including refusal by FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

Review and Approval of Drugs in the United States

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (“FDCA”), and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations.

The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- completion of extensive nonclinical, or preclinical, laboratory tests, animal studies and formulation studies in compliance with the FDA’s Good Laboratory Practice (“GLP”) regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be updated annually and when certain changes are made;
- approval by an institutional review board (“IRB”) or independent ethics committee (“IEC”) at each clinical site before each trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practices (“GCP”) requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational drug product for each proposed indication;

- preparation and submission to the FDA of an NDA after completion of all pivotal trials, together with the payment of application user fees, as applicable;
- a determination by the FDA within 60 days of its receipt of an NDA to accept the marketing application for review;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA inspections of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data; and
- FDA review and approval of the NDA.

Preclinical Studies

Before testing any drug product candidate, including our product candidates, in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of the product's chemistry, purity, toxicity, formulation, and stability as well as *in vitro* and animal studies to assess potential safety and efficacy and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety and toxicology studies.

The IND and IRB Process

Prior to beginning the first clinical trial with a product candidate in the U.S., we must submit an IND to the FDA. An IND sponsor must submit a protocol for each clinical trial, the results of the preclinical tests, manufacturing information, analytical data and any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to grant an exemption that allows an unapproved drug to be shipped in interstate commerce for use and administration in an investigational clinical trial for humans. The IND must become effective before human clinical trials may begin in the U.S. Some preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing clinical trial. Clinical holds may be imposed by the FDA when there is concern for patient safety, and may be a result of new data, findings or developments in clinical, nonclinical, and/or chemistry, manufacturing and controls or where there is non-compliance with regulatory requirements. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. Following issuance of a clinical hold or partial clinical hold, an investigation (or full investigation in the case of a partial clinical hold) may only resume after the FDA has notified the sponsor that the investigation may proceed. As a result, submission of an IND may not result in the FDA allowing clinical trials to initiate.

A separate submission to an existing IND must also be made for each successive clinical trial to be conducted, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical trial is not conducted under an IND, the sponsor must ensure that the study is conducted in accordance with GCP, including review and approval by an IEC and informed consent from subjects. FDA must be able to validate the data from the study through an on-site inspection if necessary.

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 of the study. The IRB is charged with protecting the welfare and rights of trial participants and considers whether the risks to individuals participating in the clinical trials are minimized

and are reasonable in relation to anticipated benefits. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects and must monitor the clinical trial until completion. 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.

Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects, or their legal representative, provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the exclusion and inclusion criteria, the objectives of the trial, dosing procedures, subject selection, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. As part of an IND, a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA.

Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data monitoring committee ("DMC"), which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety or health risk for subjects or other grounds, such as no demonstration of efficacy.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health ("NIH") for public dissemination on their *www.clinicaltrials.gov* website. Information related to the investigational 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 obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for some time. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government.

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

- Phase 1: The investigational drug is initially introduced into a limited population of healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion, side effects, and, if possible, to gain an early indication of its effectiveness or determine optimal dosage.
- Phase 2: The investigational drug is administered to a limited patient population with a specified disease or condition to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning Phase 3 clinical trials.
- Phase 3: The investigational drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk/benefit profile of the product, and to provide adequate information for product approval and labeling of the product. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA, although in some cases a single trial may be considered sufficient.

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, within 15 calendar days after the sponsor determines that the information qualifies for reporting, written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice.

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

FDA Review of an NDA Submission and FDA Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. An NDA is a request for approval to market a new drug for one or more specified indications and must contain proof of the drug's safety and efficacy for the requested indications. FDA must approve an NDA before a drug may be marketed in the U.S. For companies, the marketing application is required to include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, 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 effectiveness of the investigational drug product for the proposed indication to the satisfaction of the FDA. In most cases, the submission of an NDA is subject to a significant application user fee. Fee exceptions or fee waivers may be obtained under certain limited circumstances.

The FDA conducts a preliminary review of all NDAs within the first 60 days of its receipt, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

During its review of an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA, including drug component manufacturing (such as APIs), finished drug product manufacturing and control testing laboratories. The FDA will not approve an NDA unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

In addition, as a condition of approval, or post-approval if it becomes aware of a serious risk associated with the use of the product, the FDA may require the submission of a Risk Evaluation and Mitigation Strategy

("REMS"), if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without a REMS, if required. A REMS may include one or more elements, including medication guides, physician communication plans, patient package insert and/or elements to assure safe use, such as special training or certification for prescribing or dispensing, restricted distribution methods, special monitoring, patient registries or other risk minimization tools.

Under the Prescription Drug User Fee Act ("PDUFA") guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA, for a new molecular entity, to review and act on the submission, and six months from the filing date of a new molecular entity NDA with priority review. Accordingly, this review process typically takes 12 months and eight months, respectively, from the date the NDA is submitted to the FDA. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

In addition, under the Pediatric Research Equity Act of 2003, as amended ("PREA"), certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug 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 FDA may, on its own initiative or at the request of the applicant, 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 sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan ("PSP"), within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that 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 FDA and the sponsor must reach an agreement on the PSP. 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 preclinical studies, early phase clinical trials and/or other clinical development programs.

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

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter generally outlines the deficiencies in the submission and contains a statement of specific conditions that must be met in order to secure final approval of the NDA and it may require additional clinical or preclinical testing in order for FDA to reconsider the application. If a Complete Response Letter is issued, the applicant may resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application, or request a hearing. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug'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

studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, which is generally a disease or condition that affects either (i) fewer than 200,000 individuals in the U.S. or (ii) more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making the product available in the U.S. for this type of disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status 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 is entitled to orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications to market the same product for the same indication for seven years, except in certain limited circumstances, including if a subsequent product with the same active ingredient for the same indication 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, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan drug has exclusivity. 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.

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

Expedited Development and Review Programs for Drugs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs that were intended to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. Some of these programs are referred to as Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients earlier than under standard FDA development and review procedures.

The FDA has a Fast Track designation program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended, whether alone or in combination with one or more other products, to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request that the FDA grant the product Fast Track designation any time before receiving NDA approval but ideally no later than the pre-NDA meeting. Fast Track designation provides increased opportunities for sponsor interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA for a Fast Track designated product on a rolling basis before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application. The FDA's goal for reviewing a Fast Track application does not begin until the last section of the

NDA is submitted. Fast Track designation may be rescinded if the designation is no longer supported by data emerging in the clinical trial process.

Additionally, a drug may be eligible for designation as a Breakthrough Therapy if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The benefits of Breakthrough Therapy designation include the same benefits as Fast Track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Breakthrough Therapy designation comes with all of the benefits of Fast Track designation, which means that the sponsor may file sections of the NDA for review on a rolling basis if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; or taking other steps to design the clinical trials in an efficient manner.

A product may also be eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be demonstrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes and evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications and to shorten the FDA's goal for taking action on a marketing application from ten months to six months for an NDA from the date of filing. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

A product may also be eligible for accelerated approval if it treats a serious or life-threatening disease or condition, generally provides a meaningful advantage over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality ("IMM") that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Accelerated approval by the FDA is generally contingent on a sponsor's agreement to conduct, in an adequate and diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. These confirmatory trials must be completed with due diligence, and, under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw the product from the market (and withdraw its approval). As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, could result in the FDA's withdrawal of the approval and require the withdrawal of the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

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

Hatch-Waxman Amendments

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that 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. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application ("ANDA"). An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product, known as a reference listed drug ("RLD"). ANDAs are termed "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through *in vitro*, *in vivo* or other testing.

U.S. Non-Patent Exclusivity

Under the Hatch-Waxman Amendments, the FDA may not approve (or in some cases accept) an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. Market exclusivity provisions under the FDCA can delay the submission or the approval of certain follow-on applications. The FDCA provides a five-year period of non-patent data exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity ("NCE"). A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, the FDA may not accept for review an ANDA, for a generic version of the drug or a 505(b)(2) NDA for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval, until the expiration of five years unless the submission is accompanied by a paragraph IV certification, which states the proposed generic drug will not infringe one or more of the already approved product's listed patents or that such patents are invalid or unenforceable, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides three years of market exclusivity for non-NCE NDAs, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity period covers only the conditions of use associated with the new clinical investigations and often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication, but it generally would not protect the original, unmodified product from generic competition. In other words, it does not prohibit the FDA from approving follow-on applications that do not reference the protected clinical data. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of regulatory market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods for all formulations, dosage forms, indications of the active moiety, and listed patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining. The issuance of a Written Request does not require the sponsor to undertake the described clinical trials.

Hatch-Waxman Patent Certification and the 30-Month Stay

In seeking approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Upon approval, each of the patents listed by the NDA sponsor is published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Upon submission of an ANDA or 505(b)(2) NDA, an applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book that:

- no patent information on the drug product that is the subject of the application has been submitted to the FDA;
- such patent has expired;
- the date on which such patent expires; or
- such patent is invalid, unenforceable or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted.

Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired. If the ANDA or 505(b)(2) NDA applicant has provided a paragraph IV certification the applicant must send notice of the paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. If the paragraph IV certification is challenged by an NDA holder or the patent owner(s) asserts a patent challenge to the paragraph IV certification, the FDA may not approve that application until the earlier of 30 months from the receipt of the notice of the paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent was favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation. If the drug has NCE exclusivity and the ANDA is submitted four years after approval, the 30-month stay is extended so that it expires seven and a half years after approval of the innovator drug, unless the patent expires or there is a decision in the infringement case that is favorable to the ANDA applicant before then.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Amendments, which permits a patent term restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date, provided the sponsor acted with diligence. 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. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question and within 60 days of drug approval. A patent that covers multiple drugs 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 or restoration in consultation with the FDA.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling

claims are subject to prior FDA review and approval. There are also annual prescription drug product program fee requirements for marketed products.

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

FDA regulations require that products be manufactured in specific facilities and in accordance with cGMP regulations which require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs and those supplying products, ingredients and components of them are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the U.S. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval of a drug is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events 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 post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Other potential consequences include, among other things:

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

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted by a manufacturer and any third parties acting on behalf of a manufacturer only for the approved indications and in a manner consistent with the approved label for the product. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), which regulates the distribution of drugs and drug samples at the federal level and sets

minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Failure to comply with any of these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those evaluated by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees and/or imposed permanent injunctions under which specified promotional conduct is changed or curtailed.

Review and Approval of Drugs in the European Union

In the EU, the research, development and commercialization of medicinal products are also subject to extensive regulatory requirements. As in the U.S., medicinal products can only be marketed if a marketing authorization ("MA") from the competent regulatory agencies has been obtained.

Clinical Trial Approval

In April 2014, the European Union adopted a Clinical Trials Regulation (EU) No 536/2014 (the "Clinical Trials Regulation") which replaced the previous Clinical Trials Directive 2001/20/EC on January 31, 2022, subject to transitional provisions which meant that since January 31, 2025, all clinical trials in the EU have been subject to the Clinical Trials Regulation. The Clinical Trials Regulation is directly applicable in all European Union Member States, meaning no national implementing legislation in each European Union Member State is required. The legislation aims at simplifying and streamlining the approval of clinical trials in the European Union. For instance, the Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

Drug Review and Approval

In the European Union, medicinal products can only be commercialized after obtaining an MA. There are two types of MA:

The centralized MA, which is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the EMA. A centralized MA is valid throughout the entire territory of the European Union and in the additional Member States of the European Economic Area ("EEA"), which is comprised of the Member States of the European Union plus Norway, Iceland and Liechtenstein. The centralized procedure is mandatory for certain types of products, including medicines produced by certain biotechnological processes, advanced therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines), products designated as orphan medicinal products and products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the European Union, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union.

National MAs, which are issued by the competent authorities of the Member States of the European Union and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in a Member State of the European Union, this national MA can be recognized in another Member State through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the European Union make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. Following approval, MA holders are subject to ongoing obligations, including pharmacovigilance and safety reporting requirements.

Data and Market Exclusivity

In the European Union, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic applicants from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic (abbreviated) MA, for eight years from the date on which the reference product was first authorized in the European Union. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic or medicinal product can be placed on the European Union market until the expiration of the market exclusivity. The overall ten-year period may be extended to a maximum of 11 years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are determined to bring a significant clinical benefit in comparison with existing therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company could nevertheless also market another version of the product if such company obtained an MA based on an application with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Orphan Drug Designation and Exclusivity

A product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (1) the product 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 European Union when the application is made or (b) it is unlikely that the product, without the benefits derived from orphan status, would generate sufficient return in the European Union to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union or, if such method exists, the product will be of significant benefit to those affected by that condition. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers. The application for orphan designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the MA application if the orphan designation has been granted, but not if the designation is still pending at the time the MA application is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no "similar medicinal product" may be placed on the market in the European Union. 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. However, an MA may be granted to a similar medicinal product with the same indication as an authorized orphan product during the ten-year period with the consent of the MA holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same indication as an authorizes orphan product if the applicant can establish that its similar product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, 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.

The aforementioned European Union rules are generally applicable in the EEA, which consists of the European Union Member States, plus Iceland, Liechtenstein and Norway.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the European Union for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval and, in April 2024, the European Parliament proposed amendments to the legislative proposals. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into European Union law.

Other U.S. Healthcare Laws and Compliance Requirements

Healthcare providers, including physicians, and third-party payors play a significant role in determining what drug products are used by patients. Our current and future arrangements with healthcare providers, third party payors, patients and other parties within the healthcare industry as well as our business operations more generally may implicate broadly applicable fraud and abuse and other healthcare laws and regulations. Within the U.S., restrictions under applicable federal and state healthcare laws and regulations, including certain laws and regulations applicable only if we have marketed products, include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the anti-kickback statute or specific intent to violate it in order to have committed a violation;
- the federal False Claims Act (“FCA”), which imposes criminal and civil penalties on individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government and actions under the FCA may be brought by private whistleblowers as well as the government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the FCA;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary’s selection of a particular provider, practitioner or supplier of services reimbursable by Medicare or a state healthcare program;
- the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), as amended, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also establishes requirements related to the privacy, security, and transmission of individually identifiable health information which apply to many healthcare providers, physicians and third-party payors with whom we interact;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the FDCA, which, among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;
- federal laws, such as the Medicaid Drug Rebate Program, 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 governmental healthcare programs;
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the so-called federal “sunshine law” or Open Payments which requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to teaching hospitals, physicians, and other healthcare

practitioners, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and state laws which regulate interactions between pharmaceutical companies and healthcare providers, require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, require pharmaceutical companies to report information on transfers of value to other healthcare providers, marketing expenditures or pricing information and/or require licensing of sales representatives. State laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain.

Given the breadth of the laws and regulations and narrowness of any exceptions, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, 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, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

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

Healthcare Reform

In the U.S. and some foreign jurisdictions, there have been and continue to be ongoing efforts to implement legislative and regulatory changes regarding the healthcare system. Such changes could prevent or delay marketing approval of any product candidates that we may develop, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Although we cannot predict what healthcare or other reform efforts will be successful, such efforts may result in more rigorous coverage criteria, in additional downward pressure on the price that we, or our future collaborators, may receive for any approved products or in other consequences that may adversely affect our ability to achieve or maintain profitability.

Within the U.S., the federal government and individual states have aggressively pursued healthcare reform. For example, the Affordable Care Act ("ACA"), implemented in 2010, substantially changed the way healthcare is financed by both governmental and private insurers and contains a number of provisions that

affect coverage and reimbursement of drug products and/or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. Other aspects of healthcare reform, such as expanded government enforcement authority, could also affect our business.

Beyond the ACA, there have been ongoing health care reform efforts. Drug pricing and payment reform has been an ongoing focus of the Trump Administration and was a focus of the Biden Administration. For example, federal legislation enacted in 2021 eliminated the statutory cap on Medicaid drug rebate program rebates (currently set at 100% of a drug's "average manufacturer price") effective January 1, 2024. As another example, the Inflation Reduction Act of 2022 ("IRA") includes a number of changes intended to address rising prescription drug prices in Medicare Parts B and D. These changes, which have varying implementation dates, include caps on Medicare Part D out-of-pocket costs for beneficiaries, Medicare Part B and Part D drug price inflation rebates, a new Medicare Part D manufacturer discount drug program (replacing the ACA Medicare Part D coverage gap discount program) and a drug price negotiation program for certain high spend Medicare Part B and D drugs (with the first set of negotiated prices having gone into effect January 1, 2026). The focus on health care reform, including reform of drug pricing and payment, has continued in the wake of the IRA.

The One Big Beautiful Bill Act of 2025 ("OBBBA"), for example, imposed significant reductions in Medicaid funding, additional work requirements for Medicaid recipients, and more frequent reenrollment requirements. These changes are expected to place substantial pressure on state Medicaid budgets, reduce enrollment, and limit covered services, which could decrease utilization of, and reimbursement for, our products, if approved.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. The Trump Administration has issued executive orders and supported proposed regulatory initiatives in 2025 that could have a significant impact on the prices that we, or any collaborators, may receive for any approved products.

On May 12, 2025, President Trump signed an executive order directing the Secretary of HHS to set and communicate most-favored-nation ("MFN") price targets to manufacturers and propose a rulemaking plan to impose MFN pricing if "significant progress" is not made, and also directing the federal government to support regulatory paths to allow direct-to-patient sales for companies that meet these targets. The executive order further states that the Administration will take additional action (for example, examining whether marketing approvals should be modified or rescinded or considering individual drug importation waiver authorities) should manufacturers fail to offer American consumers the MFN lowest price. In July 2025, President Trump sent letters to certain pharmaceutical companies demanding that these companies extend MFN pricing to Medicaid and newly launched drugs as well as move to direct-to-consumer models priced at MFN pricing, and soliciting binding commitments by September 29, 2025. Since this time, multiple drug manufacturers have announced plans to, for certain of their drugs, lower prices to reflect similar pricing around the world, and to sell these reduced-price drugs on a direct-to-consumer purchasing platform developed by the federal government; however, it is not known what results will occur to the extent the recipients of these letters do not reduce their U.S. prices.

On December 19, 2025, CMS released two proposed rules that would incorporate MFN pricing principles into federal reimbursement for prescription drugs. The first proposal, the Global Benchmark for Efficient Drug Pricing Model ("GLOBE") for Medicare Part B, would require manufacturers of specified single source drugs and sole source biologics to pay incremental rebates based on international benchmark prices, with participation triggered for products meeting CMS's spending and eligibility criteria. The second proposal, the Guarding U.S. Medicare Against Rising Drug Costs ("GUARD") model for Medicare Part D, would similarly mandate manufacturer rebates for qualifying sole source drugs where the Medicare net price exceeds an MFN benchmark derived from international reference pricing methodologies. As proposed, GLOBE would begin a five year performance period on October 1, 2026 and GUARD would begin its performance period in 2027. These proposals will likely be subject to legal challenges that could delay their implementation or modify their impact

on manufacturer pricing and revenue. Additionally, in November 2025, CMS introduced the GENErating cost Reductions fOr U.S. Medicaid ("GENEROUS") Model, a voluntary MFN framework for manufacturers participating in the Medicaid Drug Rebate Program. Although it is voluntary, the GENEROUS Model could also impact the drug pricing landscape for manufacturers.

Individual states have also been increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. We expect that additional state and federal healthcare reform measures will be adopted in the future, particularly in light of the new presidential administration, any of which could limit the amounts that federal and state governments will pay for healthcare products and services.

Healthcare reform efforts have been and may continue to be subject to scrutiny and legal challenge. For example, with respect to the ACA, tax reform legislation was enacted that eliminated the tax penalty established for individuals who do not maintain mandated health insurance coverage beginning in 2019 and, in 2021, the U.S. Supreme Court dismissed the latest judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. As another example, revisions to regulations under the federal anti-kickback statute would remove protection for traditional Medicare Part D discounts offered by pharmaceutical manufacturers to pharmacy benefit managers and health plans. Pursuant to court order, the removal was delayed and subsequent legislation imposed a moratorium on implementation of the rule until January 2032. As another example, the IRA drug price negotiation program has been challenged in litigation filed by various pharmaceutical manufacturers and industry groups.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our potential product candidates. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. 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 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 of our products, if approved in those countries.

Coverage and Reimbursement

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

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Coverage and reimbursement

by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

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

In the U.S., there is no uniform policy of coverage and reimbursement for products among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford our product candidates, if approved, and so will significantly affect our ability to successfully commercialize any such product candidates.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Coverage may not be available for any product that we commercialize or may be subject to controls imposed by third party payors to manage utilization (e.g., requiring specific approval for use of a product in a particular patient for coverage). Even if coverage is available, the resulting reimbursement payment rates may not be adequate or may require patient out-of-pocket costs that patients find unacceptably high. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. Additionally, we, or our collaborators, will be required to obtain coverage and reimbursement for any companion diagnostic tests developed separate and apart from the coverage and reimbursement we may seek for our product candidates, once approved.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the U.S. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or requested by 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. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A Member State may approve a specific price for the medicinal product or it may instead

adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

There can be no assurance that our product candidates, even if they are approved for sale in the U.S. or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, or that coverage and an adequate level of reimbursement will be available or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations, and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information and could apply now or in the future to our operations or the operations of our partners. In the U.S., such laws and regulations include data breach notification laws, consumer privacy laws, health information privacy and security laws and consumer protection laws. Privacy and security laws, regulations and other obligations are constantly evolving and may conflict with each other to complicate compliance. The federal government and several states have also recently taken steps to restrict data transactions involving countries outside the U.S. For example, the Department of Justice's January 8, 2025, Rule on Preventing Access to U.S. Sensitive Personal Data and Government-Related Data by Countries of Concern or Covered Persons, prohibits transfers of certain types of data, including health data, genetic data, and biospecimens, to countries of concern, including China. Actual or alleged violations of these laws and regulations may be punishable by criminal and/or civil sanctions.

Employees and Human Capital Resources

As of February 15, 2026, we had 59 full-time employees, of which 15 had M.D. or Ph.D. degrees. Within our workforce, 31 employees were engaged in research and development and 28 were engaged in general and administrative activities, including business development, finance, legal and corporate administration as of February 15, 2026. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase shareholder value and support the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries and bonuses, opportunities for equity ownership, professional development programs that enable continued learning and growth and a robust employment package that promotes well-being across multiple aspects of employees' lives, including health care, retirement planning and paid time off.

Corporate Information

We were incorporated under the laws of the State of Delaware in August 2019 under the name Sling Therapeutics, Inc., and changed our name to Sionna Therapeutics, Inc. in November 2021. Our principal executive offices are located at 21 Hickory Drive, Suite 500, Waltham, MA 02451, and our telephone number is (617) 819-2020. We have one subsidiary, Sionna Therapeutics Securities Corporation (f/k/a Sling Therapeutics Securities Corporation), formed in 2020 under the laws of the Commonwealth of Massachusetts.

Available Information

Our website address is *www.sionnatx.com*. The information contained in or accessible from our website is not incorporated into this Annual Report, and you should not consider it part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and

15(d) of the Securities Exchange Act of 1934, as amended, 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 Securities and Exchange Commission (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 *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.

Our code of business conduct and ethics, corporate governance guidelines and the charters of our Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are available through the “Investors” portion of our website. Additionally, we routinely post information to the “Investors” section of our website that may be important to investors. We encourage investors and potential investors to consult our website regularly for information about our Company.

ITEM 1A. RISK FACTORS

Our future operating results could differ materially from the results described in this Annual Report due to the risks and uncertainties described below. You should consider carefully the following information about risks below in evaluating our business. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects will likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline. In addition, we cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See "Cautionary Note Regarding Forward-Looking Statements" on page 3 of this Annual Report for discussion of some of the forward-looking statements that are qualified by these risk factors. Factors that could cause or contribute to such differences include those factors discussed below.

Risks Related to Our Limited Operating History, Financial Condition and Need for Additional Capital

We are a clinical-stage biopharmaceutical company and have incurred significant operating losses since inception and anticipate that we will continue to incur significant operating losses for the foreseeable future. Our net losses were $75.3 million and $61.7 million for the years ended December 31, 2025 and 2024, respectively. We had an accumulated deficit of $256.4 million and $181.1 million as of December 31, 2025 and 2024, respectively. We may never achieve or maintain profitability.

We are a clinical-stage biopharmaceutical company with a limited operating history. We have incurred operating losses in each year since our inception. Our net losses were $75.3 million and $61.7 million for the years ended December 31, 2025 and 2024, respectively. We had an accumulated deficit of $256.4 million and $181.1 million as of December 31, 2025 and 2024, respectively. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders’ equity and working capital.

Since our inception in 2019, we have devoted substantially all of our efforts and financial resources to the development of our product candidates, the continuation of ongoing clinical trials, the commencement of new clinical trials and ongoing manufacturing to support our product candidates. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have not yet demonstrated an ability to conduct later-stage clinical trials, obtain regulatory approval, manufacture any product on a commercial scale or conduct sales and marketing activities necessary for successful product commercialization, and there is no assurance that we will accomplish any of these abilities in the future. Our limited operating history makes any assessment of our future success and viability subject to significant uncertainty. In addition, if we obtain marketing approval for any of our product candidates, we will incur significant sales, marketing and manufacturing expenses. We expect to continue to incur significant costs associated with operating as a public company. As a result, we expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or

when we will become profitable, if at all. Even if we become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

The amount of our future losses is uncertain, and our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline. Our operating losses may fluctuate significantly from quarter to quarter and from year to year. We anticipate that our expenses will increase substantially if, and as, we:

- continue to advance clinical development of our current and future product candidates, including conducting our ongoing and planned clinical trials;
- continue to advance our research and preclinical activities and seek to discover and develop additional product candidates;
- continue to utilize third parties to manufacture our product candidates and ensure sufficient supply of our manufacturing of drug substances and drug products;
- continue to develop, maintain, expand and protect our intellectual property portfolio (including intellectual property obtained through license agreements) and provide reimbursement of third-party expenses related to our patent portfolio;
- attract, hire and retain additional qualified personnel;
- seek regulatory approvals for any current or future product candidates that successfully complete clinical trials;
- make any potential milestones, royalties or other payments due under any current or future in-license, collaboration or other agreements;
- undertake any pre-commercial activities and scale up external commercial-scale manufacturing capabilities;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain regulatory approval;
- add additional operational, financial, clinical, quality and management information systems; and
- incur additional audit, legal, regulatory, tax and other expenses with being a public company.

We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

Given the numerous risks and uncertainties associated with pharmaceutical product development, it is not certain if any of our current or future product candidates will advance through late-stage development or be approved for commercial sale; therefore, we are unable to predict if or when we will generate product revenue or achieve or maintain profitability.

Even if we successfully complete development and obtain the necessary regulatory approval for commercialization for any of our product candidates, we anticipate incurring significant costs associated with launching and commercializing such products. If we fail to become profitable or do not sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or cease operations.

We will need substantial additional funding to develop and, if approved, commercialize our product candidates and identify and invest in new product candidates. We may be unable to raise capital on acceptable terms, if at all, and, as a result, we may be required to delay, reduce or eliminate our product development programs or commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approvals and achieve product sales. We expect to continue to incur significant and increasing expenses and operating losses for the foreseeable future as we initiate and conduct clinical trials of our current and any future product candidates, scale-up and manufacture our product candidates, advance our preclinical programs, seek marketing and regulatory approvals for any product candidates that successfully complete clinical trials and commercialize our products, if approved. Because the outcome of any clinical trial or preclinical study is highly uncertain, we cannot reliably estimate the actual amount of financing necessary to successfully complete the development and commercialization of any of our product candidates.

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $310.3 million, including net proceeds of $199.6 million from our initial public offering in February 2025. We believe that, based upon our current operating plans, our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations into 2028. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including but not limited to changes in progress of our development activities, acquisitions of additional product candidates and changes in regulations. Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the scope, timing, progress, costs, complexity and results of discovery, preclinical development and clinical trials for our current or future product candidates, including any additional expenses attributable to adjusting our anticipated development plans;
- the number of clinical trials required for regulatory approvals of our current or future product candidates;
- the extent to which we develop, in-license or acquire other product candidates in our pipeline;
- the costs and timing of process development and manufacturing scale-up activities associated with our product candidates and other programs as we advance them through preclinical and clinical development and, if approved, commercialization;
- the number and development requirements of product candidates that we may pursue;
- the timing and amount of the milestone, royalty or other payments we must make to Sanofi SA (“Sanofi”), the Cystic Fibrosis Foundation, AbbVie Global Enterprises Ltd. (“AbbVie”) and any other third parties;
- the costs, timing and outcome of regulatory review of our product candidates;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors (or patients’ willingness to pay out-of-pocket for any approved products in the absence of such coverage) and adequate market share and revenue for any approved products;
- the revenue, if any, received from commercial sales of any product candidates for which we receive marketing approval;
- the effect of macroeconomic trends including fluctuating inflation levels, capital markets disruption, and interest rates;

- addressing any potential supply chain interruptions or delays, which may be due in part to international tariffs; and
- the costs of operating as a public company.

We will require additional capital to achieve our business objectives. Additional funds may not be available on a timely basis, on favorable terms or at all, and such funds, if raised, may not be sufficient to enable us to continue implementing our long-term business strategy. Further, our ability to raise additional capital may be adversely impacted by potentially worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States ("U.S.") and worldwide resulting from factors that include but are not limited to, fluctuating inflation and capital markets disruptions, international tariffs, the Russia-Ukraine and Israel-Gaza conflicts, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, uncertainty about economic stability and other factors. For example, the U.S. government has imposed substantial tariffs on most countries throughout the world and has further threatened to continue to broadly impose tariffs, which could lead to corresponding punitive actions by the countries with which the U.S. trades. If the equity and credit markets continue to deteriorate, it may make any necessary debt or equity financing more difficult to obtain, more costly and more dilutive. If we are unable to raise sufficient additional capital, we could be forced to curtail our planned operations and the pursuit of our growth strategy, or even cease operations.

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

Until such time, if ever, as we can generate substantial revenues from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings or other capital sources, such as grants, collaborations, licenses or other similar 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, our stockholders' ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as a common stockholder. Debt financing and preferred equity financing may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt or making capital expenditures. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

If we raise additional funds through grants, collaborations, licenses or other similar arrangements with third parties, we may be required to relinquish valuable rights to our future revenue streams, intellectual property or product candidates, grant licenses on terms that may not be favorable to us and/or that may reduce the value of our common stock or commit us to future payment streams. If we are unable to raise additional funds through equity or debt financings when needed or on terms acceptable to us, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, or on less favorable terms than we would otherwise choose.

We maintain the majority of our cash and cash equivalents in accounts with major U.S. and multi-national financial institutions, and our deposits at certain of these institutions exceed insured limits. Market conditions and changes in financial regulations and policies can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position. In addition, changes in regulations governing financial institutions are beyond our control and difficult to predict; consequently, the impact of such changes on our business and results of operations is difficult to predict and may have an adverse effect on us.

Risks Related to the Discovery and Development of Our Product Candidates

We are substantially dependent on the success of at least one of our nucleotide binding domain 1 ("NBD1") stabilizers. If we are unable to advance an NBD1 stabilizer product candidate into later-stage clinical development or unable to obtain regulatory approval and commercialize an NBD1 stabilizer-anchored combination therapy for the treatment of cystic fibrosis, or experience significant delays in doing so, our business will be materially harmed.

To date, as an organization, we have not completed the development of any product candidates. We are substantially dependent on the success of at least one of our NBD1 stabilizer product candidates, SION-719 and SION-451, which are currently in development for the treatment of cystic fibrosis ("CF"). Our NBD1 stabilizers are being developed for use either in combination with one of our complementary modulator candidates or the standard of care. We are currently evaluating SION-719 in a Phase 2a proof-of-concept clinical trial as an add-on to the standard of care for CF and SION-451 in a Phase 1 dual combination trial with each of our two most advanced complementary modulator candidates, galicaftor (SION-2222) and SION-109.

The success of SION-719, SION-451 and our other product candidates will depend on several factors, including the following:

- successful and timely initiation and enrollment of clinical trials and completion of clinical trials with favorable results;
- the safety, tolerability and pharmacokinetic profile of our product candidates observed in clinical trials, including in combination with the standard of care;
- acceptance of regulatory submissions by the U.S. Food and Drug Administration (“FDA”) and/ or comparable foreign regulatory authorities for the conduct of clinical trials of our product candidates, and the proposed design of our planned clinical trials;
- the frequency and severity of adverse safety findings in nonclinical studies and adverse events (“AEs”) in clinical trials;
- timely and successful completion of preclinical studies, including toxicology studies, biodistribution studies and *in vitro* dose projection studies in animals, where applicable;
- acceptance of our products, if approved, by CF patients, the medical community and third-party payors, and their perspective on the cost, safety, tolerability and efficacy and perceived advantages of alternative therapies for CF, including the standard of care;
- maintaining relationships with contract research organizations (“CROs”) and clinical sites for the clinical development of our product candidates and the ability of such CROs and clinical sites to comply with clinical trial protocols, Good Clinical Practices (“GCPs”) and other applicable requirements;
- demonstrating the safety and efficacy of our product candidates to the satisfaction of applicable regulatory authorities;
- receipt and maintenance of marketing approvals from applicable regulatory authorities for our initial target indication and label expansions to include new populations;
- our ability to establish and maintain relationships with third-party manufacturers and their ability to comply with current good manufacturing practices (“cGMPs”), as well as our ability to make arrangements with third-party manufacturers to ensure adequate supply for our clinical trials and commercial manufacturing capabilities at a cost and scale sufficient to support commercialization;
- the availability of drug substance and drug product for use in production of our product candidates;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- obtaining, establishing, maintaining and enforcing patent and any potential trade secret protection or regulatory exclusivity for our product candidates;
- maintaining an acceptable safety profile of our product candidates following regulatory approvals, if any;
- the sufficiency of our financial resources to fund our operations and our ability to raise necessary additional funds;
- the impact of competition with other products approved for the treatment of CF and product candidates in development for the treatment of CF; and
- maintaining and growing an organization of people who can develop and, if approved, commercialize, market and sell our current or future product candidates.

If we are unable to develop, receive marketing approval for and successfully commercialize our product candidates, or if we experience delays as a result of any of the above factors or otherwise, our business would be significantly harmed.

We are early in our development efforts. If we are unable to successfully develop, receive regulatory approval for and commercialize any product candidate, or experience significant delays in doing so, our business will be substantially harmed.

We are early in our development efforts. Each of our product candidates will require additional preclinical and/or clinical development and regulatory approval, and will require us to obtain sufficient manufacturing supply, capacity and expertise. We have not completed any clinical trials of our product candidates in any CF patients to date. Further, we will be required to build a commercial organization or successfully outsource commercialization, and make substantial investment and significant marketing efforts before we generate any revenue from product sales, if ever. Given our early stage of development, it will take several years before we can demonstrate the safety and efficacy of a product candidate sufficient to warrant approval for commercialization, if we can do so at all.

We do not have complete control over many of the factors that affect our development efforts, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize the product candidates we develop, which would materially harm our business. If we do not receive marketing approvals for our product candidates or any future product candidate we develop or if we experience delays in such approvals, we may not be able to continue our operations.

Further, conducting clinical trials in foreign countries, as we are currently doing and plan to do in the future for our current or future product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, failure to properly translate or interpret patient-reported outcome endpoints, managing additional administrative burdens associated with foreign regulatory schemes as well as political and economic risks relevant to such foreign countries.

The foregoing makes our ability to successfully and timely complete development of our product candidates and obtain regulatory approval for them less certain. If we are unable to develop, or obtain marketing approval for, or, if approved, successfully commercialize our product candidates, our business, financial condition, results of operations and prospects would be materially harmed.

We intend to develop a proprietary dual combination of an NBD1 stabilizer with a complementary modulator and/or an NBD1 stabilizer as an add-on to the standard of care. Developing combination treatments increases complexity and risk, including risks of drug-drug interactions, unforeseen side effects or failures in our clinical trials that could delay or prevent their regulatory approval or limit the commercial profile of an approved label.

The current treatment paradigm in CF for all patients with the F508del mutation is based on a combination of drug therapies. We are currently evaluating SION-719 in combination with the standard of care in a Phase 2a proof-of-concept trial in CF patients, which we initiated in October 2025. We are also currently evaluating SION-451 in dual combinations with our two most advanced complementary modulator candidates, SION-2222 and SION-109 in a Phase 1 trial in healthy volunteers. The development of a proprietary dual combination is our prioritized development path. In either development scenario, the use of our product candidates in combination with each other or with an approved product may subject us to risks that we would not face if our product candidates were being developed to be administered as a monotherapy.

For example, either the combination of our product candidates with each other, or an NBD1 stabilizer with the standard of care, may result in adverse side effects or toxicities that the product candidates or other therapy do not produce when used alone. In addition, the product candidates may interact with each other, or with the approved product, in undesirable ways that could negatively impact the efficacy of our product candidates, any components of the approved product, or the combination as a whole. Testing product candidates in combination with each other and with an approved therapy may increase the risk of significant

adverse effects or failed clinical trials. The timing, outcome and cost of developing products to be used in combination with other therapies is difficult to predict and dependent on a number of factors that are outside our reasonable control.

In addition, to the extent we choose to develop and commercialize a product candidate for use in combination with an approved therapy, any safety, efficacy, regulatory, manufacturing or supply issues that could arise with respect to the approved therapy could have an adverse impact on us. Prescribing information for the approved therapy, such as risk information like a boxed warning, or limitations of use, could negatively impact our ability to develop and commercialize a product as an add-on to the approved therapy. If the approved therapy is replaced as the standard of care, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials, the outcome of which would be uncertain and may not be predicted by earlier trials, or we may not be able to obtain adequate reimbursement from third-party payors. Further, the FDA or comparable foreign regulatory authorities could revoke approval of a therapy we evaluate in combination with our product candidate.

The occurrence of any of these risks could result in an add-on product candidate, if developed and approved, being removed from the market or being less successful commercially. If the FDA or comparable foreign regulatory authorities revoke their approval of, or if safety, efficacy, manufacturing, or supply issues arise with respect to, therapies we choose to evaluate in combination with any of our product candidates, we may be unable to obtain regulatory approval of or to commercialize such product candidates in combination with these therapies. If we experience safety, tolerability or toxicity issues in any of our ongoing or planned combination treatment clinical trials, or the data from these trials regarding the efficacy of the combinations are not favorable, our clinical development plans could be materially negatively affected or delayed, or we may not receive regulatory approval for our product candidates, which would materially harm our business and likely cause the market price of our common stock to decline.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time-consuming and inherently unpredictable. If we are not able to obtain the required regulatory approval for any product candidate, our business will be substantially harmed.

We are not permitted to market, commercialize, sell or promote any product candidate in the U.S. until we receive regulatory approval of a new drug application (“NDA”) for such product candidate in a specific indication from the FDA. Our business is dependent on our ability to successfully complete preclinical and clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize our product candidates and any future product candidates in a timely manner. The time required to obtain approval or other marketing authorizations by the FDA and comparable foreign authorities is unpredictable, and it typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations and the type and amount of data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that we may never obtain regulatory approval for any product candidates in the future.

Prior to obtaining approval to commercialize any product candidate in the U.S. or abroad, we must demonstrate with substantial evidence from well-controlled clinical trials, to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidate is safe and effective for its intended use. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or after approval, or it may object to elements of our clinical development programs. For example, to receive regulatory approval for an NBD1 stabilizer as an add-on to standard of care, we would have to demonstrate clinically meaningful improvements in efficacy with the NBD1 stabilizer co-administered with the standard of care, as compared to the standard of care alone. It may be harder to show a clinically meaningful improvement in efficacy in a clinical trial where all participants are receiving the standard of care. Furthermore, because we intend to develop an NBD1 stabilizer product candidate in combination with one of our complementary modulator product candidates, we will have to satisfy the regulatory agencies’ requirements to demonstrate the contribution of each component in the combination. As neither product candidate in this potential combination is an approved drug, the FDA and other

regulatory authorities will require full demonstration of the safety of each component (alone and in combination), as well as the efficacy of the combination (and the contribution of each component). In either combination product scenario (proprietary dual combination or add-on to standard of care), additional safety, efficacy and/or drug-drug interaction data may be required relative to what would be required for a monotherapy.

Our current and future product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree as to the design or implementation of our clinical trials and interpretation of data from clinical trials or preclinical studies;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's benefits outweigh its risks;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA to the FDA or other submission to obtain regulatory approval in the European Union or elsewhere;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval and marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects. The FDA and comparable foreign authorities have substantial discretion in the approval process and determining when or whether regulatory approval will be granted for any product candidate that we develop. The U.S. Supreme Court's July 2024 decision to overturn prior established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which the FDA's regulations, policies and decisions may become subject to increasing legal challenges, delays or changes.

Even if we complete clinical testing and receive approval of an NDA or foreign marketing application for our current or future product candidates, the FDA or the applicable foreign regulatory agency may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post-marketing clinical trials. The FDA or the applicable foreign regulatory agency also may approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA or applicable foreign regulatory authority may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization, or failure to obtain our desired product label, would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

In addition, the FDA and other regulatory authorities may change their policies, issue additional regulations or revise existing regulations or take other actions, which may prevent or delay approval of our future product candidates under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may obtain. Further, macroeconomic and other global conditions have impacted and could in the future impact the ability of the FDA and comparable foreign regulatory authorities to provide any required approvals or marketing authorizations for our product candidates or result in the delay of such approvals or authorizations. Changes to the requirements and policies of the FDA, the SEC and other regulatory agencies with jurisdiction over our product candidates and our business could present new challenges or potential opportunities as we navigate the clinical

development and approval process for our product candidates. Some of these efforts have manifested to date in the form of personnel measures that could impact the FDA's ability to hire and retain key personnel, which could result in delays or limitations on our ability to obtain guidance from the FDA on our product candidates in development, to have preapproval inspections completed in a timely fashion, and to obtain the requisite regulatory approvals in the future.

There remains general uncertainty regarding future potential policy changes at the FDA and other regulatory agencies, which could adversely affect us or create a more challenging or costly environment to pursue the development of new therapeutic products. Additionally, state governments may attempt to address or react to changes at the federal level with changes to their own regulatory frameworks in a manner that is adverse to our operations. If we become negatively impacted by changes in regulatory policy, there could be a material adverse effect on us and our business.

Preclinical and clinical product development involves a lengthy and expensive process, with an uncertain outcome.

Our current assumptions about our product candidates' development potential are based on the data generated from preclinical studies and clinical trials; however, we may observe materially and adversely different safety results as we continue to conduct our clinical trials. In order to obtain FDA approval to market a new drug product, we must demonstrate the safety and efficacy of the drug in humans in a manner that satisfies the agency's standards. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities, including the FDA, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety, potency and efficacy of our product candidates in humans. A failure of one or more clinical trials can occur at any stage of testing or at any time during the trial process. The outcome of preclinical testing and early clinical trials may not be predictive of the results of later clinical trials as to safety or efficacy, particularly if later clinical trials have a materially different trial design. The historical failure rate for product candidates in our industry is high, particularly in the earlier stages of development. 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 products.

We have not completed all of the clinical trials required for the approval of any of our product candidates. We cannot assure you that any preclinical study or clinical trial that we are conducting, or may conduct in the future, will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

We may incur additional costs and experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We may incur additional costs and experience delays in clinical trials for our product candidates, and we do not know whether future clinical trials, if any, will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. We may experience numerous unforeseen events during or as a result of preclinical studies or clinical trials that could delay or prevent our ability to continue or complete clinical development, receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards not authorizing us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- experiencing delays in reaching, or failing to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites or prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our product candidates producing negative or inconclusive results, including failure to demonstrate statistical significance, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;

- failing to demonstrate statistical significance in clinical trials of our product candidates, which may impact the timing and design of late-stage clinical trials for such product candidates, or failing to demonstrate statistical significance in late-stage trials despite promising early stage results;
- the number of patients required for clinical trials of our product candidates being larger than we anticipate; enrollment in these clinical trials being slower than we anticipate, for example, due to the availability of standard of care therapy, changes to standard of care therapy, and the reluctance of patients to discontinue standard of care therapy in order to participate in certain of our future clinical trials; or participants dropping out of these clinical trials or failing to return for post-treatment follow-up at a higher rate than we anticipate;
- our product candidates having undesirable side effects (including drug-drug interactions), unexpected toxicology findings, or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials;
- our third-party contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or institutional review boards requiring that we or our investigators suspend or terminate clinical development for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- future collaborators, if any, conducting clinical trials in ways they view as advantageous to them but that are suboptimal to us;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary, including comparator drug, to conduct clinical trials of our product candidates being insufficient, inadequate or too costly; and
- budget reductions, hiring freezes, or similar actions at clinical trial sites and other institutions negatively impacting the ability of sites to conduct clinical trials or increasing the costs to us of conducting our trials, including, for example, a proposed action to freeze or reduce the budget of the National Institutes of Health as related to its funding for medical research.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not favorable or if there are safety concerns, we may, among other things:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

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

We have not yet completed all testing of any product candidate in clinical trials. Preclinical, interim, topline and preliminary results from our preclinical studies or clinical trials are not necessarily predictive of the results or analyses of such results of later clinical trials. If we cannot replicate the positive results from any preclinical studies or clinical trials of our current or potential future product candidates that have positive results, or if we suffer any other significant setbacks in our later clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our current or potential future product candidates.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical studies, Phase 1 and Phase 2a clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics, and to understand the side effects of product candidates at various doses and dosing schedules. Success in preclinical or animal studies and early clinical trials does not ensure that later large-scale efficacy trials will be successful, nor does it predict final results. Our product candidates may fail to show the desired safety, tolerability, pharmacokinetic profile, and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials, particularly because our NBD1 stabilizer product candidates target the NBD1 domain of the cystic fibrosis transmembrane conductance regulator ("CFTR") protein, a novel target which has not previously been tested in CF patients.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Such setbacks have occurred and may occur for many reasons, including: clinical sites and investigators may deviate from clinical trial protocols, whether due to lack of training or otherwise, and we may fail to detect any such deviations in a timely manner; patients may fail to adhere to any required clinical trial procedures, including post-treatment follow-up; our product candidates may fail to demonstrate effectiveness or safety in certain patient subpopulations or at all; or our clinical trials may not adequately represent the patient populations we intend to treat, whether due to limitations in our trial designs or otherwise. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development.

Similarly, from time to time, we may publish interim, topline or preliminary results from our preclinical studies and clinical trials, which are based on a preliminary analysis of then-available data. We make assumptions, estimations, calculations and conclusions as part of our preliminary analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, 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. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or topline results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim, topline and preliminary data should be viewed with caution until the final data are available. Adverse differences between interim, topline or preliminary data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

For example, central to our pipeline prioritization strategy is our application of an *in vitro* electrophysiology assay to measure CFTR function in a CF model, known as the cystic fibrosis human bronchial epithelial ("CFHBE") model, which uses lung cells from CF patients and has been shown to be predictive of clinical outcomes for approved CFTR modulators. In preclinical studies using our CFHBE model, the combination of either SION-719 or SION-451 with one of our complementary modulators or the components of Trikafta showed significant improvement in *in vitro* CFTR activity and the potential for restoration of CFTR function to wild-type levels. However, we have not yet replicated such results in clinical trials, and our product candidates may fail to show the desired safety and efficacy at the dose ranges we have identified using our CFHBE model. Positive results in our preclinical studies using our CFHBE model may not be predictive of the results in clinical trials and may fail to be replicated in clinical trials.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular

product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and investors or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Targeting the NBD1 domain of the CFTR protein is novel, and the time, cost of development, and likelihood of successful product development is difficult to predict.

Our NBD1 stabilizer product candidates target the NBD1 domain of the CFTR protein, which is a novel target. Other companies have discontinued programs targeting NBD1 as they were unable to develop compounds that could successfully bind to NBD1. Given the novelty of our product candidates and the inherent risk in our plans to develop a combination or add-on therapy, we may not be able to successfully develop any products.

While products modulating the CFTR protein have been approved by the FDA and comparable foreign regulatory authorities, to date, no product that directly targets the NBD1 domain has been approved, and to our knowledge, no product candidate directly targeting the NBD1 domain is currently in development. As a result, it is difficult to predict the developmental challenges we may encounter as our NBD1 stabilizers proceed through clinical trials, including our ongoing clinical trials evaluating SION-451 in combination with each of SION-2222 and SION-109, and evaluating SION-719 as an add-on to the standard of care. It is also difficult for us to predict the time and cost of development of an NBD1 stabilizer-anchored combination therapy, whether any of our clinical trials will be successful, and whether our novel approach will result in the successful development and regulatory approval of any product candidates. Any development problems we experience in the future related to our NBD1 stabilizer product candidates or any of our complementary modulator candidates may cause significant delays or unanticipated costs, and such development problems may not be able to be solved. The novelty of our product candidates and our combination therapy approach may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. For example, the FDA could require additional studies that may be difficult or impossible to perform, or prohibitively costly. Any of these factors may prevent us from completing clinical trials that we may initiate, and obtaining regulatory approval of or commercializing any product candidates we may develop, on a timely or profitable basis, if at all.

Our preclinical studies and clinical trials may fail to demonstrate the safety and efficacy of our product candidates, or serious or unacceptable adverse side effects or unexpected toxicology findings may be identified during the development of our product candidates, which could prevent or delay further clinical development, regulatory approvals and commercialization, impact the product's labeling, if approved, increase our costs or necessitate the abandonment or limitation of the development of some of our product candidates.

Clinical trials often fail to demonstrate safety or efficacy of the product candidate studied for the target indication. If our product candidates are associated with serious or significant adverse side effects in clinical trials or have adverse safety findings in nonclinical studies, we may need to abandon their development or limit development to more narrow uses in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a benefit-risk perspective. The FDA or other comparable foreign regulatory authority or an institutional review board or ethics committee may also require that we suspend, discontinue or limit our clinical trials based on safety information, or that we conduct additional animal or human studies regarding the safety and efficacy of our product candidates, which we have not planned or anticipated. Such findings could further result in regulatory authorities failing to provide marketing authorization for our product candidates or limiting the scope of the indication, if approved. Many product candidates that initially showed promise in early-stage testing have later been found to cause adverse side effects that prevented further development of the product candidate.

Additionally, if one or more of our product candidates receives marketing approval, and we or others subsequently identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend or limit approvals of such product or seek an injunction against its manufacture or distribution;
- we may be required to recall a product;
- regulatory authorities may require additional warnings on the labels, such as a boxed warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product is distributed or administered, conduct additional clinical trials or change the labeling of a product or be required to conduct additional post-marketing studies or surveillance;
- we could be sued and held liable for harm caused to patients;
- sales of the product may decrease significantly or the product could become less competitive;
- we may not be able to achieve or maintain third-party payor coverage and adequate reimbursement; and
- our reputation and physician or patient acceptance of our products may suffer.

There can be no assurance that we will resolve any issues related to any product-related AEs to the satisfaction of the FDA or comparable foreign regulatory authorities in a timely manner or at all. Moreover, any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

We may not be able to obtain orphan drug designation or exclusivity for our product candidates, and even if we do, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

We may seek orphan drug designation or exclusivity in the indications targeted by our current or future product candidates. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. For example, under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition. In order for the FDA to grant orphan drug designation to one of our product candidates, the agency must find that the product candidate is indicated for the treatment of a condition or disease that affects fewer than 200,000 individuals in the U.S. or that affects 200,000 or more individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making the product candidate available for the disease or condition will be recovered from sales of the product in the U.S. Orphan drug designation must be requested before submitting an NDA. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet the required standard, or that the data we have provided are not adequate to justify the scientific plausibility of our product candidate.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular drug for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances such as if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated.

In addition, even after an orphan drug is approved, the FDA can subsequently approve a different product candidate for the same condition without any requirement to demonstrate potential for clinical superiority (efficacy, safety, or other major contribution to patient care) relative to a product that already has orphan designation or exclusivity. 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. After the FDA grants orphan drug designation, the generic identity of the drug or biologic and its potential orphan use

are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

A similar regulatory scheme governs approval of orphan product candidates by the European Medicines Agency ("EMA") in the European Union. The orphan product marketing exclusivity period in the European Union is ten years, which can be reduced to six years if at the end of the fifth year it is determined that a product no longer meets the criteria for orphan drug designation, including if the product is sufficiently profitable so that market exclusivity is no longer justified. The EMA may conclude that our product candidate(s) may not meet the criteria to justify orphan designation.

While we may in the future seek designations for our product candidates with the FDA and comparable foreign regulatory authorities that are intended to confer benefits such as a faster development process, an accelerated regulatory pathway or priority review, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA and comparable foreign regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review of the marketing application(s). However, there can be no assurance that we will successfully obtain such designations for our product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards of product quality, safety or efficacy required to be demonstrated in support of approval. Even if we obtain such designations for our product candidates, there can be no assurance that we will realize their intended benefits.

For example, we may seek a Fast Track Designation for one or more of our product candidates. If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may rescind the Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development activities.

We may seek Breakthrough Therapy Designation for any product candidate that we develop. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval and priority review.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. Further, the receipt of Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to conventional FDA procedures and does not assure approval by the FDA. In addition, even if any product candidate we develop qualifies for Breakthrough Therapy Designation, the FDA may later decide that the drug no longer meets the conditions for qualification and rescind the designation.

Even in the absence of obtaining Fast Track and/or Breakthrough Therapy Designations, a sponsor can seek priority review at the time of submitting a marketing application. The FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness when compared with other available therapies. Significant improvement

may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting adverse reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months from FDA's acceptance of the application for review. Priority review designation may be rescinded if a product no longer meets the qualifying criteria.

We may not be able to submit investigational new drug applications "INDs" or IND amendments to commence clinical trials on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed.

We may not be able to submit INDs for our product candidates on the timelines we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing related clinical trials to begin, or that, even if such trials do begin, issues will not arise that suspend or terminate such clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs.

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them is approved.

As part of its decision to approve or grant marketing authorization for one or more of our product candidates, the FDA or other regulatory agencies may require us to perform certain post-marketing activities, such as completion of ongoing or planned studies, initiation of new studies or post-marketing clinical trials (including to assess safety risks), or additional analyses of existing data. Typically, we are required to provide annual updates on the progress of such required activities and to complete the activities by the assigned completion dates. Later discovery of previously unknown problems with our product candidates, including AEs of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of such products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on or revisions to the labeling or marketing of a medicine;
- restrictions on the distribution or use of a medicine, including under a risk evaluation and mitigation strategy ("REMS") program;
- fines, receipt of warning or untitled letters or suspension of clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of marketing approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

Additionally, the FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. Although physicians may prescribe products for uses not described in the product's labeling, known as off-label uses, in their professional medical judgment, the FDA and comparable foreign regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we market our products, if approved, in a manner inconsistent with their approved labeling, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice and other comparable foreign regulatory agencies. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or

allegations of violations of federal and state healthcare fraud and abuse laws, state consumer protection laws and laws of other comparable foreign regulatory agencies.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize any product candidates we develop and adversely affect our business, financial condition, results of operations and prospects.

If we experience delays or difficulties in the enrollment and/or retention of patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected, and our receipt of necessary regulatory approvals could be delayed or prevented.

Successful and timely completion of clinical trials will require that we identify and enroll a sufficient number of patients. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population and competition for patients with other trials. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities, or if a large number of patients withdraw. We cannot predict how successful we will be at enrolling subjects in our clinical trials. We may conduct clinical trials that would require patients to discontinue standard of care therapy, and we may experience challenges finding, enrolling and retaining CF patients who are willing to discontinue their current treatment regimens to participate in such trials. For example, AbbVie previously terminated part of a Phase 2 trial that was intended to evaluate multiple doses of SION-3067 in combination with a fixed dose of SION-2222 because this part was deemed not enrollable due to, among other reasons, the increasing availability of the standard of care for CF. Subject enrollment is affected by other factors including:

- the patient eligibility criteria as defined in the applicable protocol;
- the size of the patient population required for analysis of the trial's primary endpoints and the process for identifying patients;
- the actual and perceived risks and benefits of the product candidate in the trial;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing third-party clinical trials including trials conducted by Vertex Pharmaceuticals, Inc. ("Vertex"), enrolling currently or in the future, and clinicians' and patients' perceptions as to the potential advantages and risks of the third-party product candidate being studied in relation to other available therapies, including the standard of care, other therapies currently approved, or that may be approved in the future, for CF, or other investigational drugs in clinical development for CF;
- the willingness of patients to be enrolled in our clinical trials;
- the success of efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- our ability to obtain and maintain informed consent;
- the risk that patients enrolled in our clinical trials will drop out of the trials prior to completion;
- the cost to, or lack of adequate compensation for, prospective patients; and
- the proximity and availability of clinical trial sites to prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance. Even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients. We cannot assure you that our assumptions used in determining expected clinical trial timelines are correct or that we will not experience delays or difficulties in enrollment, or be required by the FDA or comparable foreign regulatory authorities to increase our enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

The results of clinical trials conducted at clinical trial sites outside the U.S. might not be accepted by the FDA, and data developed outside of a foreign jurisdiction similarly might not be accepted by such foreign regulatory authority.

We have conducted and are currently conducting certain of our clinical trials in Australia, and we plan to conduct additional clinical trials outside of the U.S. in the future. Clinical trials conducted in Australia using "unapproved therapeutic goods," or those that have not yet been evaluated by the Therapeutic Goods Association ("TGA") for quality, safety and efficacy, must occur pursuant to either the Clinical Trial Notification Scheme or the Clinical Trial Approval Scheme. In each case, the trial is supervised by a Human Research Ethics Committee ("HREC"), an independent review committee set up under the guidelines of the Australian National Health and Medical Research Council that reviews, approves and provides continuing oversight of trial protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. Although the FDA or comparable foreign regulatory authorities may accept data from clinical trials conducted outside the relevant jurisdiction, acceptance of these data is subject to certain conditions. For example, the FDA requires that the clinical trial must be well-designed and conducted and performed by qualified investigators in accordance with ethical principles such as institutional review board or ethics committee approval and informed consent, the trial population must adequately represent the U.S. population and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Further, the FDA may consider an on-site inspection to be necessary in which case they must be able to validate the data through such an inspection or other appropriate means. In addition, while these clinical trials are subject to the applicable local laws, acceptance of the data by the FDA will be dependent upon its determination that the trials were conducted consistent with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the U.S. as adequate support of a marketing application. Additionally, recent policy proposals in the U.S., if enacted in the future, may make acceptance by the FDA or inclusion of foreign data in a U.S. marketing application more difficult or costly. Similarly, any data submitted to foreign regulatory authorities may not adhere to their standards and requirements for clinical trials and data from trials conducted outside of such jurisdiction may not be accepted.

If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted, which may increase costs or time required to complete the clinical trial.

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

- additional foreign regulatory requirements including with respect to data privacy and security, which may impose heightened requirements and data transfer restrictions;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- inconsistent standards for reporting and evaluating clinical data and AEs;
- varying standards or availability of CF care, resulting in data that may differ from patients who have received the U.S. standard of care therapy;
- any pandemic, epidemic or public health emergencies;
- diminished protection of intellectual property in some countries; and

- political instability, civil unrest, war or similar events that may jeopardize our ability to commence, conduct or complete a clinical trial and evaluate resulting data.

If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates or increase the product yield of its manufacturing, then our manufacturing costs may increase and commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of our product candidates, our third-party manufacturers will be required to produce adequate quantities of our product candidates and meet required timelines. Further, as we seek to scale-up our manufacturing processes, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of our product candidates. The transition to larger scale production could prove difficult. In addition, if our third-party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the same quality, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operations.

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

The manufacture of our product candidates is complex and requires significant expertise. As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, various aspects of the development program, such as manufacturing methods and formulation, may be altered in an effort to reduce costs or optimize processes and product characteristics, and such outcomes may not be achieved. Any of these changes could cause our product candidates to perform differently and affect the results of our current or future clinical trials. Such changes may also require additional testing, or notification to or approval by the FDA or another comparable regulatory authority. 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 commence sales and generate revenue.

Certain of our programs may compete with our other programs, which could negatively impact our business and reduce our future revenue.

We are developing all of our product candidates for the same indication, CF, and we may develop additional product candidates for the same indication in the future. We have several programs targeting different regions of the CFTR protein, in order to support our goal of creating a differentiated combination treatment that delivers clinically meaningful benefit to CF patients. However, developing multiple programs for a single indication may negatively impact our business if the programs compete with each other. For example, if multiple programs are conducting clinical trials at the same time, they could compete for the enrollment of participants. In addition, if multiple product candidates are approved for the same indication, they may compete for market share, which could limit our future revenue.

Due to the significant resources required for the development of our pipeline, and depending on our ability to access capital, we must prioritize the development of certain product candidates over others. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and management resources, we are focused on a single indication, CF, and we focus our research and development efforts on certain selected development programs and product candidates. We are currently primarily focused on the development of SION-719 and SION-451, our NBD1 stabilizers, and our portfolio of complementary modulators. As a result, we may forego or delay pursuit of opportunities with other product candidates that later prove to have greater commercial potential. For instance, the development of a proprietary dual combination is our priority. 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 development programs and product candidates for specific indications may not yield any

commercially viable products. If we do not accurately evaluate the viability, commercial potential or target market for any of our current or future product candidates, our business, financial condition and results of operations could be materially and adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to a product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks Related to Our Dependence on Third Parties

We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing our product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we expect that we may need to enter into additional license agreements in the future. In particular, we have entered into license agreements with Sanofi and AbbVie, pursuant to which, among other things, we have secured exclusive licenses for certain intellectual property and know-how relating to CFTR modulator therapies to commercialize certain compounds, patents and proprietary information and inventions. Our existing license agreements impose, and we expect that future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. In particular, we are substantially dependent on the success of one of our NBD1 stabilizer product candidates, and to the extent we are unable to develop other product candidates at the time of such termination, it would have a material adverse effect on our business, financial condition, results of operations and prospects, including, but not limited to, cessation of our operations. See "*Business—License and Collaboration Agreements*" for a description of our license agreements.

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

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our product candidates and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed intellectual property in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and

- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We currently rely on, and in the future intend to rely on, third parties to conduct a significant portion of our clinical trials and potential future clinical trials for product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We currently engage CROs and other vendors to conduct our clinical trials, and similarly expect to engage CROs and other vendors for future clinical trials for our current and any future product candidates that we may progress to clinical development. We expect to continue to rely on third parties, including but not limited to clinical data management organizations, healthcare institutions operating as clinical sites and clinical investigators, to conduct those clinical trials. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. Switching or adding CROs or other vendors involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO or vendor commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. We may encounter challenges or delays in our CRO/vendor relationships in the future which may cause a material adverse impact on our business, financial condition and prospects.

In addition, any third parties conducting our clinical trials will not be our employees, and, except for including contractual obligations and remedies for breach of such obligations in our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approvals for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other development activities that could harm our competitive position.

We rely on these parties for execution of our preclinical studies and clinical trials, and generally do not directly control their businesses or related activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will 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 GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register certain ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Further, upon inspection by a given regulatory authority, such regulatory authority may not agree with our determination that any of our clinical trials complies with GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP conditions. Our failure to comply with these requirements may require us to repeat clinical trials, which would delay the regulatory approval process.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential revenue.

We contract with third parties for the manufacture of our product candidates for clinical drug supply and expect to continue to do so for commercialization, if our product candidates are approved. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not have any cGMP manufacturing facilities and have no plans to develop our own clinical or commercial-scale manufacturing capabilities. We currently rely, and expect to continue to rely, on contract development and manufacturing organizations (“CDMOs”) for the cGMP manufacture of our product candidates and related raw materials for clinical development. In addition, we expect to rely on CDMOs for the commercial supply of any products for which we receive marketing approval. This reliance increases the risk that we will not have sufficient quantities of our product candidates or products, if approved, or obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. For example, any of these third parties may terminate their engagements with us at any time or may face production shortages or other supply interruptions or otherwise be unable to secure the requisite raw materials to support our planned clinical activities. In addition, the availability of CDMOs to manufacture our product candidates/drugs may depend in part on the CDMOs’ schedules for manufacturing other companies’ products or product candidates. If we need to modify our development plans or enter into alternative arrangements, which may not be readily available or available on acceptable terms, it could delay our product development activities and increase our expenses.

Our reliance on CDMOs for manufacturing activities reduces our control over these activities, but does not relieve us of our responsibility to ensure compliance with all required regulations. In particular, we do not have control over a supplier’s or manufacturer’s compliance with laws, regulations and applicable cGMP standards or similar regulatory requirements and other laws and regulations, such as those related to environmental health and safety matters. If our CDMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or comparable foreign regulatory authorities, we may be unable to obtain regulatory approval of our potential future marketing applications. In addition, although we conduct routine qualification audits and have quality agreements in place with our CDMOs, we have no direct operational control over their ability to maintain adequate quality control, quality assurance and qualified personnel. Our CDMOs may face manufacturing or quality control problems causing production and shipment delays, or CDMOs may fail to maintain compliance with the applicable cGMP requirements. The facilities used by our CDMOs are subject to continual review and periodic inspections by the FDA and comparable foreign regulatory authorities. If the FDA or a comparable foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory 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 clinical holds, 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 supply of our products.

Our use of foreign CROs and CDMOs in some jurisdictions may be or may become subject to U.S. legislation, sanctions, tariffs, trade restrictions and/or other regulatory requirements, which may increase the cost of and cause delays in the procurement or supply of materials for, or manufacture of, our product candidates or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies. For example, legislation recently signed into law, known as the BIOSECURE Act, implements a prohibition on U.S. government contracts, grants, and loans from being used towards biotechnology equipment and services produced or provided by certain identified Chinese biotechnology companies and authorizes the U.S. government to name additional Chinese biotechnology companies of concern. By December 18, 2026, the Director of the Office of Management and Budget ("OMB") will publish a full list of "biotechnology companies of concern" based on recommendations from key federal Secretaries and

Directors, including Defense, Justice, HHS, Commerce, National Intelligence, Homeland Security, State, and National Cyber. The Director of OMB will thereafter review and update that list at least annually, based on recommendations from those key federal Secretaries and Directors. We have an agreement with a Chinese biotechnology company, pursuant to which it may manufacture certain of our clinical trial materials from time to time. This Chinese company was initially identified as a "biotechnology company of concern" in an earlier proposed version of the BIOSECURE Act, but that legislation did not pass, and the company is not named in the final law; however, it could be added in the future. The BIOSECURE Act has the potential to severely restrict the ability of companies, including us, to work with certain Chinese biotechnology companies of concern without losing the ability to contract with, or otherwise receive funding from, the U.S. government. Additionally, our use of foreign CROs and CDMOs, including those located in China, may be subject to unanticipated changes in the geopolitical landscape that could have negative impacts on our business operations.

There have been, and may continue to be, significant changes to U.S. trade policies, sanctions, legislation, treaties, and tariffs, including, but not limited to, trade policies and tariffs affecting products from outside of the U.S. The extent and duration of increased tariffs and the resulting impact on general economic conditions and on our business are not known and depend on various factors, such as negotiations between the U.S. and affected countries, their respective responses, potential exemptions or exclusions, and availability and cost of alternative sources of supply. Supply chain disruptions and delays could also negatively impact our cost of materials and production processes. If we are unable to obtain necessary materials in sufficient quantity and in a timely manner, the development of our product candidates may be delayed, which could significantly harm our business.

Further, any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. If our current CDMOs cannot perform as agreed, we may be required to replace such manufacturers. We may incur added costs and delays in identifying and qualifying any such replacement. In addition, our current and anticipated dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We may seek to establish collaborations, license agreements and other similar arrangements with third parties for the development or commercialization of our product candidates. If we are not able to establish them on commercially reasonable terms, or if those arrangements are not successful, we may have to alter our development and commercialization plans.

The development and potential commercialization of our product candidates will require substantial additional funding. For some of our product candidates, we may seek to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of our product candidates, including for the commercialization of any of our product candidates that are approved for marketing outside the U.S. If we enter into any such additional arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our future collaborators dedicate to the development or commercialization of our product candidates. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Whether we reach a definitive agreement for any collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors. Those factors may include the potential differentiation of our product candidate from competing product candidates, the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities outside the U.S., the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, and industry and market conditions generally. The collaborator may also consider alternative product candidates for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. 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.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected, or at all;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create 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 one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated, including for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

We may not be able to negotiate future 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 any product candidate that we planned to collaborate on, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, any future collaborations that we enter into may not be successful. The success of our future collaboration arrangements will depend heavily on the efforts and activities of our future collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. If conflicts arise between any future collaborators and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. For example, our future collaborators could conduct multiple product development efforts and could develop, either alone or with others, products in related fields that are

competitive with the product candidates we may develop. In addition, collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party, and any such termination or expiration may adversely affect us financially or harm our business.

Risks Related to Our Intellectual Property

If we or our licensors are unable to obtain, maintain and enforce intellectual property rights relating to any of our product candidates, or if the scope of the protection obtained is not sufficiently broad, our competitors or other third parties could develop and commercialize products similar or identical to ours, our ability to successfully commercialize our product candidates may be adversely affected and we may not be able to compete effectively in our markets.

We rely upon a combination of patents, access to certain third-party trade secrets and confidentiality agreements to protect the intellectual property related to our product candidates. These legal measures afford only limited protection, and competitors or others may gain access to or use our intellectual property and proprietary information. Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the U.S. and in other countries with respect to our proprietary product candidates.

We cannot predict whether the patent applications we currently or may in the future pursue will issue as patents in any particular jurisdiction or will provide sufficient protection against competitors or other third parties. Currently, much of our patent portfolio, including the applications related to our NBD1 product candidates, are in various stages of the patent prosecution process. Nor can we predict the outcome of any challenge by our competitors to the validity or enforceability of any such patents. We cannot offer any assurances that the breadth of our granted patents will be sufficient to stop a competitor from developing and commercializing a product, including a generic product that would be competitive with one or more of our product candidates. Furthermore, any successful challenge to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of the competitive advantage necessary for the successful commercialization of any of our product candidates. Further, if we encounter delays in regulatory approval, the period of time during which we could market a product candidate under patent protection could be reduced (unless we obtain a patent term extension corresponding to such delays).

Our ability to obtain and maintain valid and enforceable patents depends on our inventions being patentable in light of the prior art. Furthermore, 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 not at all. Therefore, we cannot be certain that we or our licensors were the first to invent the inventions claimed in any of our owned or licensed patents or pending patent applications, or that we or our licensors were the first to make the inventions claimed in those owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patents and patent applications may not issue as patents and even if issued, may be challenged and invalidated or rendered unenforceable. Furthermore, even if a patent is granted, our competitors or other third parties may be able to circumvent the patent by developing similar or alternative products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The patent prosecution process is expensive and time-consuming. We may not be able to prepare, file and prosecute all necessary or desirable patent applications at a commercially reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, depending on the terms of any existing and future in-licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering intellectual property in-licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our licensors' patent rights

are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued which protect our product candidates or which effectively prevent others from commercializing competitive products.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and abroad. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. We or our licensors may in the future, become subject to a third-party pre-issuance submission of prior art, opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceeding and other similar proceedings challenging our patent rights or the patent rights of others in the U.S. Patent and Trademark Office (the "USPTO") or other foreign patent office. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical products, or limit the duration of the patent protection of our product candidates.

In addition to the protection provided by our patent portfolio, we rely on access to certain third-party trade secret protection as well as confidentiality agreements to protect proprietary know-how that is not amenable to patent protection. Although we generally require all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or intellectual property to enter into confidentiality agreements, certain employees may not have signed such agreements and we cannot provide any assurances that all such agreements have been duly executed, or that such trade secrets and other confidential proprietary information will not be disclosed. Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to the above-mentioned trade secrets. Competitors could purchase our products, if approved, and replicate some or all of the competitive advantages we derive from our development efforts for intellectual property on which we do not have patent protection. If any trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that intellectual property or information to compete with us. If any trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our proprietary data and third-party trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. However, our agreements and security measures may be breached, and we may not have adequate remedies for any breach. Also, if the steps taken to maintain trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover the trade secrets and our proprietary information. Further, the FDA may change its disclosure policies from time to time and make additional information publicly available on a routine basis. If we are unable to prevent material disclosure of the non-patented intellectual property related to our product candidates to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Patent terms may be inadequate to protect our competitive position on our products, if approved, for an adequate amount of time, and if we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

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

do not have sufficient patent life to protect our product candidates, our business, financial condition, results of operations, and prospects may be adversely affected.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of any U.S. patents that may issue covering our product candidates may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product that is a new chemical entity as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent may be extended, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request, and we cannot be certain what the length of the extension would be or if we will receive an extension at all. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from any applicable products could be reduced and could have a material adverse effect on our business.

If we fail to comply with our obligations in any current intellectual property licenses with third parties, or fail to obtain such licenses in the future, we could lose rights that are material to our business.

We have licensed third-party intellectual property that is material to our business, and may enter into additional license agreements in the future. We do not and will not own the patents or patent applications that underlie these licenses, and we may not control either the prosecution or the enforcement of the patents. Under such circumstances, we may be forced to rely upon our licensors to properly prosecute and file those patent applications and prevent infringement of those patents. Therefore, we cannot be certain that the prosecution, maintenance and enforcement of these patent rights will be in a manner consistent with the best interests of our business.

If we or our licensors fail to maintain such patents, or if we or our licensors lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected.

Our rights to use the intellectual property and practice the inventions claimed in the licensed patents and patent applications are subject to our licensors abiding by the terms of those licenses and not terminating them. In addition, existing license agreements do, and future agreements may, impose diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations, including rights of first negotiation (“ROFN”) for development of certain programs. For example, under our license agreement with AbbVie, AbbVie has a ROFN pursuant to which it would have an exclusive period to negotiate in good faith the terms of a commercial license transaction if we decide to pursue a license or sublicense to commercialize a licensed product under the AbbVie agreement prior to initiating Phase 3 clinical trials. This ROFN may delay or undermine our ability to enter into an otherwise beneficial transaction. If we fail to comply with our obligations, our licensors may have the right to terminate the licenses, in which event we might not be able to develop, manufacture or market any product that is covered by the intellectual property we in-license from such licensor and may face other penalties. If any of our licenses are terminated, we may lose our patent rights on a territory-by-territory basis, and such rights may be lost worldwide. Termination of any license agreement could reduce or eliminate our rights under these agreements and may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property. Any of the foregoing outcomes could prevent us from commercializing relevant product candidates, which could have a material adverse effect on our operating results and overall financial condition.

In addition, disputes regarding obligations in licenses may require us to take expensive and time-consuming legal action to resolve, and, even if we are successful, may delay our ability to commercialize

products and generate revenue. Further, if we are unable to resolve license issues that arise, we may lose rights to practice intellectual property that is required to make, use or sell products. We may require additional licenses in the future. Licenses to additional third-party intellectual property and materials that may be required for our development programs may not be available on commercially reasonable terms, or at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more-established companies may pursue strategies to 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, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us.

In addition, disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including disputes concerning scope of rights granted under the license agreement and other interpretation-related issues; whether and the extent to which our product candidates and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; 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. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. If we are unable to successfully obtain rights to required third-party intellectual property rights, we may have to abandon development of the relevant program or product candidate or expend time and resources re-designing the program or product candidate, which could have a material adverse effect on our business.

Intellectual property rights that we in-license in the future may also be granted through sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed.

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

Our ability to obtain patents is highly uncertain because, to date, some legal principles remain unresolved, and there has not been a consistent policy regarding the breadth or interpretation of claims allowed in patents in the U.S. Furthermore, the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific, and factual issues. Changes in either patent laws or interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

Patent reform legislation in the U.S. and other countries, including the Leahy-Smith America Invents Act (the “Leahy-Smith Act”) signed into law on September 16, 2011, and its implementation could increase the uncertainties around patent protection, costs, and the enforcement or defense of our patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. The Leahy-Smith Act included a number of significant changes to U.S. patent law. Such provisions affect the way patent applications are prosecuted, redefine prior art, and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. into a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business.

The Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition. Further, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our or our licensors’ ability to obtain patents in the

future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our or our licensors' existing patents and patents that we or our licensors might obtain in the future. We cannot predict how future decisions by the courts, Congress or the USPTO may impact the value of our or our licensors' patents. Similarly, any adverse changes in the patent laws of other jurisdictions could have a material adverse effect on our business and financial condition. Changes in the laws and regulations governing patents in other jurisdictions could similarly have an adverse effect on our ability to obtain and effectively enforce our patent rights.

We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful.

While we are not currently involved in any disputes relating to our intellectual property, competitors may infringe the patents we have applied for. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. If we initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable. In patent litigation in the U.S., counterclaims alleging invalidity and/or unenforceability are common, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent.

In an infringement proceeding, a court may decide that the patent claims we are asserting are invalid and/or unenforceable, or may refuse to stop the other party from using the intellectual property at issue on the grounds that our patent claims do not cover the intellectual property in question. Third parties may also raise similar 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 and equivalent proceedings in foreign jurisdictions (for example, opposition proceedings). Such proceedings could result in revocation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of infringement, invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could have a material adverse impact on our business.

Our defense of litigation or interference proceedings may fail and require us to cease using certain intellectual property or force us to take a license under the intellectual property rights of the prevailing party, if available. Even if successful, litigation or interference proceedings may result in substantial costs and distract our management and other employees. We may not be able to prevent misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

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

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain.

While no third parties to our knowledge have initiated legal proceedings against us to date, as our current and future product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We cannot provide any assurance that our current and future product candidates do not infringe other parties' patents or other proprietary rights, and competitors or other parties may assert that we infringe their proprietary rights in any event. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and future product candidates, including infringement, interference or derivation proceedings, post-grant review and *inter partes* review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Even if we

believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize our product candidates or any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is high and requires us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would agree with us and invalidate the claims of any such U.S. patent. Similarly, the burdens on us to invalidate patent claims in foreign jurisdiction may vary substantially and courts in those jurisdictions may not agree with us that the claims are invalid. The outcome of proceedings involving assertions of infringement, invalidity and unenforceability during patent litigation is unpredictable. Furthermore, if a patent holder believes that one of our product candidates infringes its patent, the patent holder may sue us even if we have received patent protection for our intellectual property. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay manufacturing or sales of the drug or product candidate that is the subject of the actual or threatened suit. Moreover, given the vast number of patents in our field of intellectual property, we cannot be certain that our current and future product candidates do not or will not infringe existing patents or that we will not infringe patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same intellectual property rights licensed to us. If we fail to obtain a required license, we may be unable to effectively market product candidates based on our intellectual property, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Alternatively, we may need to redesign our products, which may be impossible or require substantial time and monetary expenditure. Under certain circumstances, we could be forced, including by court orders, to cease commercializing our product candidates. In addition, in any such proceeding or litigation, we could be found liable for substantial monetary damages, potentially including treble damages and attorneys' fees, if we are found to have willfully infringed the patent at issue. A finding of infringement that prevents us from commercializing our product candidates, requires us to redesign our products, or forces us to cease some of our business operations could materially harm our business.

The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information or trade secrets of third parties.

We employ individuals who were previously employed at other biotechnology or biopharmaceutical companies. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information, trade secrets or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

We may be subject to claims challenging the inventorship or ownership of our intellectual property, including any patents we obtain.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patent applications, any patents we obtain, or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of

consultants or others who are involved in developing our product candidates. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. If we no longer own intellectual property rights that are required to commercialize and protect our products, we may need to obtain a license to those rights, which may not be available on commercially reasonable terms, or at all. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Reliance on third parties requires us to share trade secrets, which increases the possibility that trade secrets will be misappropriated or disclosed, and confidentiality agreements with employees and third parties may not adequately prevent disclosure of trade secrets and protect other proprietary information.

We rely on certain third-party trade secrets, technical know-how, proprietary information and other confidential information to protect our product candidates and as otherwise useful to our business. Monitoring unauthorized uses and disclosures of trade secrets and other confidential information is difficult, and we do not know whether the steps we have taken to protect our confidential intellectual property will be effective. We seek to protect our confidential information, in part, through confidentiality and non-disclosure agreements with our employees, consultants, collaborators, suppliers and other parties. These agreements typically restrict the ability of our employees, consultants, advisors and third-party contractors to use or disclose our proprietary information or publish data potentially relating to our proprietary information. Despite our efforts to protect trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other proprietary information by the parties to these agreements. There can be no assurance that these agreements will not be breached, including by disclosure of our confidential information. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and trade secret status could be lost as a result. We also cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary product candidates and processes. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators or others is inadvertently disclosed or subject to a breach or violation, we may be liable to the owner of that confidential information. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary product candidates and processes will be effective.

To the extent that we rely on third parties to manufacture or commercialize our product candidates, or if we collaborate with additional third parties for the development of our product candidates, we must, at times, share proprietary information with them. We may also conduct joint research and development programs that may require us to share potential trade secrets under the terms of our research and development partnerships or similar agreements. Despite the contractual provisions employed when working with third parties, the need to share confidential information increases the risk that such potential trade secrets become known by our competitors, are inadvertently incorporated into the product candidates of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and other confidential information, a competitor's discovery of such information or other unauthorized use or disclosure thereof could have an adverse effect on our business and results of operations.

Enforcing a claim that a third party illegally obtained and is using trade secrets or proprietary information is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. are sometimes less willing to protect trade secrets and the enforceability of confidentiality or similar types of agreements may vary from jurisdiction to jurisdiction.

We may enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.

Filing and prosecuting patent applications and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our intellectual property in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as that in the U.S. or Europe. These products may compete with our product candidates, and our and our licensors' future patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications before they are granted. The examination of each national or regional patent application is an independent proceeding. As a result, patent applications in the same family may issue as patents in some jurisdictions, such as in the U.S., but may issue as patents with claims of different scope or may even be refused in other jurisdictions. Furthermore, the requirements for patentability differ in certain jurisdictions and countries. Some countries do not grant claims directed to methods of treatment or have additional restrictions on the scope of method of treatment claims compared to the U.S. Accordingly, depending on the country, the scope of patent protection may vary for the same product candidate.

While we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain protection efforts in all such markets. Additionally, the prosecution of patent applications in other jurisdictions is often a longer process and patents may be granted at a later date than in the U.S., potentially delaying our ability to assert such patents against competitors. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished, and we may face additional competition in those jurisdictions.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the U.S. and Europe, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property rights, which could make it difficult for us to stop the infringement of any patents we obtain or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in other jurisdictions, whether or not successful, 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 and our patent applications at risk of not issuing as patents, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In those countries, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired.

In Europe, a new unitary patent system took effect on June 1, 2023, which may significantly impact European patents, including those granted before the introduction of the new system. Under the new system, applicants can, upon grant of a patent, opt for that patent to become a unitary patent which will be subject to the jurisdiction of a new unitary patent court ("UPC"). Patents granted before the implementation of the new system can be opted out of UPC jurisdiction, remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC may be challenged in a single UPC-based revocation proceeding that, if successful, could invalidate the patent in all countries who are signatories to the UPC. Further, because the UPC is a new court system and there is no precedent for the court's laws, there is increased uncertainty regarding the outcome of any patent litigation. We are unable to predict what impact the new patent regime may

have on our ability to exclude competitors in the European market. In addition to changes in patent laws, geopolitical dynamics, such as Russia's incursion into Ukraine, may also impact our ability to obtain and enforce patents in particular jurisdictions. If we are unable to obtain and enforce patents as needed in particular markets, our ability to exclude competitors in those markets may be reduced.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the U.S. over the lifetime of our patents and/or applications and any patent rights we may obtain or license in the future. Furthermore, the USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse of a patent or patent application can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patents or patent applications, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, our competitors might be able to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

Any trademarks we have obtained or may obtain may be infringed or otherwise violated, or successfully challenged. If our trademarks and trade names are not adequately protected, or if we are unable to obtain desired trademarks or trade names, then we may not be able to build brand name recognition in our markets of interest and our business may be adversely affected.

We expect to rely on trademarks as one means to distinguish our product candidates, if approved for marketing, from the drugs of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be approved. During trademark registration proceedings in the U.S. and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties may oppose pending trademark registration applications or seek to cancel registered trademarks.

We have also not yet registered trademarks for any of our product candidates in any jurisdiction. Any trademark applications we file may be rejected and registered trademarks may not be obtained, maintained or enforced. If we do not successfully register our trademarks, we may encounter difficulty in enforcing, or be unable to enforce, our trademark rights against third parties, which could adversely affect our business and our ability to effectively compete in the marketplace.

In addition, any proprietary name we propose to use with any of our product candidate in the U.S. will need to be approved by the FDA, regardless of whether we have registered, or applied to register, the proposed proprietary name as a trademark. The FDA conducts a review of proposed proprietary names, including an evaluation of potential for confusion with other products' proprietary names, as part of the NDA review process. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

In addition, our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on, misappropriating or violating other marks. In the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademark registrations may not survive such proceedings. In the

event that our trademarks are successfully challenged, we could be forced to rebrand our drugs, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion.

Our competitors may also infringe or otherwise violate our trademarks and we may not have adequate resources to enforce our trademarks. We may not be able to protect our rights to our trademarks and trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. Any of the foregoing events may have a material adverse effect on our business.

Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. 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, then 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, trade names, domain names or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

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

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

- others may be able to make products that are similar to or otherwise competitive with our product candidates but that are not covered by the claims of our current or future patents;
- an in-license necessary for the manufacture, use, sale, offer for sale or importation of one or more of our product candidates may be terminated by the licensor;
- we or future collaborators might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we own, license or will own or license;
- we or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative product candidates or duplicate any of our product candidates without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or in-license may be held invalid or unenforceable as a result of legal challenges by our competitors;
- issued patents that we own or in-license may not provide coverage for all aspects of our product candidates in all countries;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership of our patents or patent applications may be challenged by third parties;
- we may not develop additional proprietary intellectual property that is patentable; and
- the patents of third parties may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop certain product candidates, and we may add additional licenses in the future as we expand our product candidate pipeline. Although we have succeeded in licensing intellectual property from third-party licensors, including AbbVie, in the past, we cannot assure our stockholders that we will be able to in-license or acquire the rights to any potential product candidates from third parties on acceptable terms or at all.

In addition, our license agreements may provide that our fields of use exclude particular fields. If we determine that rights to such fields are necessary to commercialize our product candidates or maintain our competitive advantage, we may need to obtain additional license rights in order to continue developing, manufacturing or marketing our product candidates. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property that is subject to our existing licenses.

Various third parties practice in competitive areas and may have issued patents or patent applications that will issue as patents in the future, which could impede or preclude our ability to commercialize our product candidates. For any third-party patents that could be relevant to our product candidates, we rely in part on the “safe harbor” or research exemption under 35 U.S.C. § 271(e)(1), which exempts activities related to pursuing FDA approval for a drug product from patent infringement. However, while U.S. patent law provides such a “safe harbor” to our clinical product candidates under this provision, that exemption may expire when an NDA is submitted. Given the uncertainty of clinical trials, we cannot be certain of the timing of their completion and it is possible that we may submit an NDA for one of our future product candidates at a time when one or more relevant third-party patents is in force. It may therefore be necessary for us to use the patented or proprietary intellectual property of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such intellectual property, or if we are forced to license such intellectual property on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same intellectual property licensed to us.

Additionally, we may collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution’s rights in intellectual property resulting from the collaboration. Even if we hold such an option, we may be unable to negotiate a license from the institution within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program.

In addition, the licensing or acquisition of third-party intellectual property rights is a highly competitive area, and a number of more established companies are also pursuing strategies to 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, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the applicable product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our product candidates, or the methods for manufacturing them or to develop or license replacement intellectual property, 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 product candidates, which could harm our business, financial condition, results of operations, and prospects significantly.

Additionally, if we fail to comply with our obligations under license agreements, 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. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or current and future 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 impede, or delay or prohibit the further development or commercialization of one or more potential product candidates that rely on such agreements.

Risks Related to Legal and Regulatory Compliance Matters

Our business operations and our relationships with healthcare providers, third-party payors, patients and other parties in the healthcare industry are subject, directly or indirectly, to significant regulation under a broad range of healthcare laws, including fraud and abuse laws. Any action against us for violation of such laws could harm our reputation and require significant resources for defense. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Pharmaceutical manufacturers, and the parties with which such manufacturers interact, are subject to extensive and complex regulation under a broad range of healthcare laws. Such laws, some of which will apply only if and when we have a marketed product, constrain our business operations, including the research and development, manufacturing, distribution, sales and promotion of our product candidates and products, if any are approved in the future, as well as educational and charitable activities. Arrangements with healthcare providers, third-party payors, patients and other parties in the healthcare industry, which may have a significant impact on our business, are regulated by fraud and abuse and other healthcare laws. For more information, see the section titled "*Business—Government Regulation—Other U.S. Healthcare Laws and Compliance Requirements*."

Healthcare laws regulating our business activities are broad and any exceptions may be narrow. Requirements may differ across jurisdictions. There may be limited guidance on the interpretation of the laws and their application to our specific activities. Interpretations of these laws by government enforcement agencies and courts are evolving. Efforts to ensure that our business operations will comply with applicable healthcare laws and regulations will involve substantial costs. We will need to develop and implement robust compliance policies and processes to seek to prevent and detect non-compliance and update such policies and processes as our operations and government expectations evolve, which will involve substantial and ongoing costs, and even with such policies and processes we cannot be certain to prevent non-compliance.

Given the broad scope, limited guidance and evolving government interpretations, our business activities may potentially be subject to challenge under these healthcare laws despite efforts to ensure compliance. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Such an action could also harm our reputation and adversely affect our business as a result. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, 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, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

Even if we obtain regulatory approvals for our product candidates or any future product candidates, they will remain subject to ongoing regulatory oversight.

Even if we obtain any regulatory approvals for our product candidates or any future product candidates, such product candidates, once approved, will be subject to ongoing regulatory requirements applicable to manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and post-marketing activities, among other things. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval. Manufacturers of approved products and their facilities are subject to continual review and periodic and unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. Any regulatory approvals that we receive for our product candidates or any future product candidates may also be subject to a REMS, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or requirements that we conduct potentially costly post-marketing testing, including additional trials and heightened surveillance to monitor the quality, safety and efficacy of the drug. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will further be required to promptly report any serious and unexpected adverse drug experiences and certain quality or production problems with our products to regulatory authorities along with other periodic reports.

Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to ensure compliance. We will also have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drug products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we will not be allowed to promote our products for indications or uses for which they do not have approval, commonly known as off-label promotion. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies, including their sales force, with respect to off-label uses of products for which marketing approval has not been issued. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The holder of an approved NDA must submit new or supplemental applications and obtain prior approval for certain changes to the approved product, product labeling, or manufacturing process. A company that is found to have improperly promoted off-label uses of their products may be subject to significant civil, criminal and administrative penalties.

In addition, drug manufacturers are subject to payment of annual fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with any product, if approved, such as adverse experiences of unanticipated severity or frequency, or problems with the facility where the product is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that product, a regulatory authority may impose restrictions relative to that product, the manufacturing facility or us, including requesting revisions to the approved labeling to add new safety information, imposing of post-market studies or clinical trials to assess new safety risks or imposing distribution restrictions or other restrictions under a REMS program, requesting a recall or requiring withdrawal of the product from the market or suspension of manufacturing. If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory authority may:

- issue an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines, disgorgement of profits or revenue, warning letters or adverse publicity requirements;
- suspend or withdraw regulatory approvals;
- restrict product distribution or use, including full or partial holds on any ongoing or planned clinical trials;
- refuse to approve a pending NDA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the drug;

- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and harm our business, financial condition, results of operations and prospects.

Healthcare and other reform initiatives may have an adverse impact on our business and results of operations.

In the U.S. and some foreign jurisdictions, there have been and continue to be ongoing efforts to implement legislative and regulatory changes regarding the healthcare system. Such changes could prevent or delay marketing approval of any product candidates that we may develop; restrict or regulate post-approval activities; and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Although we cannot predict what healthcare reform efforts will be successful, such efforts may result in more rigorous coverage criteria, additional downward pressure on the price that we, or our future collaborators, may receive for any approved products, or in other consequences that may adversely affect our ability to achieve or maintain profitability. For more information, see the section titled "*Business—Government Regulation—Healthcare Reform*."

Among policy makers and third-party payors in the U.S. and elsewhere, there is significant and ongoing interest in implementing changes in the delivery and payment for healthcare services in order to contain healthcare costs, improve quality and/or expand access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives and changing policies and practices of the third-party payors. There has also been heightened governmental scrutiny in the U.S. of pharmaceutical pricing practices considering the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several congressional inquiries and proposed and enacted legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient support programs, or reform government program reimbursement methodologies for products. Individual states in the U.S. have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

The U.S. has recently taken steps intended to reduce drug prices and establish and communicate most-favored-nation price targets to pharmaceutical manufacturers to bring prices for American patients in line with comparably developed nations. Several large pharmaceutical companies have already started to voluntarily reduce their pricing on select drugs indexed to lower prices around the globe. In addition, at the state level, legislatures have increasingly passed legislation and implemented regulations with similar goals, as well as laws designed to control pharmaceutical and biotherapeutic product pricing, including restrictions on pricing or reimbursement at the state government level, limitations on discounts to patients, marketing cost disclosure and transparency measures, restrictions or other limitations on patient assistance, and, in some cases, policies to encourage importation from other countries (subject to federal approval) and bulk purchasing.

Adoption of new legislation at the federal or state level could affect demand for, or pricing of, any future products if approved for sale. We cannot, however, predict the ultimate content, timing or effect of any federal and state reform efforts. There is no assurance that federal or state healthcare reform will not adversely affect our future business and financial results. Additionally, implementation by third party payors of policies and practices to limit coverage, manage utilization, reduce payment of drug products could adversely affect our ability to sell our products profitably. All these efforts may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

In addition, FDA regulations and guidance may be revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. If executive actions impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively

impacted. Any new regulations or guidance, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for our product candidates. We cannot determine how changes in regulations, statutes, policies or interpretations when and if issued, enacted or adopted, may affect our business in the future. Such changes could, among other things, require:

- significant changes to the design of planned clinical trials that impact their duration or cost;
- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recalls, replacements, or discontinuance of one or more of our products, if approved; and
- additional recordkeeping.

Such changes would likely require substantial time and impose significant costs, or could reduce the potential commercial value of our product candidates, and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory approvals for any of our product candidates would harm our business, financial condition, and results of operations. Further, we cannot predict the likelihood, nature, or extent of healthcare reform initiatives that may arise from future legislation or administrative action.

General legislative cost control measures may also affect reimbursement for our product candidates. For example, the Budget Control Act of 2011, as amended, resulted in the imposition of reductions in Medicare (but not Medicaid) payments to providers in 2013 and will remain in effect into 2032 unless additional Congressional action is taken. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and/or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations.

Risks Related to the Commercialization of Our Product Candidates

We face substantial competition. Our main competitor in the CF market holds substantial market share and has substantially greater resources than we do. We may not be able to compete successfully in this environment and, in particular, against a much larger competitor.

The biotechnology and pharmaceutical industries are characterized by rapid advances, intense competition and a strong emphasis on proprietary and novel products and product candidates. We face substantial competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from many different sources, including major pharmaceutical and biotechnology companies, academic institutions, governmental agencies, consortiums and public and private research institutions.

In particular, we expect to compete with Vertex, which has multiple approved products, as well as additional product candidates in development, for the treatment of CF that would compete with our product candidates, if approved. Vertex holds substantial market share in our product candidates' proposed markets, and has substantially greater name recognition, financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Our commercial opportunity could be reduced or eliminated if Vertex or another competitor develops and commercializes products that are safer or more effective, have fewer or less severe side effects, or are more convenient or are less expensive than any product candidate that we may develop. Vertex or another competitor may also obtain approval by FDA or comparable foreign regulatory authorities for its product candidates currently in development more rapidly than we may obtain approval for our product candidates. Competing products could present superior treatment alternatives and could render our product candidates obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Even if one or more of our product candidates achieves marketing approval, it may be priced at a significant premium over competitive products, or otherwise not achieve broad market access, resulting in reduced competitiveness. If we do not compete successfully, we may not generate or derive sufficient revenue from any product candidate for which we obtain marketing approval and may not become or remain profitable.

Smaller or early-stage companies could also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. This may include other small-molecule drug discovery companies using similar approaches or other types of therapies, such as gene therapy, gene editing and/or mRNA therapies. If successful, gene therapy, gene editing, and/or mRNA therapies could repair or replace the defective CFTR gene or produce functional CFTR protein and reduce or eliminate the need for CFTR modulators. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring intellectual property complementary to, or that may be necessary for, our programs. 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.

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. There is currently a well-established standard of care for CF, Trikafta, with which physicians, CF patients and payors are very familiar and for which an established benefit-risk profile exists. In addition, in December 2024, the FDA approved Alyftrek, which targets the same mechanisms as Trikafta. Even if our product candidates are successful in registrational clinical trials, they may not be successful in displacing the standard of care if we are unable to demonstrate competitive efficacy, safety, ease of administration and/or cost-effectiveness. For example, physicians may be reluctant or unwilling to take their patients off their current medication and switch their treatment regimen to our product candidates, if approved, if the current medication is effective. Further, patients often acclimate to the treatment regimen that they are currently taking and may not want to switch unless recommended to do so by their physician for clinical reasons or required to do so due to lack of coverage and adequate reimbursement. Even if we are able to demonstrate our product candidates' safety and efficacy to the FDA and other regulators and receive approval, concerns in the medical community related to the comparative efficacy or side effect profile of our products may hinder market acceptance and uptake.

Efforts to educate the medical community and third-party payors regarding the benefits of our product candidates, if approved, may require significant resources, including management time and financial resources, and may not be successful. If our product candidates do not achieve an adequate level of market acceptance, we may not generate significant revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy, safety and potential advantages compared to alternative treatments;
- whether a product candidate is approved, if ever, as an add-on to standard of care or as part of a proprietary combination therapy;
- the prevalence and severity of any side effects;
- our ability to offer our products at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- product labeling or product insert requirements of the FDA or comparable foreign regulatory authorities, including any limitations or warnings contained in a product's approved labeling, including any boxed warning;
- the product's acceptance into standard of care treatment algorithms by medical societies that could affect payor and physician uptake;
- the effectiveness of sales and marketing efforts, and the strength of sales, marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for any product candidates, once approved;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- any restrictions on the use of our products together with other medications; and

- potential product liability claims and unfavorable publicity related to our products.

Any failure by one or more of our product candidates that obtains regulatory approvals to achieve market acceptance or commercial success would adversely affect our business prospects.

The success of our product candidates or any future product candidate will depend significantly on coverage and adequate reimbursement by third party payors or the willingness of patients to pay for these products if not covered.

We believe that for any product candidates which may be approved, our success depends on obtaining and maintaining coverage and adequate reimbursement for such products for their respective approved indications, and the extent to which patients will be willing to pay out-of-pocket for such products in the absence of reimbursement for all or part of the cost. Accordingly, we will need to establish a coverage and reimbursement strategy for any approved product candidate. In the U.S. and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Government and private third-party payors decide which products they will cover and establish reimbursement levels. Coverage and reimbursement varies among third party payors and new products face significant challenges in obtaining and maintaining coverage and adequate reimbursement, particularly if approved for indications with established treatments already on the market. For more information, see the section titled "*Business— Government Regulation— Coverage and Reimbursement.*"

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage for certain products, managing utilization of covered products and restricting the amount of reimbursement for covered products. Within the U.S., net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or requested by private payors in exchange for favorable coverage. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

There can be no assurance that our product candidates, even if they are approved for sale in the U.S. or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, or that coverage and an adequate level of reimbursement will be available or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

The market for our product candidates may be smaller than we estimate.

Our estimates of the potential market opportunity for our product candidates include several key assumptions, based on our industry knowledge, industry publications and third-party research reports. These assumptions include the number of patients who have CF, as well as the estimated reimbursement levels for each product candidate, if approved. While we believe our assumptions and the data underlying our estimates are reasonable, we have not independently verified the accuracy of the third-party data on which we have based our assumptions and estimates, and these assumptions and estimates may not be correct and the conditions supporting our assumptions or estimates may change at any time, including as a result of factors outside our control, thereby reducing the predictive accuracy of these underlying factors. Further, new studies may change the estimated incidence or prevalence of these diseases, and the potentially addressable patient population for our product candidates may not ultimately be amenable to treatment with our product candidates. If the actual market for any product candidates we may develop is smaller than we estimate, our revenues, if any, may be limited and it may be more difficult for us to achieve or maintain profitability.

Clinical trial and product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

We face an inherent risk of clinical trial and product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any

products that we may develop, especially if our products are prescribed for off-label uses (even if we do not promote such uses). For example, we may be sued if our product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims may be brought against us by clinical trial participants, patients or others using, administering or selling products that may be approved in the future. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- termination of clinical trials;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards paid to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- reduced resources of our management to pursue our business strategy;
- the inability to commercialize any products that we may develop; and
- a decline in our stock price.

Although we maintain clinical trial liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval on any current or potential product candidates, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

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

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. Each of our executive officers may currently terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

The loss of the services of our executive officers or other key employees could impede the achievement of our development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approvals of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we

are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Further, job candidates and existing employees often consider the value of the stock awards they receive in connection with their employment. If the perceived benefits of our stock awards decline, either because we are a public company or for other reasons, it may harm our ability to recruit and retain highly skilled employees. Our employees may be more likely to leave us if the shares they own have significantly appreciated in value relative to the original purchase prices of the shares, or if the exercise prices of the options that they hold are significantly below the market price of our common stock.

We expect to expand our clinical development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As we continue to build our organization and execute on our strategy, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management, business, and development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. Our future financial performance and our ability to compete effectively will depend, in part, on our ability to manage our growth effectively.

Our business could be affected by litigation, government investigations and enforcement actions.

We currently operate and plan to operate in a highly regulated industry and we could now or in the future be subject to litigation, government investigation and enforcement actions on a variety of matters in the U.S. or foreign jurisdictions, including, without limitation, intellectual property, regulatory, product liability, environmental, whistleblower, false claims, privacy, anti-kickback, anti-bribery, securities, commercial, employment and other claims and legal proceedings which may arise from conducting our business. Any determination that our operations or activities are not in compliance with existing laws or regulations could result in the imposition of fines, civil and criminal penalties, equitable remedies, including disgorgement, injunctive relief and/or other sanctions against us, and remediation of any such findings could have an adverse effect on our business operations.

Legal proceedings, government investigations and enforcement actions can be expensive and time-consuming. An adverse outcome resulting from any such proceedings, investigations or enforcement actions could result in significant damages awards, fines, penalties, exclusion from the federal healthcare programs, healthcare debarment, injunctive relief, product recalls, reputational damage and modifications of our business practices, which could have a material adverse effect on our business and results of operations. Even if such a proceeding, investigation or enforcement action is ultimately decided in our favor, the investigation and defense thereof could require substantial financial and management resources and cause reputational harm.

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

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. In addition, government funding of the Securities and Exchange Commission (the "SEC") and other government agencies on which our operations

may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies, including substantial leadership, personnel and policy changes, may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times, including a 43-day period that began on October 1, 2025, due to budgetary issues and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, or if geopolitical or global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, government shutdowns or other disruptions at the FDA, SEC or other government agencies could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates FDA or other comparable regulatory authority regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA or other comparable regulatory authority, manufacturing standards, foreign, federal and state healthcare laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud and abuse, such as the payment of kickbacks in return for business. 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 or misrepresentation of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted both a code of business conduct and ethics and an insider trading policy, but it is not always possible to identify and deter misconduct, 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 be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, 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, and the curtailment or restructuring of our operations. Any of these could adversely affect our ability to operate our business and our results of operations.

If our third-party manufacturers or suppliers do not comply with laws regulating the protection of the environment and health and human safety, our business could be affected adversely.

We and any CDMOs and suppliers we engage are subject to numerous federal, state and local environmental, health, and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We

generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials by us or by one of our third party-manufacturers, we could be held liable for any resulting damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended. We and our third-party manufacturers and suppliers cannot eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities.

In addition, we and our third-party manufacturers and suppliers may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which may increase the cost of their services to us. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities for us or our third-party manufacturers and suppliers, or adversely impact our supply chain or reputation, which could in turn materially adversely affect our business, financial condition, results of operations and prospects.

Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include property, general liability, employment directors' and officers' and employment practices insurance, however, we may not be able to maintain insurance adequate levels of coverage in the future. Further, an insurance carrier may seek to cancel or deny coverage after a claim has occurred.

We may engage in strategic transactions that could increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, subject us to other risks, adversely affect our liquidity, increase our expenses, present significant distractions to our management and harm our financial condition and results of operations.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and strategic partnerships or out-licensing or in-licensing of intellectual property, product candidates or products. For example, we have entered into a license agreement with AbbVie that gives us exclusive worldwide rights to develop and commercialize three clinical-stage compounds. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. We may not be able to find suitable partners or acquisition candidates, and we may not be able to complete such transactions on favorable terms, if at all. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of our management. In addition, the integration of any licensed assets that we may acquire rights to in the future may disrupt our existing business, may cause delays related to the integration of any licensed or acquired assets, and may be a complex, risky and costly endeavor for which we may never realize the full benefits. Furthermore, we may experience losses related to our entry into any licensing or partnerships, including as a result of failure to realize expected benefits or the materialization of unexpected liabilities or risks, which could have a material negative effect on our results of operations and financial condition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

Our operations and the operations of our suppliers, CROs, CDMOs and clinical sites could be subject to earthquakes, power shortages, telecommunications or infrastructure failures, cybersecurity incidents, physical security breaches, water shortages, floods, hurricanes, typhoons, blizzards and other extreme weather conditions, fires, public health pandemics or epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely or expect to rely on third-party manufacturers or suppliers to produce our product candidates and their components and on CROs and clinical sites to conduct our clinical trials, and do not currently have a redundant source of supply for all components of our product candidates. Our ability to obtain clinical or, if approved, commercial, supplies of our product candidates or any future product candidates could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption, and our ability to commence, conduct or complete our clinical trials in a timely manner could be similarly adversely affected by any of the foregoing. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Risks Related to Ownership of Our Common Stock

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.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including:

- the timing and success or failure of clinical trials for our product candidates or competing product candidates or any other change in the competitive landscape of our industry;
- our ability to successfully recruit and retain subjects for clinical trials and any delays caused by difficulties in such efforts;
- the timing and cost of, and level of investment in, research, development, regulatory approvals and commercialization activities relating to our product candidates, which may change from time to time;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we may incur to acquire, develop or commercialize additional product candidates;
- the level of demand and the indication for any approved products, which may vary significantly;
- the risk/benefit profile, cost, coverage, and reimbursement policies with respect to our product candidates, if approved, and existing and potential future drugs that compete with our product candidates;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- the timing and amount of any milestone, royalty or other payments payable by us or due to us under any collaboration, licensing or other similar agreement; and
- general market and economic conditions, including market conditions in the pharmaceutical and biotechnology sectors.

The cumulative effects 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 common stock could decline

substantially. Such a stock price decline could occur even if we have met any previously publicly stated revenue or earnings guidance.

The trading price of the shares of our common stock may be volatile, and investors could lose all or part of their investment.

The market price for our stock has been highly volatile and may continue to be subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of particular companies, including in connection with conflicts in various regions of the world, increasing inflation rates, interest rate changes, and changes in U.S. federal policy. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- the commencement, enrollment or results of our current or future clinical trials of our product candidates;
- adverse results from, delays in, suspension or termination of current or future clinical trials or preclinical studies of our product candidates, or any delay in advancing a clinical candidate;
- the success of competitive products gaining approvals or announcements by current and future competitors of their product development efforts;
- any delay in our regulatory filings for our product candidates or any other product candidate we may develop, and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings;
- adverse regulatory decisions, including the failure to authorize or approve the conduct of one or more clinical trials of our product candidates, the failure to receive regulatory approvals of our product candidates, or the failure of a regulatory authority to accept data from clinical trials conducted in other countries;
- the reporting of unfavorable preclinical or clinical results;
- our success or failure to identify, develop, acquire or license additional product candidates;
- the degree and rate of physician and market adoption of any of our current and future product candidates, if successfully developed and approved;
- manufacturing, supply or distribution delays or shortages, including our inability to obtain adequate supply of drug product, drug substance, raw materials or any commercially available product to be used in our clinical trials, at acceptable prices, or at all;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- unanticipated serious safety concerns related to the use of our product candidates or any other product candidate;
- our cash position, and any changes in financial estimates by us or by any equity research analysts who cover our stock;
- changes in our capital structure, such as future issuances of securities and the incurrence of additional debt;
- conditions or trends in our industry;
- investors' general perception of our company and our business;
- our ability to effectively manage our growth;
- overall performance of the equity markets;
- changes in the market valuations and stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;

- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, capital commitments or divestitures;
- third-party publications and discussions about our business on social media, forums and other websites;
- recruitment or departure of key personnel;
- trading volume of our common stock;
- sales of common stock by us or our stockholders in the future;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our product candidates;
- significant lawsuits, including patent or stockholder litigation;
- changes in the structure of healthcare payment systems;
- changes in accounting standards, policies, guidelines, interpretations or principles;
- regulatory or legal developments in the U.S. and foreign countries;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, geopolitical and stock market conditions; and
- other events or factors, many of which are beyond our control.

These and other market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the risks described in this section, or any of a broad range of other risks, could have a material adverse impact on the market price of our common stock. The price of our common stock may be disproportionately affected as investors may favor traditional profit-making industries and companies during times of market uncertainty and instability.

In the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted, could result in substantial costs and divert management's attention and resources.

In addition, the trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of these analysts ceases coverage of us, fails to publish reports on us regularly or publish inaccurate or unfavorable research about our business, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

We may not be able to satisfy listing requirements of Nasdaq or obtain or maintain a listing of our common stock on Nasdaq.

Since our common stock is listed on Nasdaq, we must meet certain financial and liquidity criteria to maintain such listing. If we violate Nasdaq's listing requirements, our common stock may be delisted. If we fail to meet any of Nasdaq's listing standards, our common stock may be delisted. In addition, our board of directors may determine that the cost of maintaining our listing on a national securities exchange outweighs the benefits of such listing. A delisting of our common stock from Nasdaq may materially impair our stockholders' ability to buy and sell our common stock and could have an adverse effect on the market price of, and the efficiency of the trading market for, our common stock. The delisting of our common stock could significantly impair our ability to raise capital and the value of our stockholders' investment.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may significantly reduce the value of our shares to a potential acquiror or make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change of control was considered favorable by

our stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock and may fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change of control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors will be elected each year;
- stockholders are not entitled to remove directors other than by a two-thirds (2/3) vote and only for cause;
- stockholders are not permitted to take actions by written consent;
- stockholders cannot call a special meeting of stockholders; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change of control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in our stockholders' best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our executive officers, directors, principal stockholders, and their respective affiliates own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates beneficially own a significant percentage of our outstanding common stock. As a result, these persons, acting together, would be able to control all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions.

Some of these persons or entities may have interests different than other stockholders. For example, because many of these stockholders purchased their shares at prices substantially below the current market price of our common stock and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders. The significant concentration of ownership may adversely affect the trading price of our common stock due to investors' perceptions that it may create conflicts of interest.

We do not anticipate paying any cash dividends on our common stock in the foreseeable future.

We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future. Investors seeking cash dividends should not purchase our common stock. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

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 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 Delaware General Corporation Law, our certificate of incorporation or our bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery of the State of Delaware 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 of 1933, as amended (the "Securities Act") or the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our 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 bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, the forum selection clauses in our 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.

General Risk Factors

If our information technology systems or data, or those of third parties upon which we rely, are or were compromised, or fail, we could experience adverse consequences resulting from such compromise, or failure, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse consequences.

In the ordinary course of our business, we and the third parties upon which we rely, process, collect, receive, store, use, transfer, protect, secure, dispose of, transmit, and share proprietary, confidential, and sensitive data, including personal data (such as health-related data), intellectual property and trade secrets. The secure processing, maintenance and transmission of such sensitive information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions.

Cyber-attacks, malicious internet-based activity, online and offline fraud, security breaches and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties upon which we rely. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer “hackers,” threat actors, “hacktivists,” organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states and nation-state-supported actors. Some actors now engage and are expected to continue to engage in cyber-attacks, including, without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities.

These risks, as well as the number and frequency of cybersecurity events globally, may also be heightened during times of war or other major conflicts. We and the third parties upon which we rely are subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks (such as credential stuffing attacks), credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, electrical and telecommunications failures, earthquakes, fires, floods, and other similar threats. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, loss of sensitive data and income, reputational harm and diversion of funds.

We have a hybrid in-office/remote work environment, which, like other companies that have incorporated remote working, has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations.

Future business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

We currently rely on third-party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, cloud-based infrastructure, employee email, and other functions. We also currently rely on commercially available tools from third-party service providers to process and safeguard our sensitive information and business data. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award.

We, like others in our industry, have experienced and may continue to experience threats or system failures which could cause a security incident or other interruption that could result in unauthorized, unlawful or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties upon whom we rely. We have not yet conducted any internal audits or penetration tests on our information technology systems, nor have we enlisted any external parties to conduct security audits or penetration tests on our behalf. Such assessments, when conducted, could indicate vulnerabilities in our information technology systems which we may not be able to effectively remediate. If a security incident were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. We may expend significant resources or modify our business activities (including our clinical trial activities) to endeavor to protect against security incidents.

Certain data privacy and security obligations may require us to implement and maintain specific security measures or industry-standard or reasonable security measures to protect our information technology systems and sensitive information. While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. Additionally, certain federal, state and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular categories of personally identifiable information, which could result from breaches experienced by us or the third parties upon whom we rely. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences.

We may not be able to detect and remediate vulnerabilities in our information technology systems because the threats and techniques used to exploit vulnerabilities change frequently and are often sophisticated in nature. Therefore, such vulnerabilities could be exploited but may not be detected until after a security

incident has occurred. Such vulnerabilities could pose material risks to our business. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. It is not possible to prevent all threats to our information technology systems and those of our third-party service providers, over which we exert less control, and any controls we implement to do so may prove to be ineffective.

If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences, such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may cause delays or disruptions in our clinical trials and development of product candidates, deter customers from using our products, and negatively impact our ability to grow and operate our business.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages or claims related to our data privacy and security obligations. Further, although we maintain cyber liability insurance, we cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims. In addition to adverse impacts relating to experiencing a security incident, third parties may gather, collect or infer sensitive information about us from public sources, data brokers or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

We are subject to stringent and evolving U.S. laws and regulations and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations, reputational harm, loss of revenue or profits, and other adverse business consequences.

In the ordinary course of business, we and the third parties on which we rely process personal data and other sensitive information, including proprietary and confidential business data, trade secrets, intellectual property, data we collect about clinical trial participants and sensitive third-party data. Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security.

The legislative and regulatory framework for the processing of personal data worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. In the U.S., there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure, transfer, security and processing of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act, the California Consumer Privacy Act (the "CCPA")), and other similar laws. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to HIPAA, which imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. Depending on the facts and circumstances, we could be subject to civil and criminal penalties if we knowingly obtain, use or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

At the state level, numerous U.S. states have enacted comprehensive privacy laws that impose certain obligations on covered businesses. For example, For example, the CCPA establishes data privacy rights for individuals located in California and imposes certain requirements on how businesses can collect, use, and share personal information about such individuals. The California Privacy Rights Act, or the CPRA, significantly modified the CCPA and imposes additional obligations on companies covered by the legislation, including by expanding consumers' rights with respect to personal information, and established a state agency vested with

the authority to enforce the CCPA While these state laws exempt some data processed in the context of clinical trials, these developments may further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely. Furthermore, other states have proposed or enacted legislation that is focused on more narrow aspects of privacy. For example, a number of states have passed laws that are specifically focused upon health privacy, such as Washington's My Health My Data Act, which imposes an additional layer of protection regarding consumer health data and creates a private right of action. A smaller number of states have passed laws protecting biometric information. The effects of state and federal privacy laws are potentially significant and may require us to modify our data processing practices and policies and to incur substantial costs and potential liability in an effort to comply with them.

Additionally, through executive and legislative action, the federal government has taken steps to restrict data transactions involving certain sensitive data categories – including health data, genetic data, and biospecimens – with persons or entities affiliated with China and certain other countries of concern. These current and future data privacy laws and regulations may require us to modify our data collection or processing practices and policies, incur substantial costs and expenses in an effort to comply and increase our potential exposure to regulatory enforcement, reputational damage, and/or litigation.

Outside the U.S., an increasing number of laws, regulations, and industry standards may govern data privacy and security. For example, if we commence clinical trials in Europe, which we anticipate commencing if our product candidates advance to later stages of development, our processing of personal data in that context would become subject to the European Union's General Data Protection Regulation ("EU GDPR"), and/or the United Kingdom's so-called "UK GDPR" (together, the "GDPR"). The GDPR is wide-ranging in scope and imposes numerous requirements on companies that are subject to it, including relating to having a legal basis for processing personal data, relating to the processing of sensitive data (such as health 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, notification of data breaches, requiring data protection impact assessments for high risk processing 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 European Union and the UK, 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 (£17.5 million) or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR.

In addition, we may be unable to transfer personal data from Europe and other jurisdictions to the U.S. or other countries due to data localization requirements or limitations on cross-border data flows. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area ("EEA") and the United Kingdom ("UK") have significantly restricted the transfer of personal data to the U.S. and other countries whose privacy laws it considers inadequate. Other jurisdictions may adopt similarly stringent data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the U.S. in compliance with law, such as the EEA's standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the U.S. If there is no lawful manner for us to transfer personal data from the EEA, the UK or other jurisdictions to the U.S., or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the U.S., are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data out of Europe for allegedly violating the GDPR's cross-border data transfer limitations.

We are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. If any privacy policies, marketing materials and other statements regarding data privacy and security that we publish are found to be deficient, lacking in transparency, deceptive, unfair or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, including the Federal Trade Commission, or other adverse consequences.

Laws and regulations related to privacy, data protection and security are continuing to evolve and are becoming increasingly stringent. Additionally, these laws may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions, creating uncertainty. Preparing for and complying with these obligations requires us to devote significant resources, which may necessitate changes to the ways in which we collect and process data, our information technologies, systems and to exercise greater oversight and control over third parties that process personal data on our behalf.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties we rely on fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we may face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims); additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials and development of product candidates); inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations.

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

We may use, and our vendors may incorporate, artificial intelligence, or AI, both in our own development and implementation of AI and through the adoption of commercially available tools. The use of AI presents risks and challenges that could adversely affect our business and reputation, including cybersecurity, data privacy, IT, confidentiality, regulatory, legal, operational, competitive, reputational, intellectual property and other risks. For example, use of certain AI tools may increase the risk of unauthorized disclosure of confidential information, compromise of proprietary intellectual property, or inadvertent inclusion of third-party intellectual property or other protected material, which could result in disputes, claims of infringement, legal liabilities or financial losses. The rapidly evolving regulatory landscape surrounding AI also poses a risk, as new laws and regulations could impose additional compliance burdens, resulting in increased operational costs to comply with U.S. and non-U.S. laws concerning the use of AI, the nature of which cannot be determined at this time.

Additionally, our vendors may incorporate AI tools into their offerings, and the providers of these AI tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of AI, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. The use of generative AI models in our internal or third-party systems may create new attack surfaces or methods for adversaries, which could impact us and our vendors. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

We are subject to governmental export and import controls, economic sanctions, anti-corruption laws and regulations of the U.S. and other jurisdictions. We can face criminal liability and other serious consequences for violations of these laws and regulations, which could harm our business.

We are subject to and required to comply with various export control, import and trade and economic sanctions laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations and sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. These laws may prohibit or restrict our ability to transfer, sell or supply, our products to certain governments,

persons, entities, countries, and territories, including those that are the target of comprehensive sanctions or an embargo.

We are also subject to anti-corruption and anti-bribery laws, including the U.S. Foreign Corrupt Practices Act of 1977, as amended (the "FCPA"), the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws, including the FCPA, generally prohibit companies and their employees, agents, CROs, contractors and other partners from offering, promising, giving, soliciting or authorizing others to give or receive anything of value, either directly or indirectly, to or from 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. We can be held liable for the corrupt or other illegal activities of our employees, agents, CROs, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violation of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

If we fail to maintain an effective system of internal controls over financial reporting, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting.

Commencing with this Annual Report, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Form 10-K filing for each year, as required by Section 404 of the Sarbanes-Oxley Act. This requires that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. Prior to our initial public offering, we had never been required to test our internal control within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner. In addition, when we lose our status as an "emerging growth company" and if we do not otherwise qualify as a "non-accelerated filer," our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting, which will require additional expense, resources and management commitment.

We may identify material weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our consolidated 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.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls over financial reporting, we may not be able to produce timely and accurate consolidated financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our 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 certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, 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 realities 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 or insufficient disclosures due to error or fraud may occur and not be detected.

We might not be able to utilize a significant portion of our net operating loss carryforwards.

We have generated, and expect to continue to generate, significant federal and state net operating loss ("NOL") carryforwards. As of December 31, 2025, we had federal and state net operating loss carryforwards of $148.0 million and $155.4 million, respectively. Under current tax laws and regulations, these NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the Tax Cuts and Jobs Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act, federal NOLs incurred in taxable years beginning after December 31, 2017 generally may be carried forward indefinitely, but the deductibility of such federal NOLs is limited to 80% of our taxable income for taxable years beginning after December 31, 2020. We cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our NOLs.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "IRC"), and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change by value, in its equity ownership by certain stockholders over a rolling three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We may have experienced ownership changes in the past and may experience ownership changes as a result of subsequent shifts in our stock ownership which may be out of our control. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs by federal or state taxing authorities or other unforeseen reasons, portions of our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities.

New tax laws or regulations, changes to existing tax laws or regulations or changes in their application to us may have a material adverse effect on our business, cash flows, financial condition or results of operations.

U.S. federal, state, local and foreign tax laws, regulations and administrative guidance are subject to change as a result of the legislative process and review and interpretation by the U.S. Internal Revenue Service, the U.S. Treasury Department and other taxing authorities. For example, budget reconciliation bill H.R. 1, referred to as the One Big Beautiful Bill Act ("H.R. 1") was signed into law on July 4, 2025, and made significant changes to U.S. federal tax law. Changes to tax laws (which changes may have retroactive application), including with respect to net operating losses and research and development tax credits, could adversely affect us or holders of our common stock.

For example, under H.R. 1, taxpayers are now permitted to immediately deduct domestic research and development expenses for taxable years beginning after December 31, 2024. Taxpayers may alternatively elect to capitalize and amortize such expenses. In addition, H.R. 1 provides that for taxable years beginning after December 31, 2021 and before January 1, 2025, certain eligible taxpayers generally may elect to retroactively deduct expenses for domestic research and development expenses in such taxable years by filing amended tax returns for such taxable years, and all other taxpayers that are not eligible to make such an election and that amortized expenses for domestic research and development expenses in such taxable years generally may elect to accelerate and deduct the remaining unamortized amounts of such expenses (i) in the first taxable year beginning after December 31, 2024, or (ii) ratably over the two-taxable year period beginning with the first taxable year beginning after December 31, 2024. However, pursuant to Section 174 of the IRC, in taxable years beginning after December 31, 2021, foreign research and development expenses must continue to be capitalized and amortized.

In recent years, many changes to tax laws have been made and changes are likely to continue to occur in the future. Since early 2025, U.S. policy changes have been implemented at a rapid pace, and additional

changes, including to tax laws, are likely. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations.

We are eligible to be treated as an "emerging growth company" and a "smaller reporting company" and, as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"). For as long as we continue to be an emerging growth company, we may take advantage of certain exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- providing only two years of audited financial statements in addition to any required unaudited interim financial statements and correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least $1.235 billion or (c) in which we are deemed to be a large accelerated filer, which means, among other conditions, that the market value of our common stock that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies, and we expect to rely on this exemption. Even after we no longer qualify as an emerging growth company, we may, under certain circumstances, still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We incur significant costs and demands upon management as a result of being a public company.

As a public company, we incur significant additional legal, accounting and other costs that we did not incur as a private company. We are now subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, Sarbanes-Oxley, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and certain corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted additional rules and regulations in these areas, such as mandatory "say on pay" voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to

additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly as compared to a private company. If these requirements divert the attention of our management and personnel from other business concerns, they could have an adverse effect on our business. The increased costs will increase our net loss, and may require us to reduce costs in other areas of our business.

Unstable global economic and geopolitical conditions could adversely affect our business, financial condition, stock price, and results of operations.

The global economy and financial markets have experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, inflation, declines in economic growth, global supply chain disruptions, and uncertainty about economic stability. The global economy and financial markets may also be adversely affected by actual or anticipated changes in U.S. policies or regulatory environment, current or anticipated impact of military conflict, including the ongoing conflicts between Russia and Ukraine, and in the Middle East, terrorism or other geopolitical events. Sanctions imposed by the U.S. and other countries in response to such conflicts may adversely impact the financial markets and the global economy, and the economic countermeasures by the affected countries or others could exacerbate market and economic instability.

There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A severe or prolonged economic downturn could result in a variety of risks to our business, including weakened demand for any product candidates we may develop and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. If the equity and credit markets continue to deteriorate, it may make any necessary equity or debt financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing 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, scale back or discontinue the clinical development of one or more of our product candidates. In addition, there is a risk that our current or future service providers, manufacturers or other collaborators may not survive such difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget. We cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Changes in U.S. federal policy that affect the geopolitical landscape could give rise to circumstances outside our control that could have negative impacts on our business operations. For example, in 2025, the U.S. imposed broad-based tariffs on imports from almost all countries, including significant tariffs applicable to imports from China, where certain of our clinical trial materials are manufactured. In response to tariffs, other countries have implemented retaliatory tariffs on U.S. goods. While certain tariffs were subsequently suspended, modified, or temporarily reduced, their impact has already been seen, and we expect will continue to be seen, in global markets. Historically, tariffs have led to increased trade and political tensions between the U.S. and countries in the international community. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. Any changes in political, trade, regulatory, and economic conditions, including U.S. trade policies, could have a material adverse effect on our financial condition or results of operations.

We may become involved in litigation that could divert management's attention and harm our business, and insurance coverage may not be sufficient to cover all costs and damages.

From time to time, we may be subject to litigation claims through the ordinary course of our business operations regarding, but not limited to, securities litigation, employment matters, security of patient and employee personal data, contractual relations with collaborators and licensors and intellectual property rights. We may be exposed to such litigation even if no wrongdoing on our part has occurred. Litigation to defend ourselves against claims by third parties, or to enforce any rights that we may have against third parties, could

result in substantial costs and diversion of our resources, causing a material adverse effect on our business, financial condition, results of operations or cash flows.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 1C. CYBERSECURITY

Cyber Risk Management and Strategy

We have implemented and maintain an information security program that includes processes for the identification, assessment, and mitigation of cybersecurity risks. We conduct periodic assessments of our assets as part of our risk management process and to evaluate the effectiveness of applicable security controls. These assessments are informed by industry standards. Our cybersecurity risk management process is a part of our overall risk management program. We also have an employee education program that includes training designed to raise awareness of cybersecurity threats. We maintain an incident response plan that outlines the legal and governance process for identifying and managing material cyber risks to our information and information systems and our framework for assessing and responding to cyber incidents, as applicable.

Although risks from cybersecurity threats have to date not materially affected us, our business strategy, results of operations or financial condition, we do, from time to time, experience threats and communicate security incidents relating to our and our third party vendors' data and information systems. For more information about these risks, please refer to the section entitled "Risk Factors" in this Annual Report.

Governance Related to Cybersecurity Risks

Our head of information technology ("IT"), who reports to the Chief Financial Officer (collectively, "IT Leadership"), has primary responsibility for the strategic leadership and management of our cybersecurity program. Our head of IT has over 25 years of experience building and leading information technology and security teams. Our IT Leadership works alongside other functions to maintain and implement our cybersecurity strategy. Our IT Leadership meets as circumstances warrant with other members of our management, including executive leadership, to review and update incident response procedures and other aspects of our cybersecurity program.

The audit committee of Sionna's board of directors has ultimate oversight over cybersecurity risk. Our IT Leadership presents to the audit committee periodically regarding cybersecurity matters, including updates on security testing and assessments, cyber risks, and related cyber strategy, as applicable. The Chief Financial Officer and the Chief Legal Officer are responsible for informing the audit committee in the event of any material cybersecurity incidents and any potential disclosure obligations arising from such incidents. The audit committee will update the board of directors on matters related to cybersecurity as needed.

ITEM 2. PROPERTIES

Our principal facilities consist of office and laboratory space. Our corporate headquarters is located in Waltham, Massachusetts, where we occupy approximately 24,051 square feet of office space at 21 Hickory Drive, Suite 500, Waltham, Massachusetts 02451. The current term of our lease expires in November 2030. We have the option to extend our lease for an additional five-year term at market-based rates.

We believe these facilities are adequate for the foreseeable future and that suitable additional space will be available as and when needed. To meet the future needs of our business, we may lease additional or alternate space. We believe that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we may become involved in legal proceedings arising from the ordinary course of business. We record a liability for such matters when it is probable that future losses will be incurred and that

such losses can be reasonably estimated. Significant judgment by us is required to determine both probability and the estimated amount. Our management is currently not aware of any legal matters that could have a material effect on our financial position, results of operations or cash flows, nor are we aware of any governmental proceedings involving potential monetary sanctions of $300,000 or more.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

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

Market Information

Our common stock began trading under the symbol "SION" on the Nasdaq Global Market on February 7, 2025. Prior to this time, there was no public trading market for our common stock.

Holders of our Common Stock

As of February 1, 2026, there were approximately 10 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees.

Securities Authorized for Issuance under Equity Compensation Plans

Information about securities authorized for issuance under our equity compensation plans is incorporated herein by reference to Part III, Item 12 of this Annual Report.

Use of Proceeds from our IPO

On February 6, 2025, the SEC declared effective our registration statement on Form S-1 (File No. 333-284352), as amended (the "Registration Statement"), filed in connection with our initial public offering (the "IPO"). Pursuant to the Registration Statement, we registered the offer and sale of 12,176,467 shares of our common stock with a proposed maximum aggregate offering price of approximately $219.2 million. Goldman Sachs & Co. LLC, TD Securities (USA) LLC, Stifel, Nicolaus & Company, Incorporated, and Guggenheim Securities, LLC acted as representatives of the underwriters for the offering. On February 10, 2025, we raised aggregate net proceeds of $199.6 million from the sale of 12,176,467 shares of common stock at a price of $18.00 per share, which included 1,588,234 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares, before deducting offering costs payable by us of $4.2 million.

The offering terminated after the sale of all securities registered pursuant to the Registration Statement. There has been no material change in the expected use of the net proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b) of the Securities Act on February 7, 2025.

We continue to hold a significant portion of the balance of the net proceeds in cash equivalents and marketable securities. There has been no material change in the planned proceeds from our IPO, as described in our final prospectus filed with the SEC on February 7, 2025 pursuant to Rule 424(b) under the Securities Act.

Dividends

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Unregistered Sales of Equity Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. [RESERVED]

Not applicable.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our consolidated financial statements and related notes and other financial information included elsewhere in this Annual Report. This discussion and analysis and other parts of this Annual Report contain forward-looking statements based upon our current plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and beliefs. Our actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under "Risk Factors" and elsewhere in this Annual Report. You should carefully read the "Risk Factors" section of this Annual Report to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Also see the section titled "Cautionary Note Regarding Forward-Looking Statements." Our historical results are not necessarily indicative of the results that may be expected for any period in the future. For convenience of presentation, some of the numbers have been rounded in the text below.

Overview

We are a clinical-stage biopharmaceutical company on a mission to revolutionize the current treatment paradigm for cystic fibrosis ("CF") by developing novel medicines that normalize the function of the cystic fibrosis transmembrane conductance regulator ("CFTR") protein to deliver clinically meaningful benefit to people with CF. Our goal is to deliver differentiated medicines for people with CF that can restore their CFTR function to as close to normal as possible by directly stabilizing CFTR's nucleotide binding domain 1 ("NBD1"). We believe stabilizing NBD1 is central to unlocking dramatic improvements in clinical outcomes and quality of life for people with CF. We are also advancing a portfolio of complementary CFTR modulator candidates designed to work synergistically with our NBD1 stabilizers to improve CFTR function, as seen in preclinical models.

We believe our robust pipeline provides multiple potential pathways to achieve our mission, either through development of an NBD1 stabilizer and a complementary modulator in combination with each other to produce a proprietary dual combination, or an NBD1 stabilizer administered in combination with the standard of care for CF. While we have prioritized development of a proprietary dual combination, we believe both development pathways offer attractive commercial opportunities.

In June 2025, we announced positive topline data from our two randomized, double-blinded, placebo-controlled Phase 1 clinical trials evaluating SION-719 and SION-451, our lead NBD1 stabilizer product candidates, in healthy volunteers, and our plans to advance both compounds to the next phase of clinical development. The trials assessed the safety, tolerability, and pharmacokinetics ("PK") of single and multiple ascending doses of each product candidate, as well as food effect and tablet bioequivalence.

Both SION-719 and SION-451 were generally well tolerated in these trials, with no serious adverse events, treatment emergent adverse events that led to discontinuation of drug, or dose-limiting toxicities observed. The Phase 1 data also supported the use of a tablet formulation in future trials and indicated that both compounds could be dosed in a fed or fasted state. Both NBD1 stabilizers met target exposure thresholds. Based on the Phase 1 data and our preclinical CF human bronchial epithelial ("CFHBE") model, we believe our NBD1 stabilizers have the potential to provide clinically meaningful benefit to people with CF when SION-719 is administered as an add-on to the standard of care or when SION-451 is used in proprietary dual combinations with one of our complementary modulators.

In October 2025, we announced the initiation of a Phase 2a proof-of-concept trial in CF patients evaluating SION-719 as an add-on to the standard of care. The Phase 2a trial, called PreciSION CF, is

designed to evaluate the safety, tolerability, and PK of SION-719 when administered with the standard of care for CF, Vertex Pharmaceuticals, Inc.'s Trikafta, and to assess change in CFTR function as measured by sweat chloride levels. Additionally, in August 2025, we announced the initiation of a Phase 1 dual combination trial in healthy volunteers evaluating SION-451 in dual combinations with each of SION-2222 and SION-109, two of our complementary CFTR modulators. The trial will evaluate the safety, tolerability, and PK of varying doses of the dual combinations and will inform selection of a dual combination for further development. Topline data from both trials are anticipated in mid-2026.

Liquidity and Financial Condition

Since our inception, we have funded our operations primarily with proceeds from private placements of convertible preferred stock and through net proceeds from our IPO. During 2025, we completed our IPO and raised aggregate net proceeds of $199.6 million from the sale of 12,176,467 shares of common stock, which included 1,588,234 shares of common stock sold pursuant to the underwriters' full exercise of their option to purchase additional shares. As of December 31, 2025, we have raised aggregate net proceeds of $530.0 million. We have not generated any revenue from product sales or other sources.

Due to our significant research, development and manufacturing expenditures, we have accumulated substantial losses and negative cash flows since our inception, including net losses of $75.3 million and $61.7 million for the years ended December 31, 2025 and 2024, respectively. As of December 31, 2025, we had an accumulated deficit of $256.4 million.

We expect our expenses and operating losses will increase substantially as we:

- continue to advance the clinical development of our current and future product candidates;
- continue to advance our research activities and seek to discover and develop additional product candidates to expand our pipeline;
- pursue regulatory approvals for any current or future product candidates that successfully complete clinical trials;
- continue to utilize third parties to manufacture our product candidates;
- continue to develop, maintain, expand, enforce, defend and protect our intellectual property portfolio (including intellectual property obtained through license agreements) and provide reimbursement of third-party expenses related to our patent portfolio;
- attract, hire and retain additional qualified personnel;
- add operational, financial and management information systems;
- undertake pre-commercial activities, and scale-up external commercial-scale manufacturing capabilities, to commercialize any current or future product candidates which may obtain regulatory approval;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any current or future product candidates which may receive regulatory approval; and
- incur additional audit, legal, regulatory, tax and other expenses associated with being a public company.

In addition, we have several clinical development, regulatory, and commercial milestones, as well as royalty payment obligations under our licensing arrangements. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our ongoing and planned clinical trials and our expenditures on other research and development activities.

We do not have any products approved for sale and have not generated any revenue from product sales. We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our current or any future product candidates, which we expect will take a number of years or may never occur. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings or other capital sources, potentially including collaborations, licenses or other strategic

arrangements. See the section titled "*—Liquidity and Capital Resources*." We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates, or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

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

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $310.3 million. Based upon our current operating plans, we believe that our existing cash, cash equivalents and marketable securities, will be sufficient to fund our operations into 2028. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. In addition, we could utilize our available capital resources sooner than we expect. See the sections titled "*—Liquidity and Capital Resources*" and "*Risk Factors—Risks Related to Our Limited Operating History, Financial Condition and Need for Additional Capital*" included elsewhere in this Annual Report.

License and Collaboration Agreements

Below is a summary of the key terms for certain of our license and collaboration agreements. For a more detailed description of these agreements, see the section titled "*Business—License and Collaboration Agreements*."

Sanofi License Agreement

In December 2019, we entered into a license agreement, which has been subsequently amended (as amended, the "Sanofi License Agreement"), with Sanofi, pursuant to which we have been granted an exclusive, worldwide, sublicensable, royalty-bearing license to develop and commercialize products using the licensed compounds and know-how for CFTR modulator therapies. The licensed and derived rights are being utilized in SION-719, SION-109 and SION-451.

As initial consideration for the license, we paid a non-refundable, upfront payment of $1.5 million, as well as a reimbursement of $0.3 million for Sanofi's research and development expenses, which was previously recorded as research and development expense because the acquired license represented in-process research and development with no alternative future use. In addition, we are required to pay Sanofi a total of up to $40.0 million upon achievement of certain late-stage developmental and commercial milestones. As of December 31, 2025, no milestones were achieved. We are also required to pay royalties to Sanofi in the low single-digit percentage range based on net sales of licensed products, subject to customary reductions and offsets. Such royalty payments shall be reduced for products covered by derived patents.

CFF Payment Agreement

In December 2019, we entered into a payment agreement (the "CFF Payment Agreement") with the Cystic Fibrosis Foundation ("CFF"), pursuant to which we agreed to provide CFF with compensation in exchange for the grant of, or forbearance from exercising, certain of CFF's rights existing under the license agreement, by and between CFF (through an assignment by Cystic Fibrosis Foundation Therapeutics, Inc.) and Genzyme Corporation, an affiliate of Sanofi (the "CFFT-Genzyme Agreement"). Under the CFF Payment Agreement, we are obligated to compensate CFF in connection with our development and commercialization of licensed products under the Sanofi License Agreement.

As initial consideration for CFF's grant of, and forbearance from exercising, its rights under the CFFT-Genzyme Agreement, we paid an upfront fee of $0.2 million and issued CFF shares of our preferred stock, valued at $1.0 million, which were previously recorded as research and development expenses. In addition, we agreed to pay CFF a sub-teen double-digit percentage of any amounts paid by us to Sanofi under the Sanofi

License Agreement, other than milestone, royalty or reimbursement payments. We are required to pay CFF a total of up to $40.0 million upon achievement of certain late-stage developmental and commercial milestones. As of December 31, 2025, no milestones were achieved. We are also required to pay revenue-shares of royalty payments to CFF in the low single-digit percentage range based on net sales of licensed products, subject to customary reductions and offsets. Such milestone and royalty payments shall be reduced for products covered by derived patents. Further, a side letter was executed between us and Sanofi, which clarifies the relationship between us, Sanofi and CFF, under which we are obligated to pay Sanofi 20% of the milestones it would have been obligated to pay CFF, net of the milestone amounts it is obligated to pay under the Sanofi License Agreement.

AbbVie License Agreement

In July 2024, we entered into a license agreement (the "AbbVie License Agreement") with AbbVie, pursuant to which we have been granted a license to research, develop and commercialize certain CFTR compounds. The licensed rights are directed, among other things, to three clinical-stage CFTR modulator therapies: SION-2222, SION-2851 and SION-3067. The license granted to us under the AbbVie License Agreement is subject to certain preexisting rights held by AbbVie and Galapagos NV ("Galapagos"). In particular, certain of the licensed patents and other intellectual property rights were developed by or on behalf of Galapagos and are sublicensed to us subject to the terms of the second amended and restated collaboration agreement between Galapagos and AbbVie in October 2018 (the "Galapagos License Agreement"), as amended by a side letter between Galapagos and AbbVie in July 2024.

As initial consideration for the license, we paid a non-refundable, upfront payment of $5.0 million and issued shares of our common stock with a fair value of $8.6 million to AbbVie. We determined that the AbbVie License Agreement represented an asset acquisition as it did not meet the definition of the business. We recorded the total initial consideration of $13.6 million as research and development expense during the year ended December 31, 2024, because the acquired license represented in-process research and development with no alternative future use. In addition, we are required to pay AbbVie a total of up to $360.0 million upon achievement of certain development and commercial milestones, consisting of up to $70.0 million in late-stage development milestones and up to $290.0 million in commercial milestones. We are also required to pay royalties to AbbVie in the low to mid single-digit percentage range based on net sales of licensed products, subject to customary reductions and offsets.

In addition, we are required to pay AbbVie up to $130.0 million in commercial and sales-based milestone payments, mid to high single-digit royalties on the licensed products or other payments due to Galapagos pursuant to the Galapagos License Agreement, to the extent such payments are triggered by our use of the licensed rights owned by Galapagos under the AbbVie License Agreement. There were no milestones achieved under the AbbVie License Agreement and Galapagos License Agreement as of December 31, 2025.

Components of Results of Operations

Revenue

To date, we have not generated any revenue. In the future, we may generate revenue from product sales from any approved product, which approval we do not expect to occur for at least the next several years, if ever, as well as collaboration or license agreements we may enter into with respect to our current or future product candidates. We cannot predict if, when or to what extent we will generate revenue as we may never succeed in obtaining regulatory approval for any of our product candidates. If we fail to complete preclinical and clinical development of our current or future product candidates or fail to obtain regulatory approval for any that successfully complete clinical trials, our ability to generate future revenues, and our results of operations and financial position would be adversely affected.

Operating Expenses

Our operating expenses consist of (i) research and development expenses and (ii) general and administrative expenses.

Research and Development Expenses

Research and development expenses consist primarily of costs associated with the preclinical and clinical development of our current and potential future product candidates. In particular, our research and development expenses include:

- personnel-related costs, including salaries, payroll tax, bonuses, benefits and stock-based compensation for employees engaged in research and development functions;
- the costs to acquire in-process research and development with no alternative future use acquired in an asset acquisition;
- external expenses, including expenses incurred under arrangements with third parties, such as contract research organizations (“CROs”), contract development and manufacturing organizations (“CDMOs”), consultants and our scientific advisors;
- the cost of manufacturing our product candidates, including costs for laboratory supplies, research materials and reagents;
- facility costs, depreciation and other expenses, which include direct and allocated expenses; and
- the cost of obtaining and maintaining patent and trade secret protection for our product candidates.

We recognize research and development costs in the periods in which they are incurred. Most of our research and development expenses have been related to identifying and developing our product candidates. Typically, external expenses are recognized based on an evaluation of the progress to completion of specific tasks using information obtained from (i) internal personnel regarding the services that have been performed on the Company's behalf and estimating the associated cost incurred for those services or (ii) information provided to us by our service providers as of each reporting date. Advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses, which are expensed as the related goods are delivered or the services are performed, or when it is no longer expected that the goods will be delivered, or the services rendered. Significant judgments and estimates are made in determining the accrued or prepaid expense balances at the end of any reporting period.

External costs represent a significant portion of our research and development expenses, which we track on a program-by-program basis following the nomination of a product candidate. Our internal research and development expenses consist primarily of personnel-related expenses, including stock-based compensation expenses and allocated expenses. We do not track our internal research and development expenses on a program-by-program basis as they either relate to early-stage research expenses, such as lab supplies or our personnel expenses, consulting fees or other costs that are deployed across multiple programs.

Product candidates in later stages of development generally have higher development costs than those in earlier stages resulting from larger and more complex clinical trials, manufacturing scale-up and an increase in research and development headcount to oversee these activities. As a result, management expects that our research and development expenses will increase substantially over the next several years as we potentially advance our product candidates into later-stage development efforts.

Our future development costs may vary significantly based on a variety of factors, including:

- the timing, complexity and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the extent to which we in-license or acquire other product candidates and technologies to further develop our pipeline;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to domestic and foreign regulatory authorities;
- receipt of marketing approvals, if any, from applicable regulatory authorities;
- the development of commercial-scale manufacturing and distribution processes for our current and any future product candidates;

- our ability to obtain, maintain and protect patent, trade secret protection and regulatory exclusivity for our product candidates, both in the U.S. and internationally;
- our ability to successfully recruit and retain additional employees;
- the timing and amount of milestones, royalties or other payments we must make to our licensing partners; and
- the commercialization of our product candidates, if and when approved.

A change in the outcome of any of these variables with respect to the development of any current or future product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the U.S. Food and Drug Administration ("FDA") or another regulatory authority were to delay a planned start of a clinical trial or require us to conduct clinical trials beyond those that we currently anticipate would be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to slower than expected patient enrollment or other reasons, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate. We do not have control over many of these factors, including certain aspects of clinical development, the regulatory submissions process, potential threats to our intellectual property rights and general political and economic conditions that may negatively impact our business in the future. We may never obtain regulatory approval for any of our product candidates, and, even if we do, drug commercialization takes several years and millions of dollars in development costs.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, including salaries, payroll tax, bonuses, benefits and stock-based compensation charges for those individuals in executive, legal, finance, human resources, business development, information technology and other administrative functions. Other significant costs include legal fees relating to intellectual property and corporate matters, professional fees for auditing, accounting, tax and consulting services. Lastly, corporate overhead expenses such as information technology, insurance, facilities, and depreciation that are not allocated to the Company's research and development activities are included in general and administrative expenses. We recognize general and administrative expenses in the periods in which they are incurred.

We anticipate that our general and administrative expenses will increase in the future to support our increased research and development activities, pre-commercial preparation activities for our product candidates and any future product candidates and, if any product candidate receives marketing approval, commercialization activities. These increases will likely include increased costs related to the hiring of additional personnel and fees paid to outside consultants, among other expenses. We also anticipate increased expenses related to audit, accounting, legal and regulatory services associated with public company reporting and compliance, director and officer insurance premiums, investor and public relations costs and other administrative and professional services associated with operating as a public company.

Interest Income

Interest income consists primarily of interest earned and the amortization of discount or premiums on our cash equivalents and marketable securities. Interest income increased in 2025 primarily due to the investment of proceeds from our IPO. We expect interest income to decrease in future periods as our investment balances are reduced through operating activities.

Other Income

Other income consists of sublease income through our subleasing agreement which is further discussed within Note 7, "*Leases*" in our consolidated financial statements included elsewhere in this Annual Report.

Income Taxes

Since our inception, we have not recorded any income tax benefits for the net losses we have incurred in each period or for our earned research and development tax credits, as we believe, based upon the weight of

available evidence, that it is more likely than not that all of our net operating loss carryforwards and tax credits will not be realized.

As of December 31, 2025 and 2024, we had $148.0 million and $65.6 million of federal net operating loss ("NOL") carryforwards, and $155.4 million and $68.2 million of state NOL carryforwards, respectively. The federal NOLs are not subject to expiration and the state NOLs begin to expire in 2045. These loss carryforwards are available to reduce future federal taxable income, if any. As of December 31, 2025 and 2024, we have recorded a full valuation allowance against our net deferred tax assets.

Results of Operations

Comparison of Years Ended December 31, 2025 and 2024

The following table summarizes our results of operations (in thousands):

	Year Ended December 31,		
	2025	2024	Change
Operating expenses:			
Research and development	$ 60,263	$ 57,288	$ 2,975
General and administrative	28,719	13,268	15,451
Total operating expenses	88,982	70,556	18,426
Loss from operations	(88,982)	(70,556)	(18,426)
Other income:			
Interest income	13,295	8,170	5,125
Other income	419	698	(279)
Total other income:	13,714	8,868	4,846
Net loss	$ (75,268)	$ (61,688)	$ (13,580)

Research and Development Expenses

The following table summarizes our research and development expenses (in thousands):

	Year Ended December 31,		
	2025	2024	Change
Direct research and development expenses by program:			
NBD1 and combination development programs[1]	$ 32,865	$ 22,065	$ 10,800
Complementary modulator programs[2]	5,781	6,531	(750)
Unallocated research and development expenses:			
Personnel-related (including stock-based compensation)	14,668	9,128	5,540
Other R&D related costs	4,616	3,334	1,282
Facility, lab and depreciation	2,333	2,591	(258)
IPR&D acquisition related costs	—	13,639	(13,639)
Total research and development expenses	$ 60,263	$ 57,288	$ 2,975

[1]NBD1 and combination development program costs include NBD1 stabilizer activities and development of our proprietary combination therapy.

[2]Complementary modulator program costs include manufacturing expenses for the complementary modulators.

Research and development expenses increased by $3.0 million to $60.3 million for the year ended December 31, 2025, from $57.3 million for the year ended December 31, 2024. The increase in research and development expenses was primarily due to:

- direct research and development expenses increased by $10.1 million primarily due to an increase in clinical programs and combination development activities; and
- unallocated research and development expenses decreased by $7.1 million primarily due to IPR&D acquisition costs incurred in connection with our license agreement with AbbVie of $13.6 million in the third quarter of 2024, partially offset by a $5.5 million increase in personnel-related expenses including stock-based compensation, driven by an increase in the size of our workforce to support our clinical pipeline, and a $1.3 million increase in other R&D related costs, primarily driven by the use of third parties.

General and Administrative Expenses

The following table summarizes our general and administrative expenses (in thousands):

	Year Ended December 31,		
	2025	2024	Change
Personnel-related (including stock-based compensation)	$ 18,898	$ 7,842	$ 11,056
Professional services & fees	7,858	3,889	3,969
Facility and depreciation	1,963	1,537	426
Total general and administrative expenses	$ 28,719	$ 13,268	$ 15,451

General and administrative expenses increased by $15.5 million to $28.7 million for the year ended December 31, 2025, from $13.3 million for the year ended December 31, 2024. The increase in general and administrative expenses was primarily due to:

- $11.1 million increase in personnel-related expenses including stock-based compensation, driven by an increase in the size of our workforce; and
- $4.0 million increase in fees related to the use of third parties, including consultants and professional service organizations.

Interest Income

Interest income increased by $5.1 million to $13.3 million for the year ended December 31, 2025, from $8.2 million for the year ended December 31, 2024, primarily driven by an increased investment in debt securities due to the proceeds received from the initial public offering.

Other Income

Other income was $0.4 million and $0.7 million for the years ended December 31, 2025, and 2024, respectively, due to sublease income in connection with our subleasing agreement.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from operations. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our product candidates and any future product candidates. As such, we expect our research and development and general and administrative costs will continue to increase significantly, including the costs associated with operating as a public company. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings or strategic agreements.

As of December 31, 2025, we had $310.3 million in cash, cash equivalents and marketable securities.

Cash Flows

The following table sets forth a summary of the net cash flow activity (in thousands):

	Year Ended December 31,	
	2025	2024
Net cash used in operating activities	$ (66,297)	$ (52,787)
Net cash used in investing activities	(118,749)	(126,913)
Net cash provided by financing activities	205,710	178,967
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 20,664	$ (733)

Operating Activities

For the year ended December 31, 2025, net cash used in operating activities was $66.3 million primarily due to our net loss of $75.3 million and changes in operating assets and liabilities of $2.7 million, partially offset by $11.6 million of non-cash charges related to stock-based compensation, depreciation, non-cash operating lease expense and amortization of discounts on marketable securities.

For the year ended December 31, 2024, net cash used in operating activities was $52.8 million primarily due to our net loss of $61.7 million and changes in operating assets and liabilities of $3.1 million, partially offset by $12.0 million of non-cash charges related to stock-based compensation, depreciation, non-cash operating lease expense and amortization of discounts on marketable securities.

Investing Activities

Net cash used in investing activities was $118.7 million during the year ended December 31, 2025, which was primarily driven by purchases of marketable securities of $325.0 million and purchases of property and equipment of $0.4 million, partially offset by maturities of marketable securities of $206.7 million.

Net cash used in investing activities was $126.9 million during the year ended December 31, 2024, which was primarily driven by purchases of marketable securities for $182.8 million, partially offset by maturities of marketable securities of $56.0 million.

Financing Activities

Net cash provided by financing activities was $205.7 million during the year ended December 31, 2025, primarily due to net proceeds of $202.1 million received when the Company closed its IPO plus exercise proceeds totaling $3.6 million.

Net cash provided by financing activities was $179.0 million during the year ended December 31, 2024, during which time the Company closed its Series C Financing.

Future Funding Requirements

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $310.3 million. Based upon our current operating plans, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations into 2028. However, our forecast for the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. Additionally, conducting preclinical studies and clinical trials is costly, and the timing of progress and expenses in these studies and trials is uncertain. We will need to raise substantial additional capital in the future.

Our future funding requirements will depend largely on:

- the type, number, scope, progress, expansions, results, costs and timing of, discovery, preclinical studies and clinical trials of our current and future product candidates;
- the costs and timing of manufacturing for our current and future product candidates and commercial manufacturing;
- the costs, timing and outcome of regulatory review of our current and future product candidates;
- the timing and amount of milestones, royalties, or other payments we may be required to make to third parties, including Sanofi, CFF and AbbVie, and the terms and timing of establishing and maintaining any other similar arrangements we may enter in the future;
- the legal costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company;
- the costs associated with hiring additional personnel and consultants as our clinical and pre-commercial activities increase;
- the costs and timing of establishing or securing sales and marketing capabilities if any current or future product candidate is approved;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- the financial terms of any such agreement that we may enter into, including if we in-license or acquire additional product candidates or intellectual property; and
- costs to add additional operational, financial, clinical, quality and management information systems.

We have no committed sources of capital. Until such time, if ever, as we can generate substantial product revenue to support our cost structure, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, potentially including collaborations, licenses or other strategic arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. In addition, debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through a strategic agreement, we may have to grant rights to develop and market our current and future product candidates even if we would otherwise prefer to develop and market such product candidates ourselves. Our failure to raise capital or enter

into such other arrangements when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies.

If we are unable to raise additional funds, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts.

Contractual Obligations and Commitments

Research and Development and Manufacturing Agreements

We enter into contracts in the ordinary course of business with CROs, CDMOs and other vendors to assist in the research and development activities and other services and products for operating purposes. These contracts generally provide for termination at any time upon a certain amount of prior notice.

Leases

In May 2022, we executed a non-cancelable operating lease in Waltham, Massachusetts (the "Waltham Lease") to rent out 24,051 square feet of laboratory and office space and relocated our headquarters to Waltham in January 2023. Total expected cash payments in connection with the Waltham Lease will be $9.7 million over the term of the agreement ending in 2030. This excludes our share of facility operating expenses, real-estate taxes and other costs that are reimbursable to the landlord under the lease. For additional information regarding the lease obligations see Note 7, "Leases" in our consolidated financial statements included elsewhere in this Annual Report.

License Agreements

Our agreements with certain third parties to license intellectual property include potential milestone fees, sublicense fees and royalty fees. The milestone fees are dependent upon the development of products using the intellectual property licensed under the arrangements and contingent upon the achievement of development or regulatory approval milestones, as well as commercial milestones. These potential obligations are contingent upon the occurrence of future events and the timing and likelihood of such potential obligations are not known with certainty. For further information regarding these agreements, please see "*Business—Licenses and Collaboration Agreements*."

Critical Accounting Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which are prepared in accordance with generally accepted accounting principles in the United States of America. The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements and accompanying notes. We base our estimates and assumptions on historical experience and other factors that we believe to be reasonable under the circumstances. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience, known trends and events and on 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. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2, "*Summary of Significant Accounting Policies*" in our consolidated financial statements included elsewhere in this Annual Report, we believe that our critical accounting estimates are as follows.

Research and Development Expenses and Accruals

In preparing the consolidated financial statements, we are required to estimate our accrued research and development expenses as of each balance sheet date. 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. This process involves reviewing open contracts, communicating with internal personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the

service when we have not yet been invoiced or otherwise notified of the actual cost. We periodically confirm the accuracy of our estimates with our service providers and make adjustments, if necessary. The majority of our service providers invoice in arrears for services performed or when contractual milestones are met. The financial terms of agreements with these service providers are subject to negotiation, vary from contract-to-contract and may result in uneven payment flows. In circumstances where amounts have been paid in excess of costs incurred, we record a prepaid expense.

Contingent developmental and regulatory milestone payments will be recognized when the milestone is achieved, and commercial milestones, such as sales-based milestone payments, and royalties will be recognized when the underlying sale(s) occur.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts incurred.

Stock-Based Compensation Expense

We measure all stock options and other stock-based awards granted to employees, directors and non-employees based on their fair value on the date of the grant. We recognize compensation expense for awards to employees and directors over the requisite service period, which is generally the vesting period of the respective award. Compensation expense for awards to non-employees with service-based vesting conditions is recognized in the same manner as if we had paid cash in exchange for the goods or services, which is generally over the vesting period of the award. Our stock-based payments include stock options and grants of restricted common stock awards. For stock-based awards with service-based vesting conditions, we recognize compensation expense using the straight-line method. The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of our common stock on that same date. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option and our expected dividend yield. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require judgment to develop. See Note 12, "*Stock-based Compensation*" in our consolidated financial statements included elsewhere in this Annual Report for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted for the years ended December 31, 2025 and 2024. For awards to non-employees, the expected term of the option is equal to the contractual term of the non-employees' service agreement.

Determination of Fair Value of Common Stock Valuations

Prior to the completion of our IPO, there was no public market for our common stock. As a result, the estimated fair value of our common stock was determined by our board of directors as of the date of each option grant with input from management, considering our most recently available third-party valuations of common stock, and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the *American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, including the option pricing method and the probability-weighted expected return method. These methodologies required the use of significant management judgment and assumptions.

Since completion of our IPO in February 2025, the fair value of our common stock has been determined based on the closing market price of our common stock on the date of equity grant.

Recent 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, "*Summary of Significant Accounting Policies*" in our consolidated financial statements included elsewhere in this Annual Report.

Emerging Growth Company and Smaller Reporting Company Status

We are an “emerging growth company,” as defined in the JOBS Act, and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. We may take advantage of these exemptions until we are no longer an emerging growth company. Section 107 of the JOBS Act provides that an “emerging growth company” can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. We have elected to use the extended transition period for complying with new or revised accounting standards and as a result of this election, our consolidated financial statements may not be comparable to companies that comply with public company effective dates. We may take advantage of these exemptions up until the time that we are no longer an “emerging growth company.”

We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which we have total annual gross revenue of at least $1.235 billion or (c) in which we are deemed to be a “large accelerated filer” under the rules of the SEC, which means, among other things, the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the last business day of our most recently completed second fiscal quarter and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

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

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act, and pursuant to Item 305 of Regulation S-K we are not required to provide quantitative and qualitative disclosures about market risk
As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act, and pursuant to Item 305 of Regulation S-K we are not required to provide quantitative and qualitative disclosures about market risk.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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Consolidated Financial Statements for the Years Ended December 31, 2025 and 2024:

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Sionna Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Sionna Therapeutics, Inc., and subsidiary (the "Company") as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2025 and 2024, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ Deloitte & Touche LLP

Boston, Massachusetts

March 2, 2026

We have served as the Company’s auditor since 2021.

SIONNA THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	Year Ended December 31,	
	2025	2024
Assets		
Current assets:		
Cash and cash equivalents	$ 58,451	$ 37,788
Marketable securities, current	177,431	109,750
Prepaid expenses and other current assets	5,537	3,455
Total current assets	241,419	150,993
Property and equipment, net	2,225	2,466
Marketable securities, noncurrent	74,420	20,505
Restricted cash	963	962
Operating lease right-of-use asset	6,926	7,832
Other assets	—	2,994
Total assets	$ 325,953	$ 185,752
Liabilities, convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 769	$ 1,186
Accrued expenses	9,668	8,162
Operating lease liability, current	1,269	1,072
Other current liabilities	6	—
Total current liabilities	11,712	10,420
Operating lease liability, noncurrent	7,408	8,677
Total liabilities	19,120	19,097
Commitments and contingencies (Note 8)		
Series Seed convertible preferred stock, $0.001 par value, no shares and 3,963,963 shares authorized, issued and outstanding as of December 31, 2025 and December 31, 2024, respectively	—	13,014
Series A convertible preferred stock, $0.001 par value, no shares and 5,704,161 shares authorized, issued and outstanding as of December 31, 2025 and December 31, 2024, respectively	—	25,235
Series B convertible preferred stock, $0.001 par value, no shares and 11,370,621 shares authorized, issued and outstanding as of December 31, 2025 and December 31, 2024, respectively	—	110,791
Series C convertible preferred stock, $0.001 par value, no shares and 18,628,970 shares authorized, issued and outstanding as of December 31, 2025 and December 31, 2024, respectively	—	181,328
Total convertible preferred stock	—	330,368
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value, 10,000,000 and no shares authorized as of December 31, 2025 and December 31, 2024, respectively; no shares issued or outstanding as of December 31, 2025 and December 31, 2024	—	—
Common stock, $0.001 par value, 500,000,000 and 55,200,000 shares authorized as of December 31, 2025 and December 31, 2024, respectively; 44,723,585 and 4,798,721 shares issued, 44,723,585 and 4,722,763 shares outstanding as of December 31, 2025 and December 31, 2024, respectively	45	5
Additional paid-in capital	562,602	17,000
Accumulated other comprehensive income	540	368
Accumulated deficit	(256,354)	(181,086)
Total stockholders' equity (deficit)	306,833	(163,713)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 325,953	$ 185,752

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

SIONNA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Year Ended December 31,	
	2025	2024
Operating expenses:		
Research and development	$ 60,263	$ 57,288
General and administrative	28,719	13,268
Total operating expenses	88,982	70,556
Loss from operations	(88,982)	(70,556)
Other income:		
Interest income	13,295	8,170
Other income	419	698
Total other income	13,714	8,868
Net loss	$ (75,268)	$ (61,688)
Net loss per share, basic and diluted	$ (1.88)	$ (15.99)
Weighted-average common shares outstanding, basic and diluted	39,962,163	3,858,859
Comprehensive loss:		
Net loss	$ (75,268)	$ (61,688)
Unrealized gain on marketable securities	172	368
Total other comprehensive gain	172	368
Comprehensive loss	$ (75,096)	$ (61,320)

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

SIONNA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share amounts)

	Series Seed Preferred Stock		Series A Preferred Stock		Series B Preferred Stock		Series C Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Gain	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2023	3,963,963	$13,014	5,704,161	$25,235	11,370,621	$110,791	—	$ —	3,050,863	$ 2	$ 4,515	$ —	$ (119,398)	$ (114,881)
Issuance of Series C Preferred Stock, net of issuance costs of $528	—	—	—	—	—	—	18,628,970	181,328	—	—	—	—	—	—
Issuance of common stock from IPR&D acquisition	—	—	—	—	—	—	—	—	1,414,445	2	8,637	—	—	8,639
Exercise of common stock options	—	—	—	—	—	—	—	—	71,264	1	140	—	—	141
Vesting of restricted common stock awards	—	—	—	—	—	—	—	—	186,191	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	3,708	—	—	3,708
Unrealized gain on marketable debt securities	—	—	—	—	—	—	—	—	—	—	—	368	—	368
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(61,688)	(61,688)
Balance at December 31, 2024	3,963,963	$13,014	5,704,161	$25,235	11,370,621	$110,791	18,628,970	181,328	4,722,763	$ 5	$ 17,000	$ 368	$ (181,086)	$ (163,713)
Conversion of convertible preferred stock to common stock upon closing of initial public offering	(3,963,963)	(13,014)	(5,704,161)	(25,235)	(11,370,621)	(110,791)	(18,628,970)	(181,328)	27,149,206	27	330,340	—	—	330,367
Issuance of common stock from initial public offering, net of issuance costs of $4,265	—	—	—	—	—	—	—	—	12,176,467	12	199,558	—	—	199,570
Exercise of common stock options	—	—	—	—	—	—	—	—	599,191	1	3,638	—	—	3,639
Vesting of restricted common stock awards	—	—	—	—	—	—	—	—	75,958	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	12,066	—	—	12,066
Unrealized gain on marketable debt securities	—	—	—	—	—	—	—	—	—	—	—	172	—	172
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(75,268)	(75,268)
Balance at December 31, 2025	—	$ —	—	$ —	—	$ —	—	$ —	44,723,585	$ 45	$ 562,602	$ 540	$ (256,354)	$ 306,833

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

SIONNA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2025	2024
Cash flows from operating activities:		
Net loss	$ (75,268)	$ (61,688)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	12,066	3,708
Non-cash operating lease expense	1,962	1,962
Amortization of discount on marketable securities	(3,052)	(3,001)
Non-cash expense related to IPR&D acquisition	—	8,639
Depreciation expense	647	668
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(2,082)	(2,760)
Accounts payable	(417)	467
Accrued expenses and other current liabilities	1,975	1,080
Operating lease liability	(2,128)	(1,897)
Other assets	—	35
Net cash used in operating activities	(66,297)	(52,787)
Cash flows from investing activities:		
Purchases of property and equipment	(377)	(27)
Purchases of marketable securities	(325,025)	(182,841)
Maturities of marketable securities	206,653	55,955
Net cash used in investing activities	(118,749)	(126,913)
Cash flows from financing activities:		
Proceeds from initial public offering, net of underwriter discounts, commissions and offering costs paid during the period	202,071	—
Proceeds from issuance of Series C convertible preferred stock, net of issuance costs	—	181,328
Payment of deferred offering costs	—	(2,502)
Exercise of common stock options	3,639	141
Net cash provided by financing activities	205,710	178,967
Net increase (decrease) in cash, cash equivalents and restricted cash	20,664	(733)
Cash, cash equivalents and restricted cash at beginning of period	38,750	39,483
Cash, cash equivalents and restricted cash at end of period	$ 59,414	$ 38,750
Supplemental disclosure of non-cash investing and financing activities:		
Conversion of convertible preferred stock into common stock upon closing of initial public offering	$ 330,368	$ —
Offering costs transferred to additional paid in capital	4,265	—
Deferred offering costs in accrued expenses	—	492
Reconciliation of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 58,451	$ 37,788
Restricted cash	963	962
Total cash, cash equivalents, and restricted cash	$ 59,414	$ 38,750

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

SIONNA THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of the Business

Organization

Sionna Therapeutics, Inc. (the “Company”), formerly known as Sling Therapeutics, Inc., was incorporated in Delaware in August 2019 and is headquartered in Waltham, Massachusetts. The Company is a clinical-stage biopharmaceutical company on a mission to revolutionize the current treatment paradigm for cystic fibrosis (“CF”) patients by developing novel medicines that normalize the function of the cystic fibrosis transmembrane conductance regulator (“CFTR”) protein to deliver clinically meaningful benefit to CF patients.

Risks and Uncertainties

The Company is subject to a number of risks common to other companies in the biotechnology industry, including but not limited to, development by competitors of new technological innovations, risks of failure of preclinical studies and clinical trials, risks related to development and manufacturing of product candidates, obtaining regulatory approval for product candidates, competition from substitute products, the need to successfully commercialize and gain market acceptance of its product candidates, protection of proprietary technology, dependence on key personnel, the ability to attract and retain qualified employees, reliance on third party organizations, compliance with government regulations, and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive clinical testing and regulatory approval, prior to commercialization. These efforts will require significant amounts of additional capital, adequate personnel infrastructure, and extensive compliance-reporting capabilities. Even if the Company’s development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Initial Public Offering

In February 2025, the Company completed its initial public offering ("IPO"), in which the Company sold an aggregate of 10,588,233 shares of its common stock at a public offering price of $18.00 per share and sold an additional 1,588,234 shares of its common stock to the underwriters of the IPO pursuant to the full exercise of their option to purchase additional shares, resulting in aggregate net proceeds of approximately $199.6 million, after deducting underwriter discounts, commissions and other offering expenses. Immediately prior to the closing of the IPO, the Company's outstanding redeemable convertible preferred stock automatically converted into 27,149,206 shares of common stock. Following the closing of the IPO, no shares of redeemable convertible preferred stock were outstanding.

In connection with the closing of the IPO, the Company's certificate of incorporation was amended and restated to authorize 500,000,000 shares of common stock, par value $0.001 per share, and 10,000,000 shares of preferred stock, par value $0.001 per share.

Liquidity and Going Concern

The Company has incurred annual net operating losses and has generated negative operating cash flows in every year since inception. As of December 31, 2025, the Company had an accumulated deficit of $256.4 million. The Company expects its operating losses to continue into the foreseeable future as it continues to pursue its research and development efforts.

The Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company’s ability to continue as a going concern within one year after the date that these consolidated financial statements are issued. The Company believes that its existing cash, cash equivalents, and marketable securities of $310.3 million as of December 31, 2025 will be sufficient to allow the Company to fund operations beyond twelve months from the date of issuance of these consolidated financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP") as found in the Accounting Standards Codification ("ASC") of the Financial Accounting Standards Board ("FASB"). The accompanying consolidated financial statements include the accounts of Sionna Therapeutics, Inc., and its wholly owned subsidiary, Sionna Therapeutics Securities Corporation. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make judgments, assumptions, and estimates that affect the reported amounts of assets, liabilities and expenses and the related disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected within the consolidated financial statements include, but are not limited to, research and development expenses and accruals and the valuation of the Company's common shares in connection with the accounting for stock-based awards. The Company bases its estimates on historical experience and various other assumptions that are believed to be 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. On an ongoing basis, management evaluates its estimates, as there are changes in circumstances and facts. Changes in estimates are recorded in the period in which they become known. Actual results may differ from those estimates or assumptions.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments with original maturities of ninety days or less at the time of purchase to be cash equivalents. Cash and cash equivalents typically include cash held in deposit accounts and money market funds.

Cash accounts with any type of restriction are classified as restricted cash. As of December 31, 2025 and 2024, the Company had restricted cash of $1.0 million held to secure a letter of credit associated with the Company's leased corporate headquarters. The restricted funds are maintained in a money market account. The Company classified this amount as restricted cash in the accompanying consolidated balance sheets based on the release date of the restrictions.

Marketable Securities

The Company classifies marketable securities with a remaining maturity greater than three months at the time of purchase and less than one year from the balance sheet date as current. Marketable securities are classified as long-term assets on the consolidated balance sheets if the maturity exceeds one year, and the Company does not intend to utilize the marketable securities to fund current operations.

The Company classifies all of its investments as available-for-sale securities. Accordingly, these investments are recorded at fair value. Realized gains and losses and amortization of discounts and premiums are included in interest income, which is a component of other income. Unrealized gains and losses on available-for-sale securities are included in accumulated other comprehensive gain as a component of stockholders' equity (deficit) until realized. Interest receivables earned on marketable securities are recorded as a component of prepaid expenses and other current assets.

At each balance sheet date, the Company assesses available-for-sale debt securities in an unrealized loss position to determine whether the unrealized loss or any potential credit losses should be recognized. The Company evaluates whether it intends to sell, or it is more likely than not that it will be required to sell the security before recovery of its amortized cost basis. The Company also evaluates whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, the Company considers the severity of the impairment, any changes in interest rates, changes to the underlying credit ratings and forecasted recovery, among other factors. The credit-related portion of unrealized losses, and any subsequent improvements, are recorded in other income. There have been no impairment or credit losses recognized during any of the periods presented.

Concentration of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash, cash equivalents and marketable securities. Periodically, the Company may maintain deposits in financial institutions in excess of government insured limits. The Company believes that it is not exposed to significant credit risk as its deposits are held at financial institutions that management believes to be of high credit quality and the Company has not experienced any losses on these deposits. The Company regularly invests excess cash with major financial institutions in money market funds, U.S. Treasury securities and government agency securities, corporate bonds, and commercial paper, all of which can be readily purchased and sold using established markets. The Company believes that the market risk arising from its holdings of these financial instruments is mitigated based on the fact that many of these securities are either government-backed or of high credit rating.

Fair Value of Financial Instruments

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

Level 1—Quoted market prices in active markets for identical assets or liabilities.

Level 2—Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

Level 3—Unobservable inputs for the asset or liability (i.e., supported by little or no market activity). Level 3 inputs include management's own assumptions about the assumptions that market participants would use in pricing the asset or liability (including assumptions about risk).

A financial instrument's level within the fair value hierarchy is based on the lowest level of input that is significant to the fair value measurement. To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of the fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. The Company does not currently have recurring fair value measurements classified within Level 3.

The carrying values of prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities.

Property and Equipment, net

Property and equipment is stated at cost net of accumulated depreciation. Costs of major additions and betterments are capitalized. Maintenance and repairs to an asset that do not improve or extend its life are expensed in the period incurred. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset as follows:

	Estimated Useful Life (in years)
Lab equipment	5
Furniture & fixtures	5
Hardware & software	3
Leasehold improvements	Shorter of useful life or remaining lease term

When an item is sold or retired, the costs and related accumulated depreciation are eliminated, and the resulting gain or loss, if any, is credited or charged to the consolidated statement of operations and comprehensive loss. Property and equipment held for disposal are carried at fair value less costs to sell.

Impairment of Long-Lived Assets

Long-lived assets consist primarily of property and equipment and right-of-use assets. The Company continually evaluates whether events or circumstances have occurred that indicate that the estimated remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use or disposition of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written down to their fair values. The Company has not recognized any impairment charges during the years ended December 31, 2025 and 2024.

Leases

At the inception of an arrangement the Company determines whether the arrangement contains a lease. Operating leases are included in operating lease right-of-use lease asset (“ROU asset”), operating lease liability, current, and operating lease liability, noncurrent, on the Company’s consolidated balance sheets. Assets subject to finance leases are included in property and equipment, and the related lease obligation is included in other current liabilities and other long-term liabilities on the Company’s consolidated balance sheets. Lease expense for operating leases is recognized on a straight-line basis over the lease term as an operating expense. As of December 31, 2025 and 2024, the Company did not have any finance leases. The Company has elected the short-term lease recognition exemption for short-term leases, which allows the Company not to recognize lease liabilities and ROU assets on the consolidated balance sheets for leases with an original term of twelve months or less.

ROU assets represent the Company’s right to use an underlying asset for the lease term, and lease obligations represent the Company’s obligation to make lease payments arising from the lease. Operating lease liabilities and their corresponding ROU assets are initially recognized based on the present value of lease payments over the expected remaining lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the Company will exercise the option. Certain adjustments to the ROU asset may be required for items such as incentives received from the lessor. The interest rate implicit in lease contracts is typically not readily determinable. Therefore, the Company utilizes its incremental borrowing rate to discount lease payments. The incremental borrowing rate reflects the fixed rate at which the Company could borrow, on a collateralized basis, the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Leases generally provide for payments of non-lease components, such as common area maintenance, real estate taxes and other costs associated with the leased property. The Company accounts for non-lease components together with lease components. Variable lease payments, such as periodic adjustments for inflation, reimbursement of real estate taxes, and variable common area maintenance are expensed as incurred as variable lease costs and are not recorded on the consolidated balance sheets.

Sublease income is recognized on a straight-line basis over the term of the sublease agreement and is recorded within Other Income on the consolidated statements of operations and comprehensive loss.

Research and Development Expenses and Accruals

Research and development costs include (i) employee-related expenses, including salaries, benefits, and stock-based compensation expense; (ii) external research and development expenses incurred under arrangements with third parties, such as contract research organizations ("CRO") agreements, contract development and manufacturing organizations ("CDMOs"), consultants and scientific advisors; (iii) costs associated with preclinical and clinical activities and (iv) lab supplies, lab expenses and an allocation of rent, depreciation, and infrastructure.

The Company recognizes research and development costs in the periods in which they are incurred because these activities have no alternative future use. Typically, external expenses are recognized based on an evaluation of the progress to completion of specific tasks using information obtained from (i) internal personnel regarding the services that have been performed on the Company's behalf and estimating the associated cost incurred for those services or (ii) information provided to the Company by their service providers as of each reporting date. Advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses, which are expensed as the related goods are delivered or the services are performed, or when it is no longer expected that the goods will be delivered, or the services rendered. Significant judgments and estimates are made in determining accrued or prepaid expense balances at the end of any reporting period.

Asset Acquisitions and Acquired In-Process Research and Development Expense

The Company accounts for acquisitions of assets or a group of assets that do not meet the definition of a business as asset acquisitions based on the cost to acquire the asset or group of assets, which include certain transaction costs. In an asset acquisition, the cost to acquire is allocated to the identifiable assets acquired and liabilities assumed based on their relative fair values as of the acquisition date. No goodwill is recorded in an asset acquisition. Assets that are acquired in an asset acquisition for use in research and development activities that have an alternative future use are capitalized as in process research and development ("IPR&D"). Acquired IPR&D that has no alternative future use as of the acquisition date is recognized as research and development expense as of the acquisition date. The costs to acquire IPR&D are presented as operating activities in the consolidated statements of cash flows in the period acquired.

The Company will recognize additional research and development expenses in the future if and when the Company becomes obligated to make contingent milestone or royalty payments which are governed by the terms of the agreements by which it acquired the IPR&D assets. Developmental and regulatory milestone payments will be recorded when the milestone is achieved, and commercial milestones, such as sales-based milestone payments, and royalties will be recorded when the underlying sale(s) occur.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications such as direct application fees, and legal and consulting expenses are expensed as incurred due to the uncertainty about the recovery of the expenditure. Patent-related costs are classified as general and administrative expenses within the Company's consolidated statements of operations and comprehensive loss.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are direct and incremental costs associated with in-process equity financings as deferred offering costs until such financing is consummated. After consummation of the equity financing, these costs are recorded as a reduction of the proceeds generated as a result of the offering within additional paid-in capital. In the event that the equity financing is abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the condensed consolidated statements of operations and comprehensive loss.

Convertible Preferred Stock

Prior to the completion of the Company's IPO, the Company had outstanding convertible preferred stock, which was classified as temporary equity in the consolidated balance sheets. Upon the completion of the IPO, all outstanding shares of convertible preferred stock automatically converted into shares of common stock, and the carrying value of the convertible preferred stock was reclassified to stockholder's equity. As of December 31, 2025, no shares of convertible preferred stock were outstanding.

Fair Value of Common Stock

Prior to the completion of the Company's IPO, the Company determined the estimated fair value of common stock based on a number of objective and subjective factors, including, but not limited to, external market conditions affecting the biotechnology industry sector, the prices at which the Company sold shares of convertible preferred stock and the superior rights and preferences of securities senior to the Company's common stock at the time, and the likelihood and potential timing of achieving a liquidity event, such as an initial public offering, in light of prevailing market conditions. The Company utilized valuation methodologies to estimate the fair value of common stock that were in accordance with the guidance outlined in the *American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, including the option pricing method and the probability-weighted expected return method. These methodologies required the use of significant management judgment and assumptions.

Since completion of the IPO, the fair value of the Company's common stock has been determined based on the closing market price of the Company's common stock on the date of equity grant.

Stock-Based Compensation

The Company measures all stock options and other stock-based awards granted to employees, non-employees, and directors based on the fair value on the date of the grant and recognizes compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. The Company's stock-based payments include stock options and grants of restricted common stock awards. Generally, the Company issues stock-based awards with only service-based vesting conditions. The Company's policy is to account for forfeitures when they occur. Stock-based compensation expense is classified in the accompanying consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipients service payments are classified.

Restricted common stock awards are subject to repurchase rights until such awards meet all vesting conditions. Accordingly, the Company recorded the proceeds from the issuance of restricted common stock awards as a liability in the consolidated balance sheets. The restricted common stock liability was reclassified into stockholders' equity as the restricted common stock vested.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Due to the lack of Company-specific historical and implied volatility information, the Company estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until it has adequate historical data regarding the volatility of its own traded stock price. The Company uses the simplified method as prescribed by the Securities and Exchange Commission's Staff Accounting Bulletin No. 107, *Share-Based Payment*, to estimate the expected term for options granted to employees and non-employees as the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is zero because the Company has never paid cash dividends on common shares and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

The Company's provision for income taxes, deferred tax assets and liabilities, and reserves for unrecognized tax benefits reflect management's best assessment of estimated future taxes to be paid.

Significant judgments and estimates based on interpretations of existing tax laws or regulations in the United States are required in determining our provision for income taxes. Changes in tax laws, statutory tax rates, and estimates of our future taxable income could impact the deferred tax assets and liabilities provided for in the consolidated financial statements and would require an adjustment to the provision for 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 income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

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. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, which are considered appropriate as well as the related net interest and penalties.

Net Loss Per Share

Basic net loss per share is computed by dividing net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period.

Diluted net loss per share is computed using the weighted-average number of common shares outstanding during the period, and if dilutive, the weighted-average number of potential common shares outstanding. Potentially dilutive securities consist of stock options, restricted stock awards, and other common stock equivalents.

In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share is the same as basic net loss per share, as the inclusion of potentially dilutive common shares would be antidilutive.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholder's equity (deficit) that result from transactions and events other than those with stockholders. The Company's unrealized gains and losses on marketable securities represent the only component of other comprehensive gain that are excluded from the reported net loss and that are presented in the consolidated statements of operations and comprehensive loss.

Segment Information

The Company is managed as one operating segment, and thus reports as a single reportable segment. This operating segment is focused on the research and development of cystic fibrosis therapies. Management assessed the financial information routinely reviewed by the Company's Chief Operating Decision Maker ("CODM"), its President and Chief Executive Officer, to monitor the Company's operating performance and support decision making regarding allocation of resources to its operations, and determined that performance is continuously monitored at the consolidated level. The measure of segment assets is reported on the consolidated balance sheet as total consolidated assets. The measure used by the CODM in assessing

performance and deciding how to allocate resources is based on consolidated net loss, as reported on the consolidated statement of operations and comprehensive loss. The CODM uses consolidated net loss, as reported in the consolidated statement of operations, to assess performance and allocate resources by evaluating operating results against expectations.

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently Adopted Accounting Pronouncements

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740: Improvements to Income Tax Disclosures)* ("ASU 2023-09"). ASU 2023-09 provides more transparency about income tax information through improvements to income tax disclosures primarily related to the rate reconciliation and incomes taxes paid information. For public companies, the amendments were effective for annual periods beginning after December 15, 2024. The Company adopted the amendments retrospectively for the year-ended December 31, 2025. The adoption did not have a material impact on the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements Not Yet Adopted

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 entities to disclose additional information about specific expense categories in the notes to the financial statements. ASU 2024-03 is effective for annual periods beginning after December 15, 2026 and for interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. ASU 2024-03 may be applied retrospectively or prospectively. The Company is currently evaluating the effect of this update on its consolidated financial statements and related disclosures.

In September 2025, the FASB issued ASU 2025-07, *Derivatives Scope Refinement*, ("ASU 2025-07"). ASU 2025-07 creates a scope exception within ASC 815 for certain contracts with underlyings tied to a party's operations or activities (such as regulatory approval, clinical, or earnings milestones), which may cause some arrangements that previously met the derivative definition to no longer be accounted for as derivatives. The guidance is effective for fiscal years beginning after December 15, 2026, including interim periods. Early adoption is permitted. Entities may adopt prospectively for new or modified contracts after the adoption date, or modified retrospectively for contracts outstanding at adoption with a cumulative-effect adjustment to opening retained earnings. The Company expects to adopt prospectively and does not expect a material impact, though this guidance may affect the accounting for future milestone-linked arrangements executed after adoption.

3. Marketable Securities

The following table summarizes the amortized cost and estimated fair value of the Company's current and noncurrent marketable securities (in thousands):

	December 31, 2025			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
Marketable securities, current:				
U.S. Treasury securities	$ 135,801	$ 263	$ —	$ 136,064
Commercial paper	24,391	10	(5)	24,396
Corporate debt	11,813	3	(1)	11,815
Government agency securities	5,145	11	—	5,156
Total marketable securities, current	177,150	287	(6)	177,431
Marketable securities, noncurrent:				
U.S. Treasury securities	55,793	208	—	56,001
Government agency securities	18,368	51	—	18,419
Total marketable securities, noncurrent	74,161	259	—	74,420
Total marketable securities	$ 251,311	$ 546	$ (6)	$ 251,851

	December 31, 2024			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
Marketable securities, current:				
U.S. Treasury securities	$ 55,154	$ 176	$ —	$ 55,330
Government agency securities	31,198	62	(1)	31,259
Corporate debt	17,205	22	—	17,227
Commercial paper	5,931	3	—	5,934
Total marketable securities, current	109,488	263	(1)	109,750
Marketable securities, noncurrent:				
U.S. Treasury securities	15,266	83	—	15,349
Government agency securities	5,133	23	—	5,156
Total marketable securities, noncurrent	20,399	106	—	20,505
Total marketable securities	$ 129,887	$ 369	$ (1)	$ 130,255

The Company has determined that there were no material changes in the credit risk, therefore the Company has not recognized any allowance for credit losses on its debt securities. As of December 31, 2025, the Company holds marketable securities with an aggregate fair value of $74.4 million that had remaining maturities between one and two years. All other securities had a contractual maturity of less than a year. There were no realized gains or losses during the years ended December 31, 2025, or 2024.

4. Fair Value Measurements

The following table presents information about the Company's financial instruments that are measured at fair value on a recurring basis and indicates the fair value hierarchy of the inputs the Company utilized to determine such fair value (in thousands):

	December 31, 2025			
	Total	Level 1	Level 2	Level 3
Assets				
Cash equivalents:				
Money market funds	$ 51,962	$ 51,962	$ —	$ —
Commercial paper	5,988	—	5,988	—
Marketable securities:				
U.S. Treasury securities	192,065	192,065	—	—
Commercial paper	24,396	—	24,396	—
Government agency securities	23,575	—	23,575	—
Corporate debt	11,815	—	11,815	—
Total financial assets	$ 309,801	$ 244,027	$ 65,774	$ —

	December 31, 2024			
	Total	Level 1	Level 2	Level 3
Assets				
Cash equivalents:				
Money market funds	$ 37,288	$ 37,288	$ —	$ —
Marketable securities:				
U.S. Treasury securities	70,679	70,679	—	—
Government agency securities	36,415	—	36,415	—
Corporate debt	17,227	—	17,227	—
Commercial paper	5,934	—	5,934	—
Total financial assets	$ 167,543	$ 107,967	$ 59,576	$ —

During the year ended December 31, 2025, there were no transfers or reclassifications between fair value measurement levels of assets or liabilities. The carrying values of prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities.

5. Property and Equipment, net

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

	December 31,	
	2025	2024
Leasehold improvements	$ 1,920	$ 1,854
Laboratory equipment	1,575	1,461
Furniture & fixtures	852	722
Total property and equipment	4,347	4,037
Less: accumulated depreciation	(2,122)	(1,571)
Property and equipment, net	$ 2,225	$ 2,466

Depreciation expense was $0.6 million and $0.7 million for the years ended December 31, 2025 and 2024, respectively.

6. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2025	2024
Accrued compensation and benefits	$ 4,740	$ 2,972
Accrued research and development	4,305	3,961
Accrued professional fees	522	737
Accrued other	101	—
Accrued deferred offering costs	—	492
Total accrued expenses	$ 9,668	$ 8,162

7. Leases

Operating Leases Summary

Waltham, Massachusetts

In May 2022, the Company entered into a noncancelable facility lease agreement to lease 24,051 square feet of office and laboratory space in Waltham, Massachusetts ("Waltham Lease"), which became the Company headquarters in January 2023 following the completion of construction of the prebuilt office and lab space, and when the Company received full access and control over the leased space. At commencement of the lease the right-of-use asset was $9.5 million, which was reduced by $0.4 million of lease incentives, offset by $0.2 million of lease prepayments, and the lease liability was $9.7 million.

The original term for the Waltham Lease is for the period from January 2023 through November 2030, and the Company has the option to extend the Waltham Lease for an additional five-year term at market-based rates. The renewal option is not reasonably certain to occur, and as such, it was not considered in the measurement of the right-of-use asset and lease liability. The Waltham Lease has escalating base rent payments, which commenced in September 2023 and continue through the expiration of the lease. The Company received eight months of free rent and five additional months of 50% rent abatement. The Company is responsible for other fixed and variable payments including operating expenses and property taxes.

Sublease Agreement

In June 2023, the Company entered into a sublease agreement to sublet 6,399 square feet of its office and laboratory space under the Waltham Lease (the "Sublease"). The Company was not relieved of its obligation to the lessor for the head lease as a result of its entry into the Sublease. The Sublease is classified as an operating lease and commenced in July 2023 and expired in August 2025. Sublease income was recognized on a straight-line basis. For the years ended December 31, 2025 and 2024, the Company recognized $0.4 million and $0.7 million, respectively, of sublease income within other income on the consolidated statements of operations and comprehensive loss.

Operating Lease Tables

The following table presents inputs used in the calculation of the Company's right of use asset and lease liabilities at the end of each reporting period:

	December 31,	
	2025	2024
Weighted-average remaining lease term (years)	4.9	5.9
Weighted-average discount rate	11.0%	11.0%
Cash paid for amounts included in the measurement of operating lease liabilities (in thousands)	$ 2,128	$ 1,897

The components of lease costs were as follows (in thousands):

	December 31,	
	2025	2024
Operating lease costs	$ 1,962	$ 1,962
Variable lease costs	627	513
Total lease cost	$ 2,589	$ 2,475

Lease commitments

Future minimum lease payments were as follows (in thousands):

Year ended December 31,	Amount
2026	$ 2,190
2027	2,253
2028	2,319
2029	2,386
2030	2,246
Total future minimum lease payments	11,394
Less imputed interest	(2,717)
Present value of operating lease liability	$ 8,677

8. Commitments and Contingencies

Legal Proceedings

The Company was not subject to any material legal proceedings during the years ended December 31, 2025 and 2024, and the Company is not aware of any material legal proceedings that are currently pending or threatened.

Other Contracts

The Company is party to various contracts with CROs and CDMOs in the ordinary course of business. These agreements generally provide for termination at any time upon a certain amount of prior notice. Payments upon termination, if any, are based on the timing of the termination and the terms of the agreement.

Indemnification Agreements

In the ordinary course of business the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including arising out of the relationship between such parties and the Company. In addition, the Company has entered into indemnification agreements with members of its board of directors and senior management 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.

To date the Company has not incurred any material costs as a result of such indemnifications nor experienced any losses related to them. As of December 31, 2025 and 2024, the Company was not aware of any claims under indemnification arrangements and it has not accrued any liabilities related to such obligations.

9. License Agreements

Sanofi License Agreement

In December 2019, the Company entered into a license agreement, which has been subsequently amended (as amended, the “Sanofi License Agreement”), with Sanofi SA (f/k/a Genzyme) (“Sanofi”), pursuant

to which the Company has been granted an exclusive, sub-licensable, royalty-bearing, worldwide license to develop and commercialize products using the licensed compounds and know-how for CFTR correctors.

As initial consideration for the license, the Company paid a non-refundable, upfront payment of $1.5 million, as well as a reimbursement of $0.3 million for Sanofi's research and development expenses, which was previously recorded as research and development expense because the acquired license represented in-process research and development with no alternative future use. In addition, the Company is required to pay Sanofi a total of up to $40.0 million upon achievement of certain late-stage developmental and commercial milestones. As of December 31, 2025, no milestones have been achieved. The Company is also required to pay royalties to Sanofi in the low single-digit percentage range based on net sales of licensed products, subject to customary reductions and offsets. Such royalty payments shall be reduced for products covered by derived patents.

CFF Payment Agreement

In December 2019, the Company entered into a payment agreement (the "CFF Payment Agreement") with the Cystic Fibrosis Foundation ("CFF"), pursuant to which the Company agreed to provide CFF with compensation in exchange for the grant of, or forbearance from exercising, certain of CFF's rights existing under the license agreement by and between CFF (through an assignment by Cystic Fibrosis Foundation Therapeutics, Inc.) and Genzyme Corporation, an affiliate of Sanofi (the "CFFT-Genzyme Agreement"). Under the CFF Payment Agreement, the Company is obligated to compensate CFF in connection with the Company's development and commercialization of licensed products under the Sanofi License Agreement.

As initial consideration for CFF's grant of, and forbearance from exercising, its rights under the CFFT-Genzyme Agreement, the Company paid an upfront fee of $0.2 million and issued CFF shares of preferred stock, valued at $1.0 million which were previously recorded as research and development expenses. In addition, the Company agreed to pay CFF a sub-teen double-digit percentage of any amounts paid by it to Sanofi under the Sanofi License Agreement, other than milestone, royalty or reimbursement payments. In addition, the Company is required to pay CFF a total of up to $40.0 million upon achievement of certain late-stage developmental and commercial milestones. In conjunction with the execution of the agreements with Sanofi and CFF in December 2019, a side letter was executed between the Company and Sanofi, which clarifies the relationship between the Company, Sanofi and CFF, under which the Company is obligated to pay Sanofi 20% of the milestones it would have been obligated to pay CFF, net of the milestone amounts it is obligated to pay under the Sanofi License Agreement.

As of December 31, 2025, no milestones have been achieved. The Company is also required to pay revenue-shares of royalty payments to CFF in the low single-digit percentage range based on net sales of licensed products subject to customary reductions and offsets. Such milestone and royalty payments shall be reduced for products covered by derived patents.

AbbVie Agreement

In July 2024, the Company entered into a license agreement (the "AbbVie License Agreement") with AbbVie Global Enterprises Ltd. ("AbbVie"), pursuant to which the Company has been granted an exclusive worldwide, royalty-bearing, sublicensable license to research, develop and commercialize certain CFTR compounds. The licensed rights are directed, among other things, to three clinical-stage CFTR modulator assets. The license granted under the AbbVie License Agreement are subject to certain preexisting rights held by AbbVie and Galapagos NV ("Galapagos"). In particular, certain of the licensed patents and other intellectual property rights were developed by or on behalf of Galapagos and are sublicensed to the Company subject to the terms of the second amended and restated collaboration agreement between Galapagos and AbbVie in October 2018 (the "Galapagos License Agreement"), as amended by a side letter between Galapagos and AbbVie in July 2024.

As initial consideration for the license, the Company paid a non-refundable, upfront payment of $5.0 million and issued shares of its common stock with a fair value of $8.6 million to AbbVie. The Company determined that the AbbVie License Agreement represented an asset acquisition as it did not meet the definition of the business. The Company previously recorded the total initial consideration of $13.6 million as research and development expense, because the acquired license represented in-process research and development

with no alternative future use. In addition, the Company is required to pay AbbVie a total of up to $360.0 million upon achievement of certain development and commercial milestones, consisting of up to $70.0 million in late-stage development milestones and up to $290.0 million in commercial milestones. The Company is also required to pay royalties to AbbVie in the low to mid single-digit percentage range based on net sales of licensed products, subject to customary reductions and offsets.

In addition, the Company is required to pay AbbVie up to $130.0 million in commercial and sales-based milestone payments, mid to high single-digit royalties on the licensed products, or other payments due to Galapagos pursuant to the Galapagos License Agreement, to the extent such payments are triggered by the Company's use of the licensed rights owned by Galapagos under the AbbVie License Agreement. As of December 31, 2025, none of such milestones under the AbbVie License Agreement and Galapagos License Agreement have been achieved.

10. Convertible Preferred Stock

Series Seed

In December 2019, the Company issued and sold 2,762,762 shares of Series Seed convertible preferred stock, par value $0.001 per share ("Series Seed Preferred Stock") to certain investors at a purchase price of $3.33 per share, for gross proceeds of $8.2 million (the "Series Seed Financing"). As disclosed in Note 9, the Company issued Series Seed Preferred Stock to CFF in connection with the CFF Payment Agreement. One investor was also issued 684,415 shares of common stock in connection with the initial Series Seed Financing closing. The proceeds from that investor were allocated between the Series Seed Preferred Stock and common stock on a relative fair value basis. There were no material issuance costs incurred related to this financing.

In June 2020, the Company issued an additional 1,201,202 shares of Series Seed Preferred Stock to an additional investor at $3.33 per share for gross proceeds of $4.0 million. The Company incurred $38,887 of issuance costs in connection with this issuance.

Series A

In September 2020, the Company issued and sold 5,704,161 shares of Series A convertible preferred stock, par value $0.001 per share ("Series A Preferred Stock"), at a purchase price of $4.43 per share, for gross proceeds of $25.3 million (the "Series A Financing"). The Company incurred $0.1 million of issuance costs in connection with the Series A Financing.

Series B

In February 2022, the Company issued and sold 11,370,621 shares of Series B convertible preferred stock, par value $0.001 per share ("Series B Preferred Stock"), at a purchase price of $9.76 per share, for gross proceeds of $111.0 million (the "Series B Financing"). The Company incurred $0.2 million of issuance costs in connection with the Series B Financing.

Series C

In March 2024, the Company issued and sold 18,628,970 shares of Series C convertible preferred stock, par value $0.001 per share ("Series C Preferred Stock") at a purchase price of $9.76 per share, for gross proceeds of $181.9 million (the "Series C Financing"). The Company incurred $0.5 million of issuance costs in connection with the Series C Financing.

Upon issuance of the Series Seed, Series A, Series B, and Series C convertible preferred stock (collectively, the "Preferred Stock"), the Company evaluated the embedded conversion and liquidation features and determined that separate accounting was not required.

Upon completion of the Company's IPO, all outstanding shares of convertible preferred stock automatically converted into shares of common stock. As of December 31, 2025, no shares of convertible preferred stock were outstanding.

The Board of Directors of the Company (the "Board") is authorized to issue up to 10,000,000 shares of preferred stock and may fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The Board may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. As of December 31, 2025, the Company had no shares of preferred stock issued or outstanding and preferred stock is classified within stockholders' equity.

11. Common Stock & Equity Incentive Plans

Common Stock Rights

The holders of the Company's common stock are entitled to one vote per share on all matters submitted to a vote of stockholders, subject to applicable law. The holders of common stock are also entitled to receive dividends, if any, as may be declared by the Company's board of directors, and to share ratably in the Company's assets legally available for distribution upon liquidation, dissolution, or winding up of the Company.

Equity Incentive Plans

2020 Stock Option and Grant Plan

The Company's 2020 Stock Option and Grant Plan, as amended (the "2020 Plan"), previously provided for the Company to sell or issue common stock or restricted common stock, or to grant incentive stock options or nonqualified stock options for the purchase of common stock, to employees, members of the Board and consultants of the Company. The 2020 Plan was administered by the Board.

As of December 31, 2025, no shares of common stock remained available for future grants under the 2020 Plan. Outstanding stock options and restricted common stock awards granted under the 2020 Plan generally vest over four years and expire ten years after the date of grant, and certain awards provide for accelerated vesting upon a change in control.

2025 Stock Option and Grant Plan

In January 2025, the Board of Directors and the Company's stockholders adopted and approved the 2025 Equity Incentive Plan (the "2025 Plan"), which became effective on February 5, 2025, immediately prior to the effectiveness of the Company's registration statement on Form S-1 for its IPO. The 2025 Plan initially reserved 5,060,000 shares of common stock for issuance and includes an evergreen provision pursuant to which the number of shares reserved for issuance may be automatically increased on an annual basis. Beginning in 2026, the number of shares reserved under the 2025 Plan shall automatically increase annually on January 1 by up to 4% of the total number of shares of common stock outstanding, unless the Board of Directors determines otherwise.

The shares reserved for issuance under the 2020 Stock Option and Grant Plan ceased to be available for issuance upon the effectiveness of the 2025 Plan. Any shares subject to outstanding awards under the 2020 Plan that subsequently expire, are forfeited, cancelled, repurchased, or withheld will become available for issuance under the 2025 Plan.

As of December 31, 2025, 2,393,345 shares of common stock remained available for future grants under the 2025 Plan. Outstanding stock options and restricted common stock awards granted under the 2025 Plan generally vest over four years and expire ten years after the date of grant, and certain awards provide for accelerated vesting upon a change in control.

2025 Employee Stock Purchase Plan

In January 2025, the Board of Directors and the Company's stockholders adopted and approved the 2025 Employee Stock Purchase Plan (the "2025 ESPP"), which became effective on February 5, 2025, immediately prior to the effectiveness of the Company's registration statement on Form S-1 for its IPO. The 2025 ESPP initially reserved 390,127 shares of common stock for issuance and includes an evergreen provision pursuant to which the number of shares reserved for issuance may be automatically increased on an annual basis. Beginning in 2026, the number of shares reserved under the 2025 Plan shall automatically

increase annually on January 1 by up to 1% of the total number of shares of common stock outstanding, unless the Board of Directors determines otherwise, but not to exceed 780,254 shares.

As of December 31, 2025, no offering periods had commenced under the 2025 ESPP.

Shares Reserved for Issuance

The number of shares of common stock reserved for issuance under the Company's equity incentive plans is as follow:

	Year Ended December 31,	
	2025	2024
Convertible preferred stock	—	27,149,206
Options to purchase common stock	5,767,799	3,700,335
Remaining shares reserved for future issuance	2,393,345	1,035,891
Unvested restricted common stock	—	75,958
Total	8,161,144	31,961,390

12. Stock-Based Compensation

Restricted Common Stock

A summary of the Company’s restricted common stock activity during the year ended December 31, 2025, is presented below:

	Number of Restricted Shares	Weighted-Average Per-Share Grant-Date Fair Value
Unvested at December 31, 2024	75,958	$0.78
Vested	(75,958)	$0.78
Unvested at December 31, 2025	—	$—

The Company did not issue shares of restricted common stock to founders and officers during the years ended December 31, 2025 or 2024. For the years ended December 31, 2025 and 2024, the liability related to the payments received for shares of unvested restricted common stock was de minimis. The aggregate fair value of restricted common stock awards that vested during the years ended December 31, 2025 and 2024, was $1.0 million and $1.3 million, respectively. The final vesting conditions for the restricted common stock awards were met in June 2025.

Stock Option Valuation

The weighted-average assumptions used to determine the fair values of stock options granted to employees and directors during the years ended December 31, 2025 and 2024, are presented as follows:

	Year Ended December 31,	
	2025	2024
Expected term (in years)	6.2	6.0
Volatility	82.4%	83.9%
Interest rate	4.2%	4.2%
Dividend yield	—	—

Stock Option Activity

The following table summarizes the Company's common stock option activity for the year ended December 31, 2025:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
			(in years)	(in thousands)
Outstanding at December 31, 2024	3,700,335	$5.87	8.3	$16,522
Granted	2,725,160	19.03		
Exercised	(599,191)	6.07		
Cancelled or forfeited	(58,505)	10.97		
Outstanding at December 31, 2025	5,767,799	$12.01	8.3	$168,007
Exercisable at December 31, 2025	2,189,013	$7.58	7.3	$73,457

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the estimated 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.

The weighted-average grant date fair value of options granted during the years ended December 31, 2025 and 2024, was $13.94 and $4.61, respectively. The total intrinsic value of options exercised in the years ended December 31, 2025 and 2024, was $14.7 million and $0.4 million, respectively.

Stock-Based Compensation Expense

During the years ended December 31, 2025 and 2024, the Company recorded stock-based compensation in the accompanying consolidated statements of operations and comprehensive loss as follows (in thousands):

	Year Ended December 31,	
	2025	2024
Research and development expense	$ 4,116	$ 1,500
General and administrative expense	7,950	2,208
Total	$ 12,066	$ 3,708

As of December 31, 2025, there was $35.3 million of unrecognized stock-based compensation expense for common stock option awards that are expected to be recognized over a weighted-average period of 2.6 years. The stock-based compensation expense for restricted common stock awards was de minimis and fully recognized as of June 30, 2025, when the final vesting conditions were met.

13. Income Taxes

The Company's loss is attributable to domestic activity, and the Company does not have foreign operations. The Company had no current or deferred federal or state income tax expense due to operating losses incurred for the years ended December 31, 2025 and 2024, and the full valuation allowance recorded on net deferred tax assets.

A reconciliation of income tax expense (benefit) from continuing operations to the amount computed by applying the statutory federal income tax rate to the net loss from continuing operations is summarized as follows (in thousands):

	Year Ended December 31,			
	2025		2024	
Tax expense (benefit) at the U.S. statutory rate	$ (15,806)	21.0%	$ (12,954)	21.0%
State income taxes, net of federal income tax effect[1]	—	—%	—	—%
Effects of changes in tax laws or rates enacted in the current period	—	—%	—	—%
Tax credits				
Research and development tax credits	(1,969)	2.6%	(1,452)	2.4%
Nontaxable or nondeductible Items				
Stock-based compensation	(1,371)	1.8%	304	(0.5%)
Limitations on executive compensation	1,068	(1.4%)	—	—%
Other permanent differences	(54)	0.1%	25	—%
Other adjustments	(43)	0.1%	—	—%
Change in valuation allowance	18,175	(24.2%)	14,077	(22.9%)
Effective tax rate	$ —	0.0%	$ —	0.0%

[1]State taxes in Massachusetts make up the majority of the tax effect in this category.

The components of the Company's deferred tax assets and liabilities are comprised of the following (in thousands):

	Year Ended December 31,	
	2025	2024
Net operating loss carryforward	$ 40,906	$ 18,075
Tax credits	6,848	4,056
Fixed assets	64	36
Stock-based compensation	2,268	885
Capitalized research costs	20,330	23,229
Accrued expenses	1,256	524
Intangibles	4,098	4,362
Lease liability	2,327	2,582
Other temporary differences	23	21
Total deferred tax assets	$ 78,120	$ 53,770
Less valuation allowance	(76,144)	(51,606)
Net deferred tax asset	$ 1,976	$ 2,164
Right of use assets	$ (1,857)	$ (2,083)
Other deferred tax liabilities	(119)	(81)
Total deferred tax liabilities	$ (1,976)	$ (2,164)
Net deferred tax asset (liability)	$ —	$ —

As of December 31, 2025 and 2024, the Company had federal net operating loss carryforwards of approximately $148.0 million and $65.6 million, respectively, which may be available to offset future income tax liabilities. The 2017 Tax Cuts and Jobs Act ("TCJA") will generally allow losses incurred after 2017 to be carried over indefinitely but will generally limit the net operating loss deduction to the lesser of the net operating loss carryover or 80% of a corporation's taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended (the "Internal Revenue Code")). Also, there is no carry back for losses incurred after 2017. All net operating loss carryforwards were generated after 2017.

In addition, the Company has state net operating loss carryforwards of $155.4 million and $68.2 million as of December 31, 2025 and 2024, respectively, which will expire at various dates through 2045.

As of December 31, 2025 and 2024, the Company had federal research and development tax credit ("Federal R&D Tax Credit") carryforwards of $4.7 million and $2.7 million, respectively, available to reduce future tax liabilities, which will expire at various dates through 2045.

As of December 31, 2025 and 2024, the Company had state research and development credit ("State R&D Tax Credit") carryforwards of approximately $2.7 million and $1.7 million, respectively, available to reduce future tax liabilities, which will expire at various dates through 2040.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize its deferred tax assets, which are comprised primarily of net operating loss carryforwards, the capitalization of research and experimental expenditures, and tax credits. Management has considered the Company's history of cumulative net losses in the United States, estimated future taxable income and prudent and feasible tax planning strategies and has concluded that it is more likely than not that the Company will not realize the benefits of its U.S. federal and state deferred tax assets. Accordingly, a full valuation allowance of $76.1 million and $51.6 million has been established against these net deferred tax assets as of December 31, 2025 and 2024, respectively. The Company reevaluates the positive and negative evidence at each reporting period. The Company's valuation allowance increased during 2025 by approximately $24.5 million, primarily due to the increase in net operating loss and tax credit carryforwards.

Under the provision of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative change in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Section 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership change may further affect the limitation in future years. The Company has not yet completed a change in control analysis, as defined under Section 382 and 383 of the Internal Revenue Code, through December 31, 2025, and the Company has not determined whether the future utilization of net operating loss carryforwards may be materially limited based on past financings. In addition, the Company may complete future financings that could result in a change in control in the future which may limit the amount of tax attributes available to offset future tax liabilities.

The Company accounts for income taxes by evaluating a probability threshold that a tax position must meet before a financial statement benefit is recognized. The minimum threshold is a tax position that is more likely than not to be sustained upon examination by the applicable taxing authority, including resolution of any related appeals or litigation processes, based on the technical merits of the position.

The Company did not have any unrecognized tax benefits as of December 31, 2025 or 2024, respectively. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2025 and 2024, the Company's balance of interest and penalties was zero.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In a normal course of business, the Company is subject to examination by U.S. federal and states. The Company's tax years are still open since inception. To the extent that the Company has tax attribute carryforwards, the tax year in which the attributes were generated may still be adjusted upon examination by the U.S. Internal Revenue Services or state tax authorities to the extent utilized in a future period. The Company is not currently under examination by any tax authorities.

14. Segment Information

The following table presents segment net loss, including significant expense categories (in thousands):

	Year Ended December 31,	
	2025	2024
Research and development expenses:		
External research and development expenses[1]	$ 43,535	$ 31,873
Fees paid to licensors[2]	23	5,525
Personnel-related expenses, excluding stock-based compensation	10,553	7,628
Facility and information technology allocated expenses	1,826	1,838
General and administrative expenses:		
Personnel-related expenses, excluding stock-based compensation	10,947	5,634
General corporate and facility expenses[3]	8,401	4,222
Other segment items[4]	(17)	4,968
Net loss	$ 75,268	$ 61,688

[1]External research and development expenses consist primarily of costs paid to third-parties including CROs, CDMOs, consultants, advisors and lab-related vendors.

[2]Fees paid to licensors consists primarily of upfront and annual licensing fees paid pursuant to the Company's license agreements.

[3]General corporate and facility expenses consists primarily of professional services fees for legal, finance, human resources, medical affairs in addition to information technology expenses and rent expense, net of sublease income.

[4]Other segment items consists primarily of interest income, partially offset by taxes and non-cash expenses, such as stock-based compensation, depreciation, the fair value of equity issued pursuant to the AbbVie License Agreement (Note 9) recognized in 2024, and amortization of discounts and premiums on marketable securities.

15. Net Loss Per Share

The Company excluded the following shares from the computation of diluted net loss per share attributable to common stockholders as of December 31, 2025 and 2024, because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2025	2024
Convertible preferred stock	—	27,149,206
Options to purchase common stock	5,767,799	3,700,335
Unvested restricted common stock	—	75,958
Total	5,767,799	30,925,499

16. Employee Benefit Plan

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers all employees and allows participants to defer a portion of their annual compensation on a pre-tax basis. Company contributions to the plan may be made at the discretion of the Board. For the year ended December 31, 2025 the Company contributed $0.2 million to the plan, no contributions were made for year ended December 31, 2024.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURES

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer (our principal executive officer) and our Chief Financial Officer (our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (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. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our 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 the end of the period covered by this Annual Report, our 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.

Inherent Limitations Over Internal Controls

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for the company. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company’s principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company’s board of directors, management, and other personnel, 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 and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company’s assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company’s receipts and expenditures are being made only in accordance with authorizations of a company’s management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of a 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. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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.

Management's Annual Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended. Management, with the participation of our Chief Executive Officer and our Chief Financial Officer, conducted an evaluation of the effectiveness of the Company's internal control over financial reporting as of December 31, 2025 based on the criteria established in Internal Control—*Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Our internal control system was designed to provide reasonable assurance to our management and our Board regarding the preparation and fair presentation of published financial statements. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Based on this evaluation, management concluded that the Company's internal control over financial reporting was effective as of December 31, 2025.

Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of the Company's independent registered public accounting firm regarding internal control over financial reporting. Management's assessment was not subject to attestation by the Company's independent registered public accounting firm pursuant to the exemption provided to emerging growth companies under the Jumpstart Our Business Startups Act of 2012, as amended.

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the year ended December 31, 2025, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

(a)

None.

(b)

Rule 10b5-1 Trading Plans

During the quarter ended December 31, 2025, none of our directors or executive officers adopted, modified, or terminated any contract, instruction or written plan for the purchase or sale of our securities that was intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) or any "non-Rule 10b5-1 trading arrangements" as defined in Item 408(c) of Regulation S-K.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item 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.

There have been no material changes to the procedures by which security-holders may recommend nominees to our board of directors.

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 and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNER 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 ACCOUNTING FEES AND SERVICES

Our independent public accounting firm is Deloitte & Touche LLP, Boston, Massachusetts, PCAOB Auditor ID 34.

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) Financial Statements

For a list of the consolidated financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report, which is incorporated into this Item by reference.

(b) Exhibits

Exhibit Number	Description
3.1	Fifth Amended and Restated Certificate of Incorporation of Sionna Therapeutics, Inc. (Incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 001-42504) filed on February 10, 2025).
3.2	Amended and Restated Bylaws of Sionna Therapeutics, Inc. (Incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K (File No. 001-42504) filed on February 10, 2025).
4.1	Specimen Common Stock Certificate (Incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
4.2+	Third Amended and Restated Investors' Rights Agreement, by and between the Registrant and certain of its stockholders, dated as of March 4, 2024 (Incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
4.3	Description of Securities of the Registrant (Incorporated by reference to Exhibit 4.3 of the Registrant's Annual Report on Form 10-K (File No. 001-42504) filed on March 20, 2025).
10.1#	2020 Stock Option and Grant Plan and form of award agreements thereunder (Incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.2#	Sionna Therapeutics, Inc. 2025 Stock Option and Incentive Plan and form of award agreements thereunder (Incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.3#	Sionna Therapeutics, Inc. 2025 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.4#	Form of Indemnification Agreement by and between the Registrant and its directors and executive officers (Incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.5#	Senior Executive Cash Incentive Bonus Plan (Incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.6#	Severance and Change in Control Plan (Incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.7#*	Amended and Restated Non-Employee Director Compensation Policy.
10.8†+	License Agreement by and between the Registrant and Sanofi Genzyme, dated as of December 20, 2019, as amended (Incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).

Exhibit Number	Description
10.9†+	License Agreement by and between the Registrant and AbbVie Global Enterprises Ltd., dated as of July 11, 2024 (Incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.10†+	Payment Agreement by and between the Registrant and Cystic Fibrosis Foundation, dated as of December 20, 2019 (Incorporated by reference to Exhibit 10.11 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.11#+	Offer Letter by and between the Registrant and Michael Cloonan, dated as of March 8, 2021 (Incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.12#+	Offer Letter by and between the Registrant and Charlotte McKee, dated as of May 7, 2021 (Incorporated by reference to Exhibit 10.13 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.13#+	Offer Letter by and between the Registrant and Elena Ridloff, dated as of August 20, 2021 (Incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
10.14+	Lease by and between the Registrant and BP3-BOS6 21 Hickory LLC, dated as of May 18, 2022, as amended (Incorporated by reference to Exhibit 10.15 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
19.1	Sionna Therapeutics, Inc. Insider Trading Policy (Incorporated by reference to Exhibit 19.1 of the Registrant's Annual Report on Form 10-K (File No. 001-42504) filed on March 20, 2025).
21.1	Subsidiaries of Registrant (Incorporated by reference to Exhibit 21.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).
23.1*	Consent of Deloitte & Touche LLP, independent registered public accounting firm.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1	Compensation Recovery Policy (Incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1/A (File No. 333-284352) filed on February 3, 2025).

* Filed herewith.

** The certification furnished in Exhibit 32.1 hereto is deemed to be furnished with this Annual Report and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

# Indicates a management contract or any compensatory plan, contract or arrangement.

† Certain portions of this document that constitute confidential information have been redacted pursuant to Item 601(b)(10) of Regulation S-K.

+ Certain exhibits and schedules to these agreements have been omitted pursuant to Item 601(a)(5) and (6) of Regulation S-K. The registrant will furnish copies of any of the exhibits and schedules to the Securities and Exchange Commission upon request.

(c) Financial Statement Schedules

No financial statements have been submitted because they are not required or are not applicable or because the information required is included in the consolidated financial statements or the notes thereto.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

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

SIONNA THERAPEUTICS, INC.

By: /s/ Michael Cloonan
Name: Michael Cloonan, M.B.A.
Title: President and Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

Each individual whose signature appears below hereby constitutes and appoints Michael Cloonan, M.B.A., and Elena Ridloff, C.F.A., as such person's true and lawful attorney-in-fact and agent with full power of substitution and resubstitution, for such person in such person's name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and all documents in connection therewith, with the Securities and Exchange Commission granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that any said attorney-in-fact and agent, or any substitute or substitutes of any of them, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report and Power of Attorney has been signed by the following person in the capacities and on the date indicated.

Signature	Title	Date
/s/ Michael Cloonan Michael Cloonan, M.B.A.	President, Chief Executive Officer and Director (*Principal Executive Officer*)	March 2, 2026
/s/ Elena Ridloff Elena Ridloff, C.F.A.	Chief Financial Officer (*Principal Financial Officer and Principal Accounting Officer*)	March 2, 2026
/s/ Paul Clancy Paul Clancy, M.B.A.	Chair of the Board of Directors	March 2, 2026
/s/ Bruce Booth Bruce Booth, D.Phil.	Director	March 2, 2026
/s/ H. Edward Fleming, Jr. H. Edward Fleming, Jr., M.D.	Director	March 2, 2026
/s/ Lucian Iancovici Lucian Iancovici, M.D.	Director	March 2, 2026
/s/ Joshua Resnick Joshua Resnick, M.D., M.B.A.	Director	March 2, 2026

Signature	Title	Date
/s/ Marcella K. Ruddy Marcella K. Ruddy, M.D.	Director	March 2, 2026
/s/ Laurie Stelzer Laurie Stelzer, M.B.A.	Director	March 2, 2026
/s/ Peter A. Thompson Peter A. Thompson, M.D.	Director	March 2, 2026
/s/ Joanne Viney Joanne Viney, Ph.D.	Director	March 2, 2026

SIONNA THERAPEUTICS, INC.

AMENDED AND RESTATED
NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

The purpose of this Non-Employee Director Compensation Policy (the "Policy") of Sionna Therapeutics, Inc., a Delaware corporation (the "Company"), is to provide a total compensation package that enables the Company to attract and retain, on a long-term basis, high-caliber directors who are not employees or officers of the Company or its subsidiaries ("Outside Directors"). This Policy will become effective as of the effective time of the registration statement for the Company's initial public offering of its equity securities. In furtherance of the purpose stated above, all Outside Directors shall be paid compensation for services provided to the Company as Outside Directors as set forth below:

Cash Retainers

Annual Retainer for Board Membership: $40,000 for general availability and participation in meetings and conference calls of our Board of Directors, to be paid quarterly in arrears, pro-rated based on the number of actual days served by the director during such calendar quarter. No additional compensation will be paid for attending individual meetings of the Board of Directors.

Additional Annual Retainer for Non-Executive Chairperson: $30,000

Additional Annual Retainers for Committee Membership:

Audit Committee Chairperson: $20,000

Audit Committee member (other than Chairperson): $10,000

Compensation Committee Chairperson: $15,000

Compensation Committee member (other than Chairperson): $7,500

Nominating and Corporate Governance Committee Chairperson: $10,000

Nominating and Corporate Governance Committee member (other than Chairperson): $5,000

Equity Retainers

All grants of equity retainer awards to Outside Directors pursuant to this Policy will be automatic and nondiscretionary and will be made in accordance with the following provisions:

Initial Award: Upon his or her initial election to the Board of Directors, each Outside Director will receive an initial, one-time stock option award (the "Initial Award") to purchase 34, 680 shares, which shall vest in equal annual installments over three years from the date of grant,

provided, however, that all vesting shall cease if the director ceases to have a Service Relationship (as defined in the Company's 2025 Stock Option and Grant Plan, as amended from time to time (the "2025 Plan")) with the Company, unless the Board of Directors determines that the circumstances warrant continuation of vesting. The Initial Award shall expire ten years from the date of grant, and shall have a per share exercise price equal to the Fair Market Value (as defined in the 2025 Plan) of the Company's common stock on the date of grant.

Annual Award: On the date of each Annual Meeting of Stockholders of the Company (each, an "Annual Meeting"), each continuing Outside Director, other than a director receiving an Initial Award on the date of such Annual Meeting, will receive an annual stock option award (the "Annual Award") to purchase 17,340 shares, which shall vest in full upon the earlier of (i) the first anniversary of the date of grant or (ii) the date of the next Annual Meeting; provided, however, that all vesting shall cease if the director ceases to have a Service Relationship with the Company, unless otherwise determined by the Board of Directors. If an Outside Director joins the Board of Directors on a date other than the date of the Annual Meeting, then, at the next Annual Meeting, in lieu of a full Annual Award, such Outside Director will be granted a pro-rata portion of the Annual Award based on the number of full months between such Outside Director's initial election or appointment and such Annual Meeting (a "Pro-Rated Annual Award"), which shall vest according to the same terms as an Annual Award. Annual Awards and Pro-Rated Annual Awards shall expire ten years from the date of grant, and shall have a per share exercise price equal to the Fair Market Value of the Company's common stock on the date of grant.

Value: For purposes of this Policy, "Value" means with respect to (i) any stock option award, the grant date fair value of the option (i.e., Black-Scholes Value) determined in accordance with the reasonable assumptions and methodologies employed by the Company for calculating the fair value of options under Financial Accounting Standard Board ("FASB") Accounting Standards Codification ("ASC") Topic 718; and (ii) any award of restricted stock or restricted stock units the product of (A) the average closing market price on the Nasdaq Global Market (or such other market on which the Company's common stock is then principally listed) of one share of the Company's common stock over the trailing 20-trading day period ending on the last trading day immediately prior to the grant date and (B) the aggregate number of shares of common stock underlying such award.

Sale Event Acceleration: All outstanding Initial Awards and Annual Awards (including Pro-Rated Annual Grants) held by an Outside Director shall become fully vested, exercisable (if applicable) and nonforfeitable upon a Sale Event (as defined in the 2025 Plan).

Expenses

The Company will reimburse all reasonable out-of-pocket expenses incurred by Outside Directors in attending meetings of the Board of Directors or any committee thereof.

Maximum Annual Compensation

The aggregate value of all equity compensation and cash compensation paid by the Company to any Outside Director for services as an Outside Director in any calendar year shall not exceed $750,000 (or such other limit as may be set forth in Section 3(b) of the 2025 Plan or any similar provision of a successor plan); provided, however, that in the first calendar year in which an individual becomes an Outside Director, the aggregate value of all equity compensation and cash compensation paid by the Company to such Outside Director for services as an Outside Director shall not exceed $1,000,000 (or such other limit as may be set forth in Section 3(b) of the 2025 Plan or any similar provision of a successor plan). In the event that the Annual Award or Initial Award causes an Outside Director to exceed his or her applicable maximum annual compensation limit, the Annual Award or Initial Award to such Outside Director, as the case may be, shall automatically and with no further action by the Board of Directors be adjusted downwards to the value that is required to remain below the applicable maximum annual compensation limit.

For the purpose of this limitation, the value of any equity compensation shall be its grant date fair value, as determined in accordance with FASB ASC Topic 718 or successor provision but excluding the impact of estimated forfeitures related to service-based vesting provisions.

Adopted January 31, 2025, subject to effectiveness of the Company's Registration Statement on Form S-1.

Amended effective as of January 1, 2026.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-284778 on Form S-8 of our report dated March 2, 2026, relating to the financial statements of Sionna Therapeutics, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2025.

/s/ Deloitte & Touche LLP

Boston, Massachusetts

March 2, 2026

CERTIFICATION PURSUANT TO
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael Cloonan, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2025 of Sionna Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 2, 2026

By: /s/ Michael Cloonan

Michael Cloonan

President and Chief Executive Officer

(Principal Executive Officer)

CERTIFICATION PURSUANT TO
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Elena Ridloff, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2025 of Sionna Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 2, 2026

By: /s/ Elena Ridloff

Elena Ridloff

Chief Financial Officer

(Principal Financial Officer and Principal Accounting Officer)

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

In connection with the Annual Report on Form 10-K of Sionna Therapeutics, Inc. (the "Company") for the fiscal year ended December 31, 2025 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned hereby certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Date: March 2, 2026 By: /s/ Michael Cloonan

Michael Cloonan

President and Chief Executive Officer

(Principal Executive Officer)

Date: March 2, 2026 By: /s/ Elena Ridloff

Elena Ridloff

Chief Financial Officer

(Principal Financial Officer and Principal Accounting Officer)