Aura Biosciences, Inc.

2024 Annual Report

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, 2024

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 001-40971

AURA BIOSCIENCES, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**32-0271970**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
80 Guest Street Boston, MA	**02135**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 500-8864

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.00001 per share	AURA	Nasdaq Global Market LLC

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

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

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

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

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

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

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

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

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

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 Exchange Act). YES ☐ NO ☒

As of June 30, 2024 (the last business day of the Registrant's most recently completed second fiscal quarter), the Registrant's aggregate market value of its voting common equity held by non-affiliates was $191.7 million based on the closing sale price of $7.56 per share as reported on the Nasdaq Global Market on that date.

The number of shares of Registrant's Common Stock outstanding as of March 19, 2025 was 50,225,312.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's proxy statement for the 2025 annual meeting of stockholders to be filed pursuant to Regulation 14A within 120 days after the registrant's fiscal year ended December 31, 2024, are incorporated by reference in Part III of this Form 10-K.

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Special Note Regarding Forward-Looking Statements

This Form 10-K, or Annual Report, contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “will”, “should”, “expects”, “intends”, “plans”, “anticipates”, “believes”, “estimates”, “predicts”, “potential”, “continue” or the negative of these terms or other comparable terminology. These statements are not guarantees of future results or performance and involve substantial risks and uncertainties. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- the initiation, timing, progress, results and cost of our research and development programs and our current and future nonclinical, preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- our ability to efficiently develop our existing product candidates and discover new product candidates;
- our ability to successfully manufacture our drug substances and product candidates for preclinical use, for clinical trials and on a larger scale for commercial use, if approved;
- the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates;
- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our ability to commercialize our products, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, and strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- estimates of our future expenses, revenues, capital requirements and our needs for additional financing;
- the potential benefits of strategic collaboration agreements, our ability to enter into strategic collaborations or arrangements and our ability to attract collaborators with development, regulatory and commercialization expertise;
- future agreements with third parties in connection with the commercialization of product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets;
- our financial performance;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States and foreign countries;
- our ability to produce our products or product candidates with advantages in turnaround times or manufacturing cost;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the impact of laws and regulations;
- developments relating to our competitors and our industry;
- the effects of macroeconomic conditions, including rising interest rates and inflation, on our business operations; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

Summary of the Material Risks Associated with Our Business

Our business is subject to numerous material and other risks and uncertainties that you should be aware of in evaluating our business. These risks are described more fully in Part II, "Item 1A—Risk Factors," in this Annual Report on Form 10-K and include, but are not limited to, the following:

- We have incurred significant net losses since our inception and anticipate that we will continue to incur losses for the foreseeable future.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish proprietary rights to our technologies or product candidates.
- Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve our objectives relating to the discovery, development, regulatory approval and commercialization of our product candidates.
- We are heavily dependent on the success of belzupacap sarotalocan, or bel-sar, our only product candidate to date.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for bel-sar, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.
- We have initiated but not yet completed a pivotal clinical trial nor have we commercialized any pharmaceutical products, which may make it difficult to evaluate our future prospects.
- If we fail to develop additional product candidates, or obtain additional indications of our first product candidate our commercial opportunity could be limited.
- The U.S. Food and Drug Administration's agreement to a Special Protocol Assessment with respect to the study design of our global Phase 3 trial of bel-sar for the treatment of early-stage choroidal melanoma does not guarantee any particular outcome from regulatory review, including ultimate approval, and may not lead to a successful review or approval process.
- We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and expect to continue to do so, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.
- We currently rely on third-party contract development and manufacturing organizations, or CDMOs, for the production of clinical supply of bel-sar and may continue to rely on CDMOs for the production of commercial supply of bel-sar, if approved. This reliance on CDMOs increases the risk that we will not have sufficient quantities of such materials, product candidates, or any therapies that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.
- If bel-sar or any future product candidates do not achieve broad market acceptance, the revenue that we generate from their sales may be limited, and we may never become profitable.
- If the market opportunity for bel-sar is smaller than we estimate or if any regulatory approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.
- Our ability to compete may decline if we do not adequately protect our proprietary rights, and our proprietary rights do not necessarily address all potential threats to our competitive advantage.
- If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to pursue our business strategy will be impaired, could result in loss of markets or market share and could make us less competitive.
- Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.
- Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval.

PART I

Item 1. Business.

Overview

We are a clinical-stage biotechnology company developing precision therapies to treat solid tumors designed to preserve organ function. Our lead candidate bel-sar is in late-stage clinical development for the treatment of patients with primary choroidal melanoma and is also in clinical development for other ocular oncology indications and bladder cancer.

There is significant unmet need for novel treatments for patients with choroidal melanoma, given the limitations of the current standard of care, or SoC, and patient reluctance to undergo radiotherapy in the form of either plaque brachytherapy or proton beam therapy, both highly-invasive therapies that result in significant vision loss, and potential legal blindness in the treated eye. Enucleation, or surgical removal of the affected eye, is another treatment option for patients with choroidal melanoma, in which patients lose all vision without the possibility of vision restoration. We are evaluating the safety and efficacy of bel-sar as a potential vision-sparing therapy in our ongoing global Phase 3 CoMpass trial for the first-line treatment of adult patients with small choroidal melanoma and indeterminate lesions, or early-stage choroidal melanoma. Moreover, we intend to assess the safety and efficacy of bel-sar in treating a range of other solid tumors, beginning with metastases of the choroid and bladder cancer where bel-sar is in clinical development. We believe bel-sar, if approved, has the potential to change the current treatment paradigm for patients with ocular and urologic cancers and other solid tumors.

Bel-sar has shown clinical benefit and has been generally well-tolerated in clinical trials to date. In a Phase 2 study (ClinicalTrials.gov ID: NCT04417530) evaluating suprachoroidal, or SC, administration of bel-sar for the first-line treatment of early-stage choroidal melanoma, patients were closely monitored over a twelve-month follow-up period to assess tumor control, visual acuity preservation, and tumor growth rate. A total of 22 patients were enrolled in the study. Bel-sar achieved an 80% tumor control rate (n=8/10) among Phase 3-eligible patients who received the therapeutic regimen, with complete cessation of growth following treatment among responders (post-treatment average growth rate of 0.011 mm/yr among responders compared to 0.351 mm/yr prior to study entry; $p<0.0001$). Visual acuity preservation was achieved in 90% of these ten patients. Importantly, 80% of these ten patients were at high risk for vision loss with tumors close to the fovea or optic disc, highlighting the potential for vision preservation with this novel class of drugs. The safety profile of bel-sar was highly favorable in all participants regardless of dose. We believe the Phase 2 results are a significant achievement considering the typically poor prognosis associated with choroidal melanoma, a rare and life-threatening ocular cancer, where there are no approved vision-preserving therapies to date. We believe bel-sar has the possibility to transform the field of ocular oncology beyond choroidal melanoma and we plan to expand clinical development in two additional indications: metastases to the choroid and cancers of the ocular surface. We have initiated a Phase 2 clinical trial in metastases to the choroid and have activated sites with patients in prescreening. We also plan to continue to advance our preclinical work designed to be IND-enabling in cancers of the ocular surface.

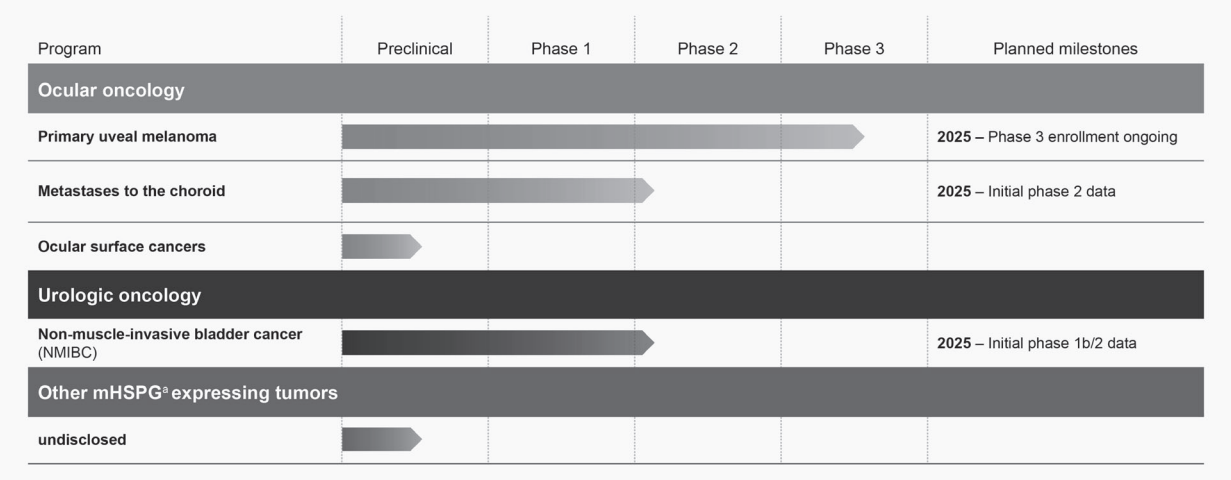
Virus-like drug conjugates, or VDCs, are a novel class of drugs with a dual mechanism of action that promote cancer cell death by both the delivery of the cytotoxic payload to generate acute necrosis and activation of a secondary immune mediated response. Bel-sar, our lead VDC candidate, consists of modified capsid proteins of the human papilloma virus, or HPV, conjugated to hundreds of light-activated molecules.

Light activation of bel-sar is designed to result in precise tumor cell killing with minimal damage to surrounding healthy tissues. In the absence of bel-sar activation or binding to the tumor cell membrane, there is no cytotoxic effect. Multiple light activations, following a single dose of bel-sar, increase antitumor activity because of the reoxygenation of the tumor and the photostability of bel-sar. Finally, acute necrosis triggers immunogenic cell death leading to the generation of an adaptive, long-term antitumor immune response. The tumor targeting specificity of VDCs is driven by the selective binding of the virus-like particles, or VLPs, to a subset of modified tumor associated glycosaminoglycans, or GAGs, that are part of the heparan sulphate chain of heparan sulfate proteoglycans or HSPGs, expressed on the tumor cell membrane. This targeting mechanism enables the delivery of multiple types of cytotoxic payloads directly to a wide range of solid tumors.

Beyond ocular cancers, bel-sar is in early-stage clinical development in bladder cancer. Bladder cancer is the ninth most common cancer worldwide and it is diagnosed early as non-muscle invasive bladder cancer, or NMIBC, with a prevalence of approximately 80,000 cases per year in the United States. Despite the early diagnosis, patients with NMIBC have a high risk of recurrence and progression with current SoC treatments. In March 2025, we announced positive data from our Phase 1 trial in NMIBC (NCT05483868).

Our vision is to innovate the future of cancer care to cure patients and preserve organ function. We are developing bel-sar in a number of indications in ocular oncology, with the goal of preserving vision and preventing blindness in patients. Our lead indication is a potential multi-billion dollar market opportunity. We are also evaluating bel-sar in urologic oncology indications, initially in bladder cancer, which is one of the most expensive cancers to treat on a per patient basis. The global market for bladder cancer is expected to be greater than $8.0 billion by 2032.

Our initial focus is in ocular and urologic oncology, both areas of high unmet medical need where local targeted therapies may enable early intervention, as shown in our pipeline below.



a. Virus-like drug conjugates (VDCs) bind to a subset of modified tumor associated glycosaminoglycans (GAGs) that are part of the heparan sulphate chain of heparan sulfate proteoglycans (HSPGs).[1]

1. Kines RC, and Schiller JT. Viruses. 2022;14(8):1656. ***mHSPG****, modified heparan sulphate proteoglycan;* ***MIBC****, muscle invasive bladder cancer;* ***NMIBC****, non-muscle-invasive bladder cancer*

We envision the potential for development of additional therapeutic areas in addition to ocular and urologic cancers.

Our Team

Our management team includes industry executives with extensive biopharmaceutical experience in developing and commercializing drugs in oncology and ophthalmology. Elisabet de los Pinos, Ph.D., our Chief Executive Officer, led the marketing strategy and European commercialization of Alimta® for the treatment of lung cancer at Eli Lilly and Company. Our Chief Medical Officer and President of Research & Development, J. Jill Hopkins, M.D., is an ophthalmologist and retinal specialist with more than 30 years of experience in ophthalmology, including serving as Senior Vice President, Global Head of Ophthalmology and Exploratory Development at Novartis AG, or Novartis, and Chief Executive Officer of Gyroscope Therapeutics, a Novartis company, where she was responsible for the global ophthalmic pipeline. Amy Elazzouzi, our Senior Vice President, Finance, interim principal financial officer and interim principal accounting officer, has served as Director of Finance and Operations at KEW Group, Inc. and Controller at AVEO Pharmaceuticals, Inc. Conor Kilroy, our Chief Legal Officer and Secretary, served as general counsel and secretary at Neurogastrx, Inc. from September 2021 to May 2023. Mr. Kilroy also served in roles of increasing responsibility at Ironwood Pharmaceuticals, Inc. (Nasdaq: IRWD) from June 2013 to February 2021, serving as senior vice president, general counsel and secretary beginning in April 2020 and vice president, general counsel and secretary beginning in April 2019. Earlier in his carrier, Mr. Kilroy held roles at Boston Scientific Corporation and in the business law department of Goodwin Procter LLP. Mark Plavsic, Ph.D. is our Chief Technology Officer and brings 30 years of global biopharmaceutical experience including end-to-end technical operations in the United States, Europe, and Australasia and successful translation and scale-up of complex biologics from preclinical development through commercial launch and distribution. He previously served as Chief Technology Officer at Fate Therapeutics, Inc. and at Lysogene. We believe the breadth and depth of experience amongst our management team will enable us to advance the clinical and development strategy for bel-sar and, if approved, its commercialization. Our Chairman of the Board of Directors, David Johnson, is a biopharmaceutical industry veteran with more than 25 years of experience in drug development. Mr. Johnson is currently Chief Executive Officer and founder of Solve Therapeutics, Inc., a biotechnology company developing next-generation mAb-based oncology therapeutics. Prior to founding Solve Therapeutics, he was Chief Executive Officer of VelosBio Inc., an oncology company acquired by Merck & Co. for $2.75 billion in 2020. He was also Chief Executive Officer at Acerta Pharma, which was acquired by AstraZeneca for $7 billion. Mr. Johnson has extensive experience leading the development of first-in-class cancer therapies and has made significant contributions to drugs which ultimately garnered regulatory approvals, including bortezomib (Velcade®), romidepsin (Istodax®), idelalisib (Zydelig®), and acalabrutinib (Calquence®).

Our Strategy

At Aura Biosciences, our vision is to innovate the future of cancer care to cure patients and preserve organ function, with an initial focus on ocular and urologic oncology. Key elements of our strategy to accomplish this objective include:

- **Complete the ongoing global Phase 3 CoMpass trial of bel-sar as a first-line treatment of small choroidal melanoma and/or indeterminate lesions and pursue U.S. Food and Drug Administration, or FDA, approval.** If approved, this would represent the first therapy for primary choroidal melanomas as a potential first-line treatment option for small tumors and indeterminate lesions, reserving radiotherapy for a second-line treatment option. If approved, we see the potential to independently commercialize bel-sar in choroidal melanoma, which has an incidence of 11,000 patients diagnosed per year in the United States and Europe. There are approximately 50 ocular oncologists in the United States and approximately 50 ocular oncologists in Europe, representing a focused call point and providing an opportunity for our company to capture the value of the market with a manageable sales team globally.
- **Expand the development of bel-sar in additional ocular oncology indications, starting with metastases to the choroid and cancers of the ocular surface**. We believe bel-sar's dual mechanism of action has potential to treat tumors while preserving key ocular structures, in other ocular cancers that affect a large number of patients. We have initiated a Phase 2 clinical trial in metastases to the choroid and have activated sites with patients in prescreening. Metastases to the choroid has an annual incidence rate of 20,000 patients in the Unites States and Europe. In addition, we are advancing bel-sar for cancers of the ocular surface, including both melanomas and squamous cell carcinomas, that has an incidence rate of 35,000 patients a year in the United States and Europe, based on strong interest from the ocular oncology community to develop better treatment options for patients.
- **Advance the development of bel-sar in NMIBC.** We believe that bel-sar has the opportunity to become a front-line treatment option with a paradigm shifting approach driven by its unique dual mechanism of

action and the possibility to generate a robust cell mediated immune response against the tumor to prevent recurrence of the disease. As such, our goal is to evaluate two different front-line interventions in a Phase 1b/2 trial: neoadjuvant treatment in combination with transurethral resection of bladder tumor, or TURBT, and immune-ablative treatment (without TURBT), with the opportunity to not only evaluate the dose and treatment regimen but also to assess durability of response at up to 12 months in patients with intermediate and high-risk NMIBC. Bel-sar has received FDA Fast Track Designation in NMIBC.

- **Continue to evaluate bel-sar, to potentially further enhance its clinical utility across additional solid cancers based on its mechanism of action.** Due to our preclinical data and robust publications in collaboration with our scientific founder at the National Institutes of Health, or NIH, demonstrating the binding of our proprietary VLPs to tumor associated GAGs across a wide range of solid tumors, we plan to expand our clinical pipeline across multiple solid cancer indications.
- **Build our operational capabilities to successfully commercialize bel-sar (if approved) in ocular oncology**.

Our Strengths in Ocular Oncology

Bel-sar is in development in multiple indications in ocular oncology: early-stage choroidal melanoma, metastases to the choroid, and cancers of the ocular surface. We believe bel-sar has several strengths that support our goal of developing bel-sar as a potential vision-sparing therapy in ocular oncology, including:

- Demonstrated clinical utility in choroidal melanoma, with Phase 2 end of study results of patients at twelve months of follow-up who received three cycles of therapy in Cohorts 5 and 6, and who match the criteria for our ongoing global Phase 3 trial.
- Tumor control rate of 80% (8/10) and visual acuity preservation rate of 90% (9/10), with the majority of patients being at high-risk for vision loss with tumors close to the fovea or optic disc.
- Favorable safety profile, with no posterior inflammation, treatment-related serious adverse events or grade three to five treatment-related adverse events reported**.**

Primary Choroidal Melanoma

Primary choroidal melanoma is our most advanced clinical program, with an ongoing global Phase 3 trial. We have received Orphan Drug Designation, or ODD, for the treatment of early-stage choroidal (also referred to as uveal) melanoma from the FDA and the European Medicines Agency, or EMA, and Fast Track Designation from the FDA for the treatment of early-stage choroidal melanoma. SC administration of bel-sar in a completed Phase 2 trial, provided data which supported this SC route of administration in the Phase 3 trial.

We have received written agreement from the FDA under a Special Protocol Assessment, or SPA, for the design and planned analysis of the global Phase 3 trial indicating concurrence by the FDA with the adequacy of the study, if successful, to address the objectives necessary to support our planned biologics license application, or BLA, submission. Disease state overview and the clinical development plan with key findings and updates from each stage of development are found below.

Choroidal Melanoma Overview

Choroidal melanoma is the most common primary malignant intraocular tumor and the second most common type of primary malignant melanoma in the body. More than 11,000 patients are diagnosed annually in the United States and Europe. This comprises approximately 90% of all cases of uveal melanoma, consisting of melanomas in the choroid, ciliary body and iris, which are collectively referred to as the uvea. Most choroidal melanomas result from transformation of a benign choroidal nevus. In early-stage lesions, most of the tumor is composed of benign nevus cells with a small cluster of malignant melanoma cells. Benign choroidal nevi are found in approximately 5% of adults in the United States 40 years or older. Most cases are found in adults with a median age of 55, light eye color and fair skin. It is often discovered in patients who are asymptomatic, although some patients report decreased vision or non-specific visual symptoms such as flashes, floaters, blurry or distorted vision or visual field defects and are referred to the ocular oncologist.

Most patients with choroidal melanoma are diagnosed with early-stage disease localized to the eye with no evidence of metastatic disease. It is estimated that 96% of patients are diagnosed without clinical evidence of metastatic disease. These patients are not treated immediately as there are no effective targeted therapies that can

preserve vision. Early-stage patients are defined as patients with small choroidal melanoma and/or indeterminate lesions representing approximately 8,000 patients in the United States and Europe. The only current treatment option for patients with primary choroidal melanoma is radiotherapy which leaves patients with vision loss and other comorbidities. Approximately 2,300 patients are diagnosed with medium to large tumors and are treated with radiotherapy or enucleation, or full surgical removal of the eye, which results in total vision loss and is irreversible.

[a]Each figure represents approximately 250 persons.

Figure 1. Distribution of Stages of Choroidal Melanoma Cases

We are developing bel-sar as a potential first line vision-sparing treatment option for early intervention in small choroidal melanoma and/or indeterminate lesions, avoiding the need for radiotherapy and reducing the risk for metastasis for these patients. Earlier diagnosis and treatment intervention of lesions in the eye has the potential to dramatically improve outcomes for patients and reduce the risk of blindness caused by radiotherapy.

Current Treatment Options for Primary Choroidal Melanoma

There are no FDA-approved therapies for primary choroidal melanoma. There are three common treatments routinely used as SoC for local control of choroidal melanoma: plaque brachytherapy; proton beam irradiation; and enucleation, or removal of the affected eye, each of which represent invasive surgical procedures and are associated with significant vision loss.

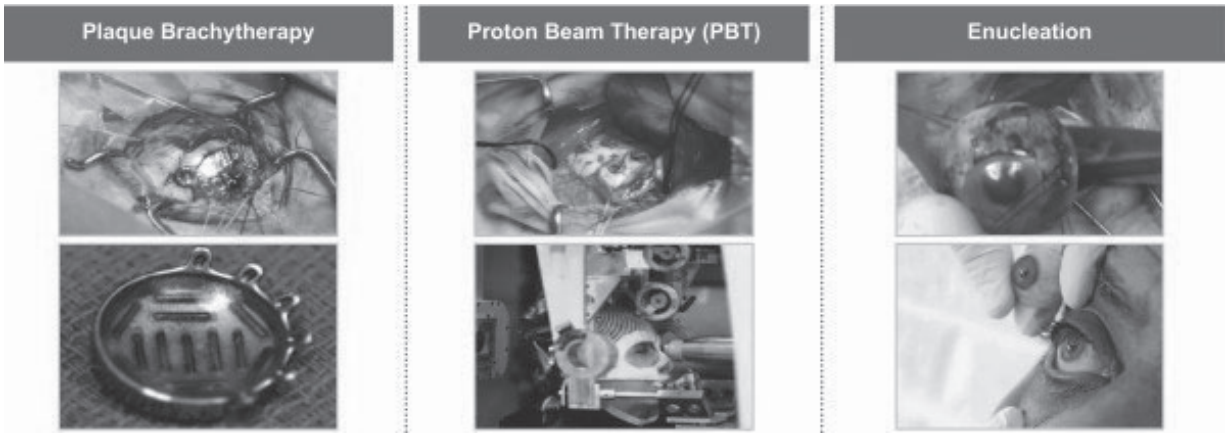


Figure 2. Three Treatment Options for Primary Choroidal Melanoma

There are limited treatment options to treat primary choroidal melanoma, which pose a challenge to clinicians and patients. The current treatments are invasive procedures and are associated with irreversible loss of visual acuity and other side effects. Lesions that are detected early are often monitored without treatment since the current SoC is invasive and causes vision loss and is therefore typically reserved for medium to large or growing lesions. As choroidal melanoma tends to metastasize early, even with radical treatments such as enucleation, metastatic disease still occurs, which results in a high degree of mortality. There is an urgent unmet medical need for an effective, vision-sparing therapy and the availability of such a therapy may encourage treatment of small choroidal melanomas and indeterminate lesions at the time of early detection. This could subsequently increase the awareness of the importance of early diagnosis and intervention for this life-threatening disease and increase the number of patients treated annually.

Bel-sar in Primary Choroidal Melanoma

Bel-sar is a VDC consisting of an HPV-derived VLP and a phthalocyanine dye, a light activated cytotoxic payload. Our VLP was created using the capsid proteins of HPV that have been genetically modified to avoid cross-reactivity with pre-existing immunity against the virus and bind with high affinity to modified tumor associated GAGs that are part of the heparan sulphate chain of HSPGs expressed on the surface of tumors cells, including ocular melanoma cells.

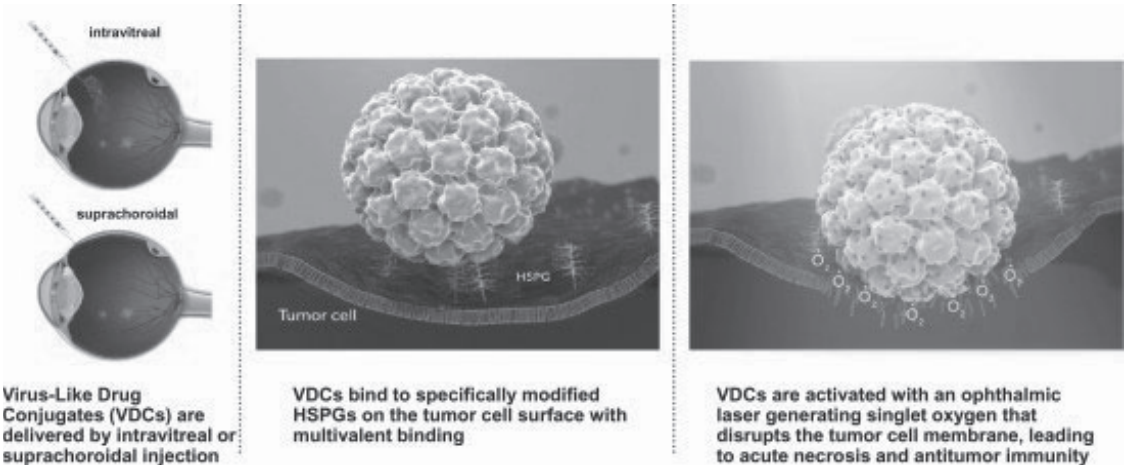


Figure 3. Bel-sar, Administered by Intraocular Injection, Binds to Tumor Cells. Activation Using an Ophthalmic Laser Leads to Rupture of the Tumor Cell Membrane, Acute Necrosis and a Secondary Immune Activation Leading to Long Term Antitumor Immunity.

Goal of Treatment with Bel-sar

In ocular oncology, early detection, and timely local intervention has the goal of achieving a local complete response, or CR, which in ocular oncology is described as tumor control. This involves completely halting tumor growth while safeguarding critical ocular structures, such as the retina, essential for maintaining visual function. Early treatment is believed to reduce the risk of metastasis. After treatment, if tumors do not have an increase in thickness by ultrasound or an increase in diameter as evaluated with digital photography, it is believed that the malignant cells have been killed, and a local complete response has been achieved and the treatment is considered equivalent to a local cure. Ocular oncologists measure the antitumor activity after plaque brachytherapy by evaluating tumor control as well as systemic disease to detect the presence of metastasis.

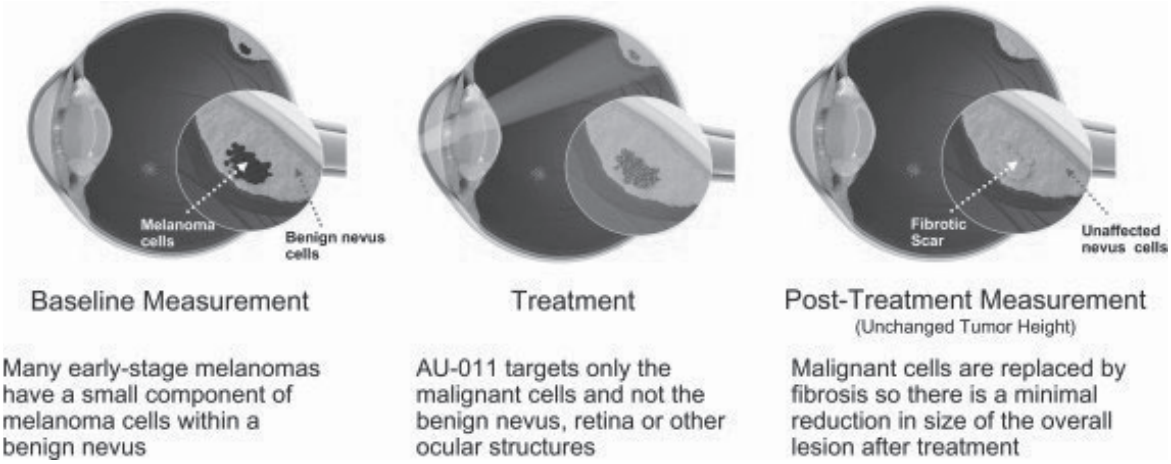


Figure 4. Goal of Treatment with Bel-sar is a Local Complete Response Achieving Tumor Control with Targeted Killing of Melanoma Cells and Preservation of Key Ocular Structures.

We believe that patients with small choroidal melanoma or indeterminate lesions would gain the most advantage from bel-sar treatment. These tumors are not only the most likely to respond to our therapy but, based on historic data, these patients also have the lowest risk of having developed life-threatening metastatic disease, and as such, bel-sar has the potential to confer the greatest long-term benefit.

Clinical Development Plan in Primary Choroidal Melanoma:

Phase 1b/2 Intravitreal Study: This study evaluated the safety and efficacy of bel-sar delivered via intravitreal, or IVT, administration followed by light activation in a dose escalation design in 56 patients. The majority of patients treated at the therapeutic regimen with two cycles of therapy at the highest dose achieved a local complete response showing a tumor control rate of 70% at 12 months. Visual acuity preservation was demonstrated in >70% including a high percentage of patients with tumors close to the fovea or optic disc considered at high risk for vision loss when treated with radiotherapy. Treatment with bel-sar was generally well-tolerated at all doses including the highest treatment regimen with two cycles of therapy. Adverse events were generally mild or moderate, transient and manageable with SoC treatments in most patients. Adverse events of vitreous inflammation, anterior chamber inflammation and increased intraocular pressure were manageable with steroid treatment and ocular antihypertensives. There were only two drug-related serious adverse events of vision loss related to pigmentary changes around the edge of the tumor.

Phase 2 Suprachoroidal Study: We also evaluated and developed the SC route of administration to optimize the delivery of bel-sar directly to the choroid where the tumor is located. The suprachoroidal space, or SCS, is a potential space bound between the external surface of the choroid and the internal surface of the sclera and encompasses the full circumference of the posterior segment of the eye. The Phase 2 study was an open-label, ascending single and repeat dose escalation trial in patients with early-stage choroidal melanoma designed to evaluate the safety, tolerability and efficacy of up to three cycles of bel-sar treatment. (ClinicalTrials.gov ID: NCT04417530)

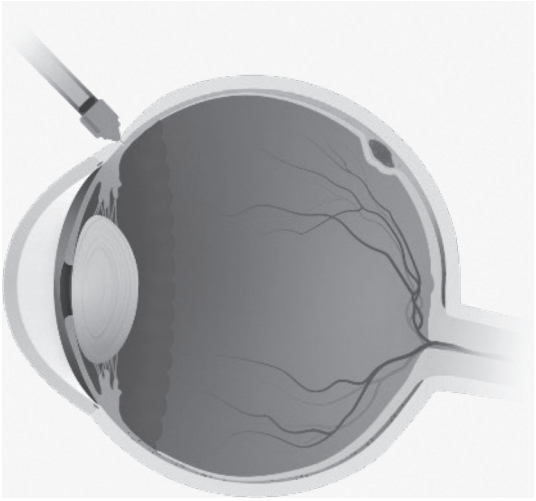


Figure 5. SC Administration with SCS Microinjector™.

The trial included both single and multiple ascending dose cohorts, with a total of 22 patients enrolled. Patients were closely monitored over a twelve-month follow-up period to assess tumor control, visual acuity preservation and tumor growth rate. The Phase 2 end of study results demonstrated that bel-sar achieved an 80% tumor control rate (n=8/10) among Phase 3-eligible patients who received the therapeutic regimen, with complete cessation of growth following treatment among responders (post-treatment average growth rate of 0.011 mm/yr among responders compared to 0.351 mm/yr prior to study entry; $p<0.0001$). Visual acuity preservation was achieved in 90% of these ten patients. Importantly, 80% of these ten patients were at high risk for vision loss with tumors close to the fovea or optic disc, highlighting the potential for vision preservation with this novel class of drugs. Of note, the current standard of care is radiotherapy, which leads to visual acuity of <20/200 (the cutoff for legal blindness) in the treated eye in up to 87% of patients. The safety profile of bel-sar was highly favorable in all participants regardless of dose. There were no treatment-related serious adverse events reported. Ocular treatment-related adverse events were mild (Grade 1), included anterior chamber inflammation (18%) or cell (9%) and resolved without sequelae. The vast majority (~70%) of the anterior chamber inflammation/cell events were self-limited, requiring no treatment, and resolved in a median of six days. For those events that did require treatment, topical steroid eye drops, administered for a median of six days, achieved complete resolution of the inflammation. Eye pain occurred in 9% of patients and was mild (Grade 1). Importantly, no treatment-related posterior inflammation events (no vitritis, choroiditis, retinitis, retinal pigment epithelium changes or vasculitis) were reported. We believe the Phase 2 results are a significant achievement considering the typically poor prognosis associated with choroidal melanoma, a rare and life-threatening ocular cancer, where there are no approved vision-preserving therapies to date.

Phase 2 safety outcomes (bel-sar/laser-related)

Drug/laser-related adverse events	All treated participants (n=22)*			
	Grade I	Grade II	Grade III-V	Total
Anterior chamber inflammation**	4 (18.2%)	0	0	4 (18.2%)
Anterior chamber cell**	2 (9.1%)	0	0	2 (9.1%)
Eye pain	2 (9.1%)	0	0	2 (9.1%)
Anisocoria	1 (4.5%)	0	0	1 (4.5%)
Conjunctival edema	1 (4.5%)	0	0	1 (4.5%)
Cystoid macular edema	1 (4.5%)	0	0	1 (4.5%)
Pupillary reflex impaired	1 (4.5%)	0	0	1 (4.5%)
Salivary gland enlargement	0	1 (4.5%)	0	1 (4.5%)

***Median duration 6 days (IQR: 3–10 days); All resolved with no or minimal treatment; If topical steroids given, median treatment duration 6 days*

* Table presents participants with AEs related to bel-sar or laser by severity and overall; participants with >1 AE are counted in the highest severity group
AE, adverse event; **SAE,** serious adverse event; **IQR,** interquartile range
ClinicalTrials.gov Identifier: NCT04417530; AU-011-202. **Data on file, Aura Biosciences.**

Figure 6. Adverse Events among the 22 Patients Enrolled in the Phase 2 SC Trial.

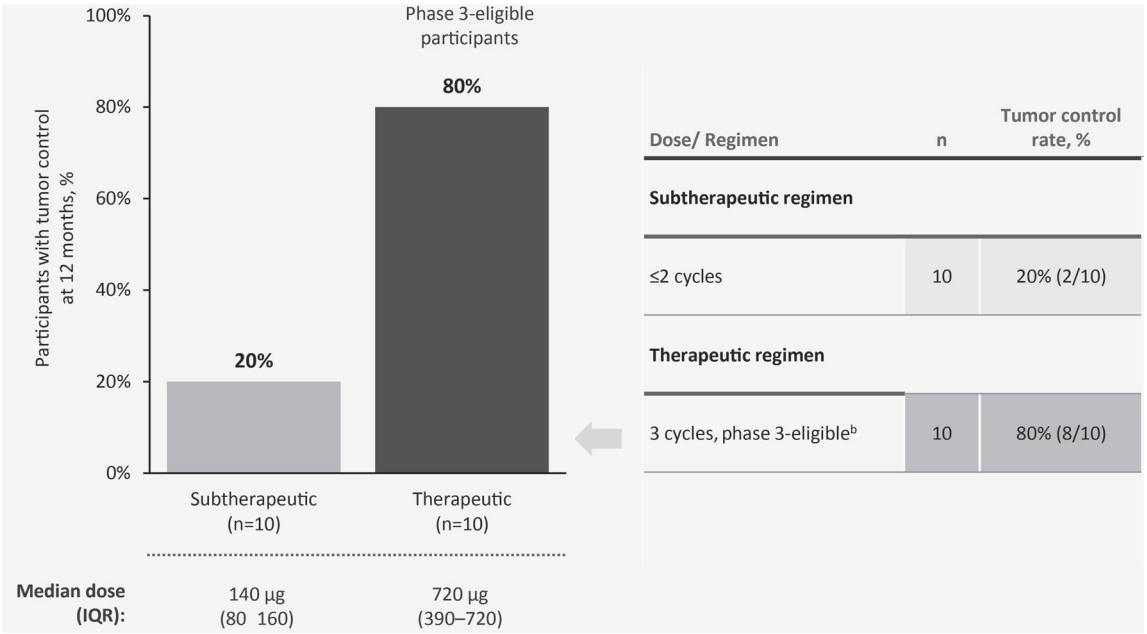
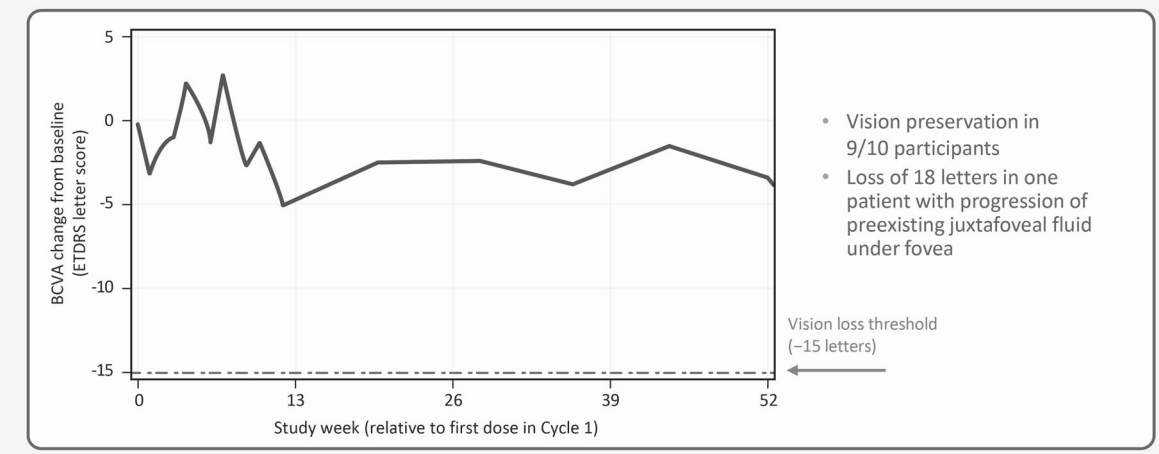


Figure 7. Dose Response and Tumor Control Rates Demonstrate Meaningful Clinical Benefit



Populations	Patients (n)	Vision failures[b] (n)	Vision preservation rate (%)
All dose cohorts			
All treated patients	22	1	95%
Subtherapeutic			
≤2 cycles	10	0	100%
Therapeutic			
3 cycles and phase 3-eligible[a]	10	1	90%

[a]One participant with circumpapillary tumor that did not meet phase 3 criteria is not included. [b]Vision acuity loss defined as ≥15 letters decrease from baseline in ETDRS BCVA letter score.
BCVA, best-corrected visual acuity; **ETDRS,** Early Treatment Diabetic Retinopathy Study.
ClinicalTrials.gov Identifier, NCT04417530: AU-011-202. **Data on file, Aura Biosciences.**

Figure 8. High Vision Preservation Rates with 12 Months of Follow Up.

Phase 3 Randomized Controlled Trial: The Phase 3 trial is designed as a superiority trial comparing bel-sar versus sham delivered via SC injection followed by laser light activation. The trial is a global, randomized, multi-center, masked study. It is intended to enroll approximately 100 patients randomized 2:1:2 to receive the high dose regimen of bel-sar, low dose regimen of bel-sar, or a sham control. The primary endpoint is time to tumor progression, and the first key secondary endpoint is a composite time to event analysis. Endpoints will only compare the bel-sar high dose regimen to sham when the last patient completes 15 months of follow up. The trial is powered at greater than 90%. (ClinicalTrials.gov ID: NCT06007690)

The design of the trial and the endpoints utilized have been agreed upon through an SPA with the FDA.

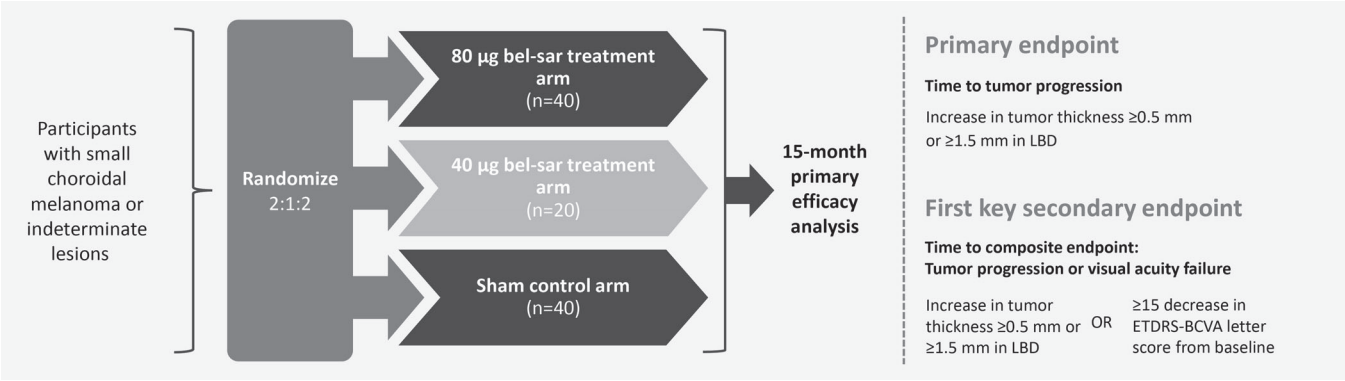


Figure 9. Global Phase 3 Trial Design

The trial is patient, assessor (VA examiners and Independent Reading Center, or IRC, readers) and sponsor-masked. Masked readers at the IRC will assess the imaging data-based efficacy assessments including tumor thickness and largest basal diameter, or LBD, during the trial. Best corrected visual acuity will be assessed using the ETDRS protocol by masked, certified, VA examiners. All measures will be taken to mask the patients during their trial participation period including the use of sham SC injections and sham laser on assigned treatment days.

Any patient in the trial who meets the tumor progression definition will be treated with SoC therapies as rescue treatment per Investigator judgment. SoC therapies will include, but are not limited to, brachytherapy and proton beam therapy. This will ensure that no patient has a delayed treatment if the tumor is progressing, and importantly, that all of the sham patients receive their SoC treatment in a timely manner and no later than in regular clinical practice.

The trial is powered at greater than 90%. Since there is no drug approved for the treatment of choroidal melanoma, we have aligned with FDA that a statistically significant difference on the primary endpoint will provide support from a regulatory perspective to meet the requirement of clinical effectiveness. Based on the SPA, the FDA has agreed that the design and planned analysis of the study can adequately address objectives in support of a regulatory submission.

If warranted by the data, we plan to submit the results of the Phase 3 trial to support approval of bel-sar for the treatment of primary small choroidal melanoma and indeterminate lesions. Based on the results of the Phase 3 trial, if positive, and a lack of therapies approved for the treatment of this rare disease, with the current SoC with radiotherapy causing patients irreversible vision loss, the FDA and EMA may agree to grant approval based on a single Phase 3 trial. However, the FDA and/or EMA may require two Phase 3 trials for approval, which will be addressed subsequent to reviewing the data from the Phase 3 trial with the regulators.

As we previously reported, there was an administrative error in the original International Nonproprietary Name, or INN, application (INN: belzupacap sarotalocan) with the World Health Organization, or WHO. In subsequent communications with the WHO, the WHO has confirmed an amendment to the existing INN allowing the continued use of belzupacap sarotalocan.

Registry Study

Based on discussions with the FDA and EMA, we will monitor patients in a long-term registry study, for a total of five years after start of dosing in the parent study. All 57 patients enrolled in the Phase 1b/2 trial (AU-011-101) with intravitreal administration completed the trial and 45/57 elected to enter the registry study. In addition, 18/22 patients from the Phase 2 trial (AU-011-202) with SC administration also elected to enter the registry study. The data collected in the registry study is intended to assess the long-term (5 total years) safety, rate of metastatic disease, and mortality from bel-sar treatment.

Retrospective natural history study to evaluate long-term visual acuity benefit versus plaque brachytherapy

The ability to demonstrate tumor control with long-term visual acuity preservation supports the potential of bel-sar to become the SoC for the first-line treatment of patients with small choroidal melanoma/indeterminate lesions compared to an invasive radiotherapy procedure that leaves most patients with irreversible vision loss and other long-term comorbidities. To demonstrate the long-term visual decline that patients (who would otherwise have been eligible for our clinical trials) experienced by undergoing radiotherapy, we have conducted a retrospective natural history study to evaluate the visual acuity of patients treated with plaque brachytherapy who were matched to actual patients in our Phase 1b/2 study with IVT administration to provide an estimate of the vision benefit of bel-sar. This study is discussed below.

We conducted a retrospective natural history study comparing a group of historic patients that underwent radiotherapy, who were matched to the 43 patients in our Phase 1b/2 trial with IVT administration, in terms of patient and tumor factors such as tumor size and location. Like the patients in our Phase 1b/2 study, tumors in the matched patients were at high risk for vision loss due to their locations close to the fovea or optic disc. The matched patients had all been previously treated with brachytherapy at the Wills Eye Hospital Ocular Oncology Service led by Dr. Carol Shields, and had long-term follow-up. This study matched patients up to 5:1 using the key baseline characteristics that impact long-term visual acuity – tumor location, tumor size and baseline visual acuity – to determine the visual acuity after radiation treatment for small tumors that might otherwise have been considered for bel-sar treatment in a clinical trial. As shown in Figure 10, matched patients who underwent radiotherapy demonstrated progressive vision loss. At five years post-treatment, mean visual acuity was <20/200 (20/200 is the definition of “legal blindness”), with a mean loss in vision of almost 50 letters.

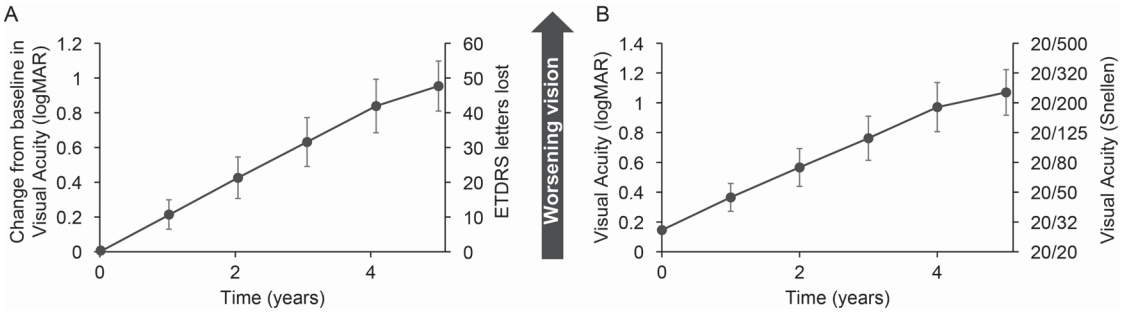


Figure 10. A) Vision Loss, and B) Visual Acuity Outcomes, after Treatment with Brachytherapy

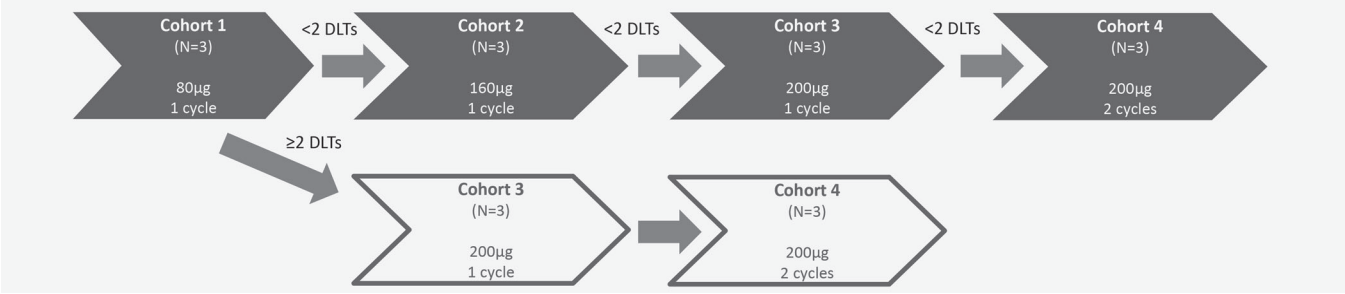
We believe that the results of this retrospective study validate and strengthen our data supporting that treatment with bel-sar provides an important advantage in terms of vision preservation compared to brachytherapy, as a first line treatment option for early-stage disease.

In addition to these data, we plan to develop a long-term follow up plan to assess visual acuity and other outcomes from the Phase 3 trial, to continue to support the long term benefit of visual acuity preservation with bel-sar compared to SoC brachytherapy.

Metastases to the Choroid

Metastases to the choroid, where different types of primary cancers from elsewhere in the body (e.g., breast and lung cancer) metastasize to the eye, is an even more common cause of intraocular malignancy than primary (i.e., originating within the eye) choroidal melanoma. There is a high unmet need in these patients, as current therapy consists primarily of external radiotherapy, which is typically given daily for four weeks, which comes with a very high treatment burden and with ocular morbidity. As such, an easier-to-apply treatment that preserves vision is needed. These patients are treated by the same ocular oncologists that treat choroidal melanoma. We have an open IND in the United States and have received Fast Track Designation from the FDA’s Division of Oncology in metastases to the choroid. We have initiated a Phase 2 clinical trial in metastases to the choroid and have sites activated with patients in prescreening. We expect initial data from this trial in 2025.

The Phase 2 trial is expected to enroll approximately 12-24 patients with unilateral/unifocal metastasis to the choroid, arising from breast or lung primary tumors. The goal of the study is to evaluate safety and early efficacy, including tumor shrinkage and visual acuity, to establish the dose and the dosing regimen for future development.



DLT: dose-limiting toxicity

Figure 11. Metastases to the choroid Phase 2 Trial Design

Cancers of the Ocular Surface

We are also evaluating the development of bel-sar in cancers of the ocular surface. Ocular surface tumors are tumors that start in the conjunctiva and are treated by the same ocular oncologists that treat choroidal melanoma and metastases to the choroid. These tumors are diagnosed early, when they are not yet metastatic, not unlike choroidal melanoma. However, they remain life-threatening – despite early diagnosis and therapeutic options including disfiguring surgeries, 5-year mortality for conjunctival melanoma remains approximately 25%. Ocular surface tumors are known to be immunologically 'hot', that is, susceptible to control through normal immune mechanisms and immune-modulating therapies. This could allow us to benefit from the immune activation that is part of our mechanism of action, as we have demonstrated with bladder tumors (see below).

There are currently no drugs approved for cancers of the ocular surface, and patients are treated with surgery, off-label chemotherapy, and radiation. The readily accessible location of these tumors, on the surface of the eye, would be expected to facilitate local treatment with bel-sar in clinic. We continue to advance our preclinical work designed to be IND-enabling in cancers of the ocular surface.

Urologic Oncology

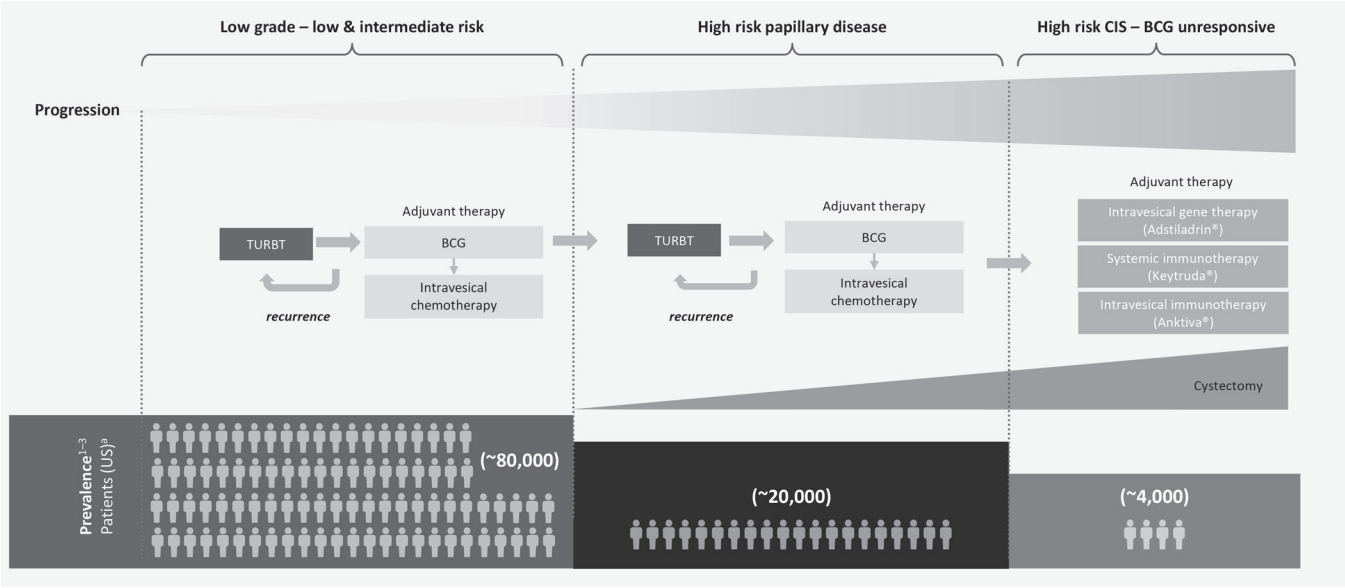
We are actively leveraging our precision oncology platform to advance the development of bel-sar in urologic oncology, with ongoing clinical development. We believe bel-sar has the potential, if approved, to serve as an immune-based, function-preserving and organ-sparing treatment approach, offering a novel therapeutic option for patients.

Bladder Cancer Overview

Bladder cancer is the most common malignancy of the urinary system and remains a significant global health concern, with over 600,000 new cases diagnosed annually, making it the ninth most diagnosed cancer worldwide. In the United States, it ranks as the eighth leading cause of cancer-related deaths in men. The disease primarily affects men and individuals over the age of 65. The primary risk factor is smoking, responsible for approximately half of all cases, followed by occupational exposure to certain chemicals, chronic infections, and genetic predispositions. Most patients are diagnosed at a localized stage; within this group, about 75% have NMIBC, while 25% present with muscle-invasive bladder cancer, or MIBC. Early detection and reducing exposure to known carcinogens, particularly tobacco, are crucial for prevention and improved outcomes.

Current Treatment Options for Bladder Cancer

Although several adjuvant intravesical therapies are utilized for patients with NMIBC, there are currently no FDA-approved treatment options specifically indicated for low-grade, intermediate-risk NMIBC. In high-risk NMIBC, various intravesical therapies, including BCG, are approved and commonly used as adjuvant treatments following surgical resection. However, their efficacy is limited by several factors, including BCG shortages and treatment-related adverse events that often lead to early discontinuation, ultimately leaving patients at a substantial risk of recurrence, disease progression, and long-term bladder function impairment.



[a]Each figure represents 1000 persons.

***1**. Holzbeierlein JM et al. J Urol. 2024;212(1):3–10. **2**. Holzbeierlein JM et al. J Urol. 2024 Apr;211(4):533-538. **3**. Internal Aura epidemiology of market size; data on file. **4**. Shalata AT, et al. Cancers (Basel). 2022;14(20):5019. **5**. van Rhijn BWG, et al. Eur Urol. 2009;56(3):430–42.*

***BCG**, Bacillus Calmette-Guérin; **CIS**, carcinoma in situ; **IR**, intermediate risk; **NMIBC**, non-muscle-invasive bladder cancer; **TURBT**, transurethral resection of bladder tumor.*

Figure 12. Distribution of Risk Categories and Associated Treatments of NMIBC

For MIBC, the current standard of care consists of neoadjuvant systemic therapy followed by radical cystectomy or adjuvant systemic treatment post-cystectomy. Despite available therapies, there remains a significant unmet medical need in both NMIBC and MIBC for safe and effective function- and organ-sparing treatment options.

Bel-sar in Bladder Cancer

Our nonclinical in vivo data support bel-sar's dual mechanism of action, demonstrating its potential to induce cytotoxicity and promote long-term antitumor immunity, which may help reduce the risk of recurrence and progression. Additionally, we have shown in preclinical studies that bel-sar exhibits strong synergy with checkpoint inhibitors, which are approved for a subset of patients with NMIBC, further enhancing its therapeutic potential. Given the well-documented sensitivity of bladder cancer to immune activation, we believe this immune response can play a critical role in improving treatment outcomes. We have announced positive data from our Phase 1 clinical trial of bel-sar in patients with NMIBC and have initiated a Phase 1b/2 trial in patients with NMIBC with enrollment expected to begin in the second quarter of 2025. We anticipate initial data from this Phase 1b/2 trial in 2025. We received Fast Track Designation from the FDA for bel-sar for the treatment of NMIBC in June 2022.

We believe the immune response induced by bel-sar could play an even greater role in improving outcomes, given the well-documented immune sensitivity of bladder cancer. The immune sensitivity is further supported by the effectiveness of immune-modulating therapies such as BCG. In nonclinical studies, bel-sar effectively targeted bladder cancer cells in both in vitro and in vivo tumor models. Light activation of bel-sar resulted in selective cytotoxicity, eliminating bladder tumor cells while sparing normal surrounding tissue. This targeted cell killing triggered a pro-immunogenic antitumor response, leading to complete and durable tumor regressions in mouse xenograft models and preventing tumor re-implantation. These preclinical findings highlight bel-sar's potential to generate lasting antitumor immunity and prevent tumor recurrence. Additionally, nonclinical data indicate that bel-sar exhibits strong synergy with checkpoint inhibitors, including those with mechanisms of action similar to already approved and emerging immunotherapies for bladder cancer patients.

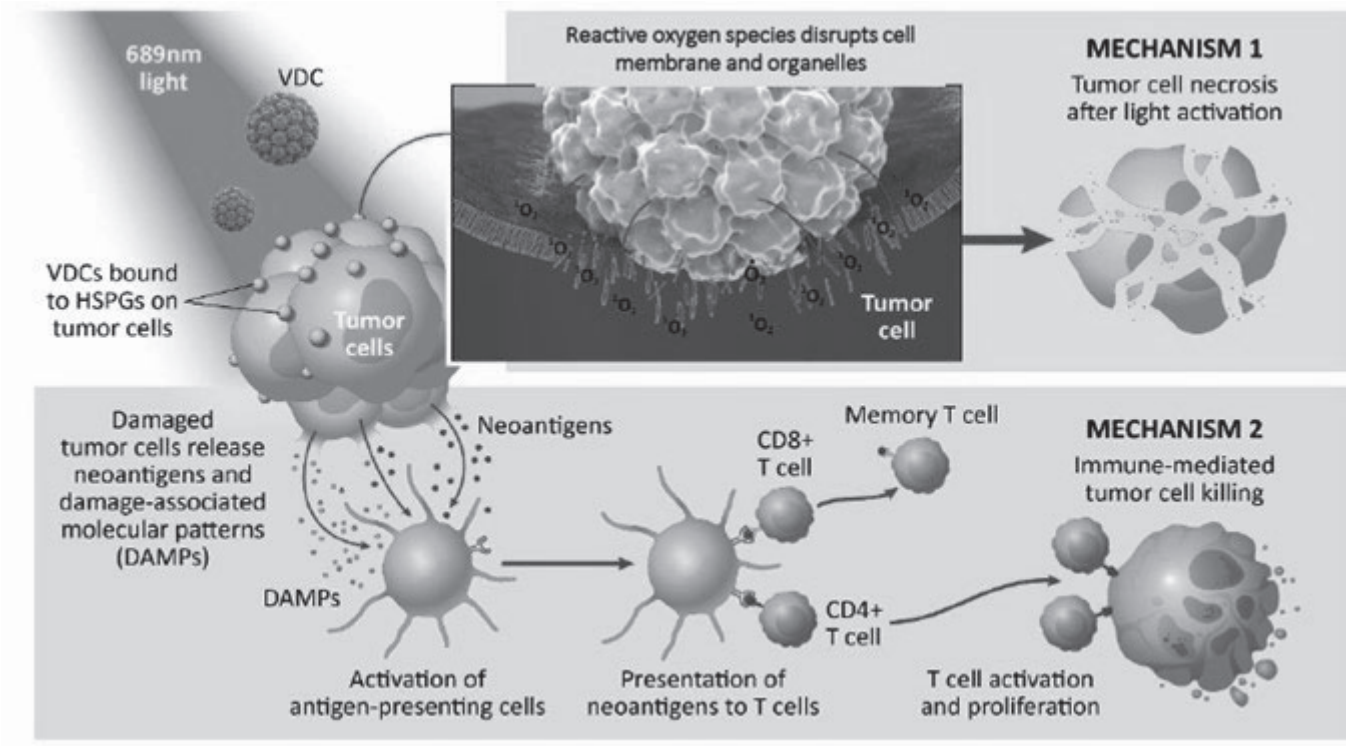


Figure 13. Overview of Bel-sar's Dual Mechanism of Action with Acute Tumor Cell Necrosis and Secondary Antitumor Immunity.

Clinical Development in Bladder Cancer

Phase 1 Window of Opportunity Study: The Phase 1 multi-center, open-label clinical trial was designed to evaluate the safety and feasibility of bel-sar as a monotherapy. The study treatment was administered seven to 12 days before the scheduled TURBT, the standard of care procedure. The participants were followed for safety monitoring over a 56-day period. The trial also evaluated bel-sar's biological activity with histopathological evaluation of tissue samples collected at the time of TURBT (regardless of tumor response) with evaluation of focal necrosis and immune changes in the tumor microenvironment as secondary endpoints. The study design is presented in Figure 14 below.

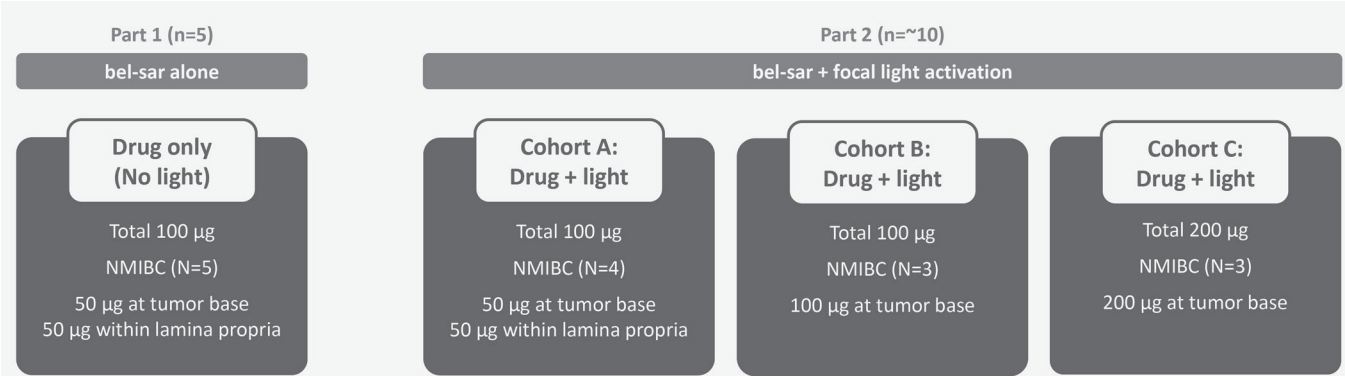


Figure 14. Phase 1 Window of Opportunity Trial to Establish Safety and Tumor Response by Histopathology after Focal Administration.

In October 2024, we announced positive early data from our ongoing Phase 1 clinical trial of bel-sar in patients with NMIBC. Subsequent data was presented in March 2025.

In Part 1 of the study (n=5), patients received a single dose of bel-sar without light activation to evaluate its safety profile. Part 2 of the study (n=11) was designed to evaluate three different cohorts of patients with a confirmed tumor at time of treatment, who received either 100ug or 200ug of bel-sar as a single dose.

Ten of the patients enrolled in part 2 of the study were evaluable for biological activity. Among these ten patients, five had intermediate-risk NMIBC and five had high-risk NMIBC. Eight of these ten patients had a history of recurrent bladder cancer and had undergone multiple TURBTs and adjuvant treatments such as BCG, mitomycin, gemcitabine, cetrelimab and tamoxifen prior to trial enrollment.

Bel-sar was well-tolerated, with less than 10% of patients reporting Grade 1 drug-related adverse events and no reports of Grade 2 or higher drug-related adverse events. No serious adverse events were reported, and no significant differences between the light-activated and non-light activated cohorts were observed.

In Part 2, the ten patients who received bel-sar with light activation showed clinical activity detectable as soon as seven days after a single low dose of bel-sar with light activation. This was demonstrated by histopathological evidence of clinical complete response, necrosis, immune activation, or visual tumor shrinkage observed on cystoscopy. In contrast, no clinical activity was seen in the five patients receiving bel-sar with no light activation. For this analysis, a “clinical complete response” was defined as the absence of tumor cells on histopathologic evaluation, with results as follows:

- **Intermediate-risk NMIBC:** Four out of five patients exhibited a clinical complete response, with no tumor cells detected in histopathological evaluation post-treatment in the target and several non-target bladder tumors and necrosis was observed in three out of five patients. In addition, visual tumor shrinkage was observed in several non-target tumors on cystoscopy.
- **High-risk NMIBC:** One of the patients with high-risk disease (based on BCG failure) had a clinical complete response in the target lesion and in one of three non-target lesions. Visual tumor shrinkage was observed in three of five patients on cystoscopy, while tumor cells were still present on histopathological evaluation.

Additionally, immune activation was noted in all ten patients in both target and non-target bladder tumors. Furthermore, 4 out of 7 patients with multiple tumors (57%) demonstrated a clinical complete response in at least one non-target lesion with infiltration of effector CD8+ and CD4+ T-cells. This data provides evidence of a bladder urothelial field effect with a single low-dose of bel-sar with light activation, potentially indicating a broader immune response and immune surveillance in the bladder beyond the target tumor in these patients.

To evaluate the local immune response after the treatment with bel-sar in the tumor microenvironment, or TME, multiplex immunofluorescence staining for key immune cell types was performed on tumor biopsies. Initial post-treatment results from three patients showed significant infiltration per unit area of cytotoxic effector cells demonstrating early activation of both innate and adaptive immunity (Natural Killer cells, CD4+ and CD8+ T cells). In addition, de novo formation of mature tertiary lymphoid structures, or TLS, post-treatment was observed in two of these three participants. Early TLS were also observed in distant, non-target lesions, suggestive of an immune mediated urothelial field effect. These early observations showing induction of effector immunity and the development of local active immunosurveillance, highlight key features of bel-sar’s dual mechanism of action and the potential to translate into durable treatment responses.

Phase 1b/2 Trial: We are advancing the development of bel-sar in bladder cancer, with an initial focus on intermediate risk and high risk NMIBC patients through a Phase 1b/2 trial. This study is designed to evaluate additional doses and treatment regimens, allowing for the assessment of clinical response at three months and durability of response at up to 12 months. We have initiated this Phase 1b/2 trial in patients with NMIBC with enrollment expected to begin in the second quarter of 2025. We expect initial data from this trial in 2025. Additionally, we are planning further regulatory discussions focused on defining a registrational strategy to guide clinical development. The Phase 1b/2 study design is illustrated in Figure 15 below.

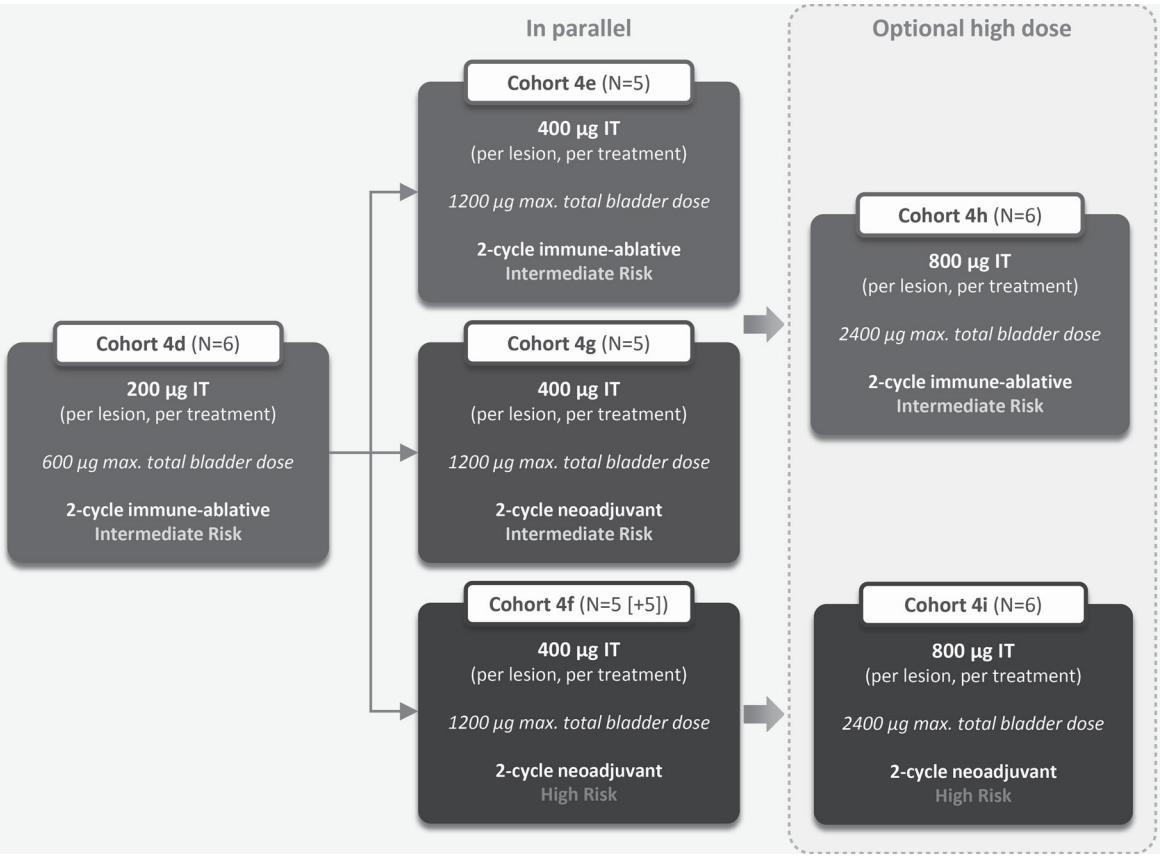


Figure 15. Phase 1b/2 Trial in Intermediate and High Risk NMIBC Patients.

Our goal is to establish bel-sar, if approved, as an immune-based frontline treatment, either as an immune-ablative approach that eliminates the need for TURBT or as a neo-adjuvant multimodal therapy prior to TURBT in NMIBC patients. We also plan to evaluate bel-sar's efficacy in patients with MIBC.

Other mHSPG-Expressing Tumors

Our HPV-derived VLPs have a unique tropism towards cancer cells based on their multivalent binding to modified HSPGs that are specifically found in tumor cells. In vitro, we have observed our VLPs bind to multiple cancer cell lines. In vivo, we have also observed binding using our HPV-derived VLPs using xenografts of human tumor cell lines and allografts of murine tumor cell lines, like lung, ovarian, bladder, melanoma and colon. These results help to corroborate the thesis that multiple tumors appear to consistently express and specifically modify HSPGs. Accordingly, we believe we may be able treat a broad spectrum of solid tumors.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid innovation of new technologies, fierce competition and a strong defense of intellectual property. While we believe that bel-sar's mechanism of action provides the opportunity and competitive advantage for an early intervention approach in cancer indications that do not have existing approved therapies, we may face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others.

We compete in the segments of the pharmaceutical, biotechnology, and companies focusing on developing oncology therapies . These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes. Any product candidates that we successfully develop and commercialize will compete with currently approved therapies and new therapies that may become available in the future from segments of the pharmaceutical, biotechnology and other related markets that pursue oncology therapeutics. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety and convenience of our products.

Our competitors may obtain regulatory approval of their products more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize bel-sar and any future product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products.

Ocular Oncology

Currently we are not aware of any other company that has a drug in clinical development for early intervention in small choroidal melanoma or indeterminate lesions, or for the treatment of metastases to the choroid, which are our first two planned ocular oncology indications. The SoC as a first line treatment for patients is radiotherapy – plaque brachytherapy for melanoma, and external beam radiotherapy for metastases. Verteporfin (Visudyne) is currently used off label in some cases of very small choroidal metastases, but is generally not utilized for melanomas. Transpupillary thermotherapy is generally used as an adjunct to previous radiotherapy for melanoma, but in most cases is no longer used as a standalone treatment modality. Proton beam radiotherapy is sometimes used for choroidal melanoma and metastases to the choroid, and can be associated with similar vision loss as other radiotherapy techniques. It is possible that there may be other companies with compounds in preclinical development but we are not aware of any data that has been published or presented at any conference. Given our stage of development, we believe we are the furthest along in development. Our focus in ocular oncology is the early treatment of the primary cancer in the eye before it metastasizes. Immunocore Holdings PLC, or Immunocore, received FDA approval for KIMMTRAK® (tebentafusp-tebn) injection for metastatic uveal melanoma. Immunocore's drug is indicated for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma and has not been developed to treat early-stage disease in the eye. Ideaya Biosciences is in Phase 2 clinical development to treat metastatic uveal melanoma. In addition, they have an ongoing Phase 2 study with neoadjuvant treatment in patients with large melanomas that are selected to receive enucleation, or neoadjuvant treatment in patients with medium-to-large tumors that are scheduled to receive radiotherapy, with the goal of either preventing enucleation or reducing the dose of radiotherapy. Neither of those drugs and the patient population they target overlap with our development plan and path to approval.

Urologic Oncology

There are multiple companies that have drugs in clinical development for the treatment of NMIBC and MIBC. Pembrolizumab has been approved for the treatment of BCG-unresponsive NMIBC with carcinoma in situ, or CIS, (with or without papillary tumors) for patients who are unfit or unwilling to undergo radical cystectomy. Ferring Pharmaceuticals has obtained FDA approval for ADSTILADRIN for the treatment of adult patients with high-risk BCG-unresponsive NMIBC with CIS, with or without papillary tumors. ImmunityBio, Inc. has an approved drug, Anktiva, in combination with BCG in patients with BCG-unresponsive NMIBC. CG Oncology's cretostimogene grenadenorepvec, or CG0070, has presented data in a global Phase 3 clinical trial as a monotherapy for the treatment of BCG-unresponsive NMIBC and has received breakthrough therapy designation and Fast Track Designation. The same drug is being studied as monotherapy for intermediate risk NMIBC, in combination with KEYTRUDA for BCG-unresponsive NMIBC, and in combination with Nivolumab in MIBC.TAR-200 (from Johnson & Johnson Innovative Medicine) has also received breakthrough therapy designation for BCG-unresponsive NMIBC and is being studied in multiple trials in NMIBC and MIBC. A New Drug Application was initiated for TAR-200 for patients with BCG-unresponsive high-risk NMIBC in 2025. UroGen Pharma Ltd., or UroGen, has a drug, Jelmyto, which is a gel reformulation of mitomycin that is currently approved to treat low grade upper tract urothelial cancer. UroGen has also announced that another drug, UGN-102, has met its primary endpoint in a Phase 3 study for NMIBC, and has submitted a BLA with a Prescription Drug User Fee Act, or PDUFA, date of June 13, 2025 for this drug. In addition, there are several additional immune checkpoint inhibitors, or ICIs, in development as a monotherapy and there are several combination trials with ICIs in an effort to improve efficacy and durability of response. In addition, there are several early-stage treatments in clinical development such as Protara Therapeutics, Inc.'s TARA-002 and Asieris Pharmaceuticals' APL-1202. While there are multiple drugs in development, we believe our competitive advantage as an early intervention approach may help reduce the risk of recurrence and metastasis. In addition, the utilization of bel-sar may be synergistic with other approved therapies like checkpoint inhibitors.

Our License Agreements

NIH Patent License Agreement

In September 2013, we entered into an exclusive patent license agreement, or the NIH License Agreement, with the NIH for certain intellectual property rights, which was amended in September 2015, August 2018 and April 2019. Under the NIH License Agreement, NIH granted us a worldwide, exclusive, sublicensable license to certain patent rights related to VLPs and papilloma pseudovirus for our development and use in combination with our proprietary nanoparticle encapsulation technology both (1) for the treatment, diagnosis and imaging of cancer tumors and metastases as well as their respective pre-cursor dysplasia states and (2) conjugated with light activated drugs for the diagnosis and treatment of cancer tumors and metastases as well as their respective pre-cursor dysplasia states.

Pursuant to the NIH License Agreement, we are required to use commercially reasonable efforts to develop the licensed products using the licensed processes to make the licensed products available to the United States public on reasonable terms, including by adhering to a commercial development plan and meeting specified benchmarks with regards to specified deadlines for regulatory filings, initiation of clinical trials, and gaining regulatory approval for the licensed products.

In consideration of the rights granted under the NIH License Agreement, we paid NIH a one-time upfront payment of $0.1 million. We are required to make low single-digit percentage royalty payments based on specified levels of annual net sales of licensed products subject to certain specified reductions. We are required to make development and regulatory milestone payments up to $0.7 million in the aggregate and sales milestone payments up to $0.6 million in the aggregate. We are also required to pay NIH a mid-single to low teen-digit percentage of any sublicensing revenue we receive. Additionally, our payment obligations to NIH are subject to an annual minimum royalty payment of low five figures. We recognized milestones related to this agreement and related amendments of $0.03 million and $0.2 million for the years ended December 31, 2024 and 2023. In addition to milestones under the agreement, we reimburse NIH for any patent prosecution costs incurred.

The NIH License Agreement will terminate upon the last expiration of the patent rights, or we may terminate the entirety of the agreement upon written notice thereof to NIH. The expiry of the last to expire patent licensed under the agreement is September 2034.

Rakuten License and Supply Agreement

In May 2024, we received notice from LI-COR, Inc., or LI-COR, that as of April 16, 2024, LI-COR assigned, and Rakuten Medical, Inc., or Rakuten, assumed, the 2014 Exclusive Agreement and the 2014 Non-Exclusive Agreement (each described below), each originally entered into by and between us and LI-COR. The 2014 Exclusive Agreement and 2014 Non-Exclusive Agreement were not otherwise modified by this assignment and assumption and remain in effect.

In January 2014, we entered into an Exclusive License and Supply Agreement, or the 2014 Exclusive Agreement, with LI-COR for the license of IRDye 700DX and a related licensed patent (now expired) for the treatment and diagnosis of ocular cancers, ocular pre-cancer and indeterminate lesions in humans, as amended in January 2016, July 2017, April 2018 and April 2019. The 2014 Exclusive Agreement required a one-time upfront license issue fee of $0.1 million and requires aggregate milestone payments of up to $0.2 million upon certain regulatory and development milestones. We are also required to pay Rakuten low-single digit royalties on net sales.

The term of the 2014 Exclusive Agreement expires on a country-by-country basis, until the longer of (i) ten years from the first commercial sale of a licensed product in such country and (ii) the last to expire valid claim in such country.

Clearside License Agreement

In July 2019, we entered into a license agreement, as amended, or the Clearside License Agreement, with Clearside Biomedical, Inc., or Clearside, for the license of Clearside's SC microinjector technology. Upon execution of the Clearside License Agreement, we paid Clearside a one-time upfront payment of $0.1 million. Under the Clearside License Agreement, we are required to pay milestones up to $21.0 million in the aggregate to Clearside upon the achievement of specified regulatory and development milestones, and upon the achievement of certain commercial sales milestones. We are also required to pay low to mid-single digit royalties on net sales. If we sublicense a product for which royalties are payable, then we are required to pay the greater of 20% received or low single digit royalties on net sales.

The Clearside License Agreement expires on a country-by-country basis upon the later of the last to expire patent or ten years from the date of the first commercial sale of a product. The expiry of the last to expire patent licensed under the agreement is August 2034.

We recognized $0 million and $1.0 million in expense related to this agreement and related amendments for the years ended December 31, 2024 and 2023.

Intellectual Property

Our success depends in part on our abilities to (1) obtain and maintain proprietary protection for our lead virus-like drug conjugate product candidate bel-sar, (2) defend and enforce our intellectual property rights, in particular, our patent rights, (3) preserve the confidentiality of our know-how relating to, for example, certain manufacturing steps, material components and characteristics of our formulations, and (4) operate without infringing valid and enforceable intellectual property rights of others. We seek to protect our proprietary position by, among other things, exclusively licensing United States and certain foreign patents and patent applications and filing United States and certain foreign patent applications related to bel-sar, where patent protection is available. We also rely on know-how, continuing technological innovation and confidential information as well as pursue licensing opportunities to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technology, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and others who may have access to proprietary information, under which they are bound to assign to us inventions made during the term of their employment or term of service. We also seek to preserve the integrity and confidentiality of our data by maintaining physical security of our premises and physical and electronic security of our information technology systems.

We cannot be sure that patents will be granted with respect to any patent applications we have licensed or filed or may license or file in the future, and we cannot be sure that any patents we have licensed or which have been granted to us, or patents that may be licensed or granted to us in the future, will not be challenged, invalidated or circumvented or that such patents will be commercially useful in protecting our technology. For more information regarding the risks related to our intellectual property, see "*Risk Factors—Risks related to our intellectual property*."

Our patent portfolio includes a combination of issued patents and pending patent applications that are owned by us, co-owned by us or licensed by us from third parties. As of March 24, 2025, we have an exclusive license (with regard to ocular cancers) and a non-exclusive license (with regard to solid tumors in humans for a specific indication) from Rakuten under one United States patent, which expired December 19, 2023; an exclusive license from NIH under four issued United States patents and three issued foreign patents; an exclusive license from INSERM-TRANSFERT, or Inserm, under three issued United States patents, and six granted foreign patents; and exclusive rights under a Cooperative Research and Development Agreement, or CRADA, with the United States Department of Health and Human Services, or DHHS, as represented by the National Cancer Institute, and Institute, Center, or Division of the NIH, under five issued United States patents, two pending non-provisional United States patent applications, twelve foreign patents, and eleven pending foreign patent applications.

In addition, as of March 24, 2025, we solely own four issued United States patents, one pending non-provisional United States patent application, four pending provisional United States patent applications, two granted foreign patents, and five pending foreign patent applications. We intend to pursue, when possible, additional patent protection, including composition of matter, method of use and process claims related to bel-sar.

Patent Families

We license one patent family from Rakuten and one patent family from the NIH, co-own and license one patent family from Inserm, co-own two patent families with DHHS/NIH and have exclusive rights under a CRADA, and solely own three patent families, all of which are generally directed to the bel-sar product and related methods of use and production.

The first family, licensed from Rakuten, includes one United States patent, which expired December 19, 2023. This patent includes claims directed to (1) fluorescent phthalocyanine dyes and (2) processes for making the dyes (e.g., the IRDye 700DX® dye molecules used in bel-sar).

The second family, licensed from NIH, includes four issued United States patents, one issued European patent, and one issued patent in each of Australia and Canada. Patents in this family include claims directed to (1) methods for inhibiting the proliferation of and/or killing of cancer cells using a therapeutic agent formulated with a papilloma VLP, (2) methods that include administering to a patient (e.g., a patient having a melanoma) a papilloma VLP having a fluorescent dye and exposing the dye to an excitation wavelength of light, and (3) methods for detecting cancer cells using a papilloma VLP having a detectable label. The patents in this patent family have a standard expiration date of May 1, 2028, subject to potential extensions.

The third family, which we co-own with and license from Inserm, includes three issued United States patents, two issued European patents, an issued patent in each of Canada, Hong Kong, India and Japan. Patents in this family include claims directed to (1) a modified papillomavirus (HPV16) L1 protein having reduced immunogenicity relative to wild-type HPV16 L1 protein and an FG loop having the specific amino acid sequence that is present in bel-sar, (2) nanoparticles comprising the modified L1 protein, (3) methods of using the modified L1 protein to deliver therapeutic agents, and/or (4) methods of producing nanoparticles comprising the modified L1 protein. The patents in this patent family have a standard expiration date of July 24, 2029, subject to potential extensions.

The fourth patent family, which we own, includes four issued United States patents. Patents in this family include claims directed to (1) codon-optimized nucleic acids having the particular nucleotide sequence that encodes the modified papillomavirus (HPV16) L1 protein present in bel-sar, (2) methods of producing nanoparticles that include the modified HPV16 L1 protein encoded by the codon-optimized nucleic acids, and (3) methods of using the nanoparticles that include the modified HPV16 L1 protein encoded by the codon-optimized nucleic acids to deliver a therapeutic agent to a patient having cancer. The patents in this patent family have a standard expiration date of February 7, 2033, subject to potential extensions.

The fifth patent family, which we co-own with DHHS/NIH and have exclusive rights under a CRADA, includes five issued United States patents, two issued patents in each of Europe, Australia, and Japan, an issued patent in each of Brazil, Canada, Hong Kong, Republic of Korea and Mexico, one pending patent applications in the United States, and one pending patent application in each of Australia, China and Europe. Patents in this family include claims directed to (1) tumor-targeting papilloma VLPs containing near infrared phthalocyanine dye molecules that become toxic or produce a toxic molecule upon light activation, (2) methods that include delivering the papilloma VLPs to an ocular tumor, and/or (3) methods of producing tumor-targeting bioconjugates that include the papilloma VLPs and near infrared phthalocyanine dye molecules. The patents in this patent family have a standard expiration date of September 18, 2034, subject to potential extensions.

The sixth patent family, which we co-own with DHHS/NIH and have exclusive rights under a CRADA, includes a granted patent in Israel, a pending patent application in each of the United States, Australia, Brazil, Canada, China, Europe, and Israel, and two pending patent applications in Japan. Patent applications in this family include claims to a combination therapy that uses (1) tumor-targeting papillomavirus nanoparticles containing photosensitive molecules and (2) a checkpoint inhibitor. Patents issuing from this family would have a standard expiration date of April 11, 2038, subject to potential extensions.

The seventh patent family, which we own, includes a granted patent in each of Europe and China, and a pending patent application in each of the United States, Australia, Canada, Japan and Republic of Korea with claims directed to an ophthalmic composition that includes a near-isotonic solution of VLP drug conjugates in suspension. Patents issuing from national stage applications based on this international application would have a standard expiration date of March 25, 2040, subject to potential extensions.

The eighth patent family, which we own, includes four pending provisional United States patent applications with claims directed to methods for treating a target tumor while simultaneously inducing a therapeutic field effect. Patents issuing from this family would have a standard expiration date of October 16, 2045, subject to potential extensions.

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing. We, along with our vendors, collaboration partners, contract research organizations, or CROs, and contract manufacturers, will be required to navigate the various preclinical, clinical, manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our product candidate. The process of obtaining regulatory approvals of drugs and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

In the United States, where we have initially focused our product development, the FDA regulates biologics under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and their implementing regulations. Biologics are also subject to other federal, state and local statutes and regulations. Our product candidate, bel-sar, has not been approved by the FDA for marketing in the United States.

The process required by the FDA before any product candidates we develop are approved for therapeutic indications and may be marketed in the United States generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with Good Laboratory Practice, or GLP, requirements;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an Institutional Review Board, or IRB, or independent ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with Good Clinical Practice, or GCP, requirements and other clinical trial-related regulations to establish the safety, purity and potency of the proposed biological product candidate for its intended purpose;

- preparation and submission to the FDA of a BLA after completion of all pivotal trials, accompanied by payment of FDA user fees;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the product will be produced to assess compliance with current Good Manufacturing Practice requirements, or cGMPs, to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency;
- potential FDA audit of the clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the biologic in the United States.

Nonclinical Studies and Clinical Trials for Biologics

Before testing any drug or biologic in humans, the product candidate must undergo rigorous nonclinical testing. Nonclinical studies include laboratory evaluations of chemistry, formulation and stability, as well as in vitro and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of nonclinical studies is subject to federal and state regulations and requirements, including GLP requirements for safety and toxicology studies. The results of the nonclinical studies, together with manufacturing information and analytical data must be submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and it must become effective before clinical trials may begin. The central focus of an IND submission is on the protocol(s) for the initial clinical trial and the general investigational plan. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational product. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Some long-term preclinical testing may continue after the IND is submitted. Accordingly, submission of an IND may or may not result in FDA authorization to begin a trial. A separate protocol submission to an existing IND must also be made for each successive clinical trial conducted in the United States, each of which may begin following a 30 day period unless the FDA issues a clinical hold on the clinical trial.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol to be conducted in the United States, and any subsequent amendments to the protocol, must be submitted to the FDA as an amendment to the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted, or by a central IRB, to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable related to the anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trials to public registries. Information about applicable clinical trials, including clinical trials results, must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website.

A sponsor who wishes to conduct a clinical trial outside of the United States under its IND may need to obtain waivers for certain regulatory compliance requirements such as those requiring IRB review and approval. However, the FDA does not require that all foreign clinical trials be conducted under United States INDs. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials to evaluate therapeutic indications to support BLAs for marketing approval are typically conducted in three sequential phases, which phases may overlap or be conducted in combination.

- Phase 1—Phase 1 clinical trials involve initial introduction of the investigational product into healthy human volunteers or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, evaluate the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- Phase 2—Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3—Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA, although there are known exceptions, particularly for rare diseases.

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 of a BLA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators fifteen days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human participants exposed to the biologic 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 must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the biological 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 and to identify appropriate storage conditions for the product candidate.

Expanded Access

Expanded access, sometimes called "compassionate use," is the use of investigational products outside of intended clinical development to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. FDA regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes for the following expanded access requests: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or treatment IND application. There is no requirement for a company to provide expanded access to its investigational product.

BLA Submission and Review by the FDA

We intend to seek data exclusivity or market exclusivity for our product candidates. Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of a BLA. A BLA is a request for approval to market a new biologic for one or more specified indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the investigational product to the satisfaction of the FDA. FDA approval of a BLA must be obtained before a biologic may be marketed in the United States.

In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate 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. A sponsor who is planning to submit a marketing application for a biological product that includes a new clinically active component, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

The FDA reviews all submitted BLAs before it accepts them for filing, and may request additional information rather than accepting the BLA for filing. The FDA must make a decision on accepting a BLA for filing within 60 days of receipt, and such decision could include a refusal to file by the FDA. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews a BLA to determine, among other things, whether the product is safe, pure and potent 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. Under the goals and polices agreed to by the FDA under the PDUFA, the FDA targets ten months from the filing date in which to complete its initial review of an original BLA and respond to the applicant, and six months from the filing date of an original BLA filed for priority review. The FDA does not always meet its PDUFA goal dates for standard or priority BLAs, and the review process is often extended by FDA requests for additional information or clarification.

Further, under PDUFA, as amended, each BLA must be accompanied by a user fee, and the sponsor of an approved BLA is also subject to an annual program fee. FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions may be available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA may refer an application for a biologic to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation, for example, as to whether the biologic is sufficiently safe and efficacious in a given indication for a given population and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making marketing approval decisions.

Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and

facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP and other requirements and the integrity of the clinical data submitted to the FDA.

The FDA also may require submission of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition for approving the BLA to ensure that the benefits of the product outweigh its risks. The REMS could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk-minimization tools.

After evaluating the BLA 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 is not ready for approval. A Complete Response Letter will usually describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. 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 product with specific prescribing information for specific indications.

Even if the FDA approves a product, depending on the specific risk(s) to be addressed, the FDA 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 product's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing 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.

Expedited Development and Review Programs for Biologics

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs and biologics to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include fast track designation, breakthrough therapy designation, priority review and accelerated approval.

A new biologic is eligible for fast track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. Fast track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

In addition, a new drug or biological product may be eligible for breakthrough therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the biologic, alone or in combination with or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation provides all the features of fast track designation in addition to intensive guidance on an efficient development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with fast track or breakthrough therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including priority review and accelerated approval. A product is eligible for priority review if it is intended to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness. For original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

A product intended to treat serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than on irreversible morbidity or mortality which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

Accelerated approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is 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. Sponsors are also required to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the sponsor fails to conduct such studies in a timely manner and send the necessary updates to the FDA, or if a confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, unless otherwise informed by the FDA, the FDA currently requires, as a condition for accelerated approval, that all advertising and promotional materials that are intended for dissemination or publication within 120 days following marketing approval be submitted to the agency for review during the pre-approval review period, and that after 120 days following marketing approval, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

Fast track designation, breakthrough therapy designation, priority review and accelerated approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval but may expedite the development or review process.

Orphan Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant ODD to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with either a patient population of fewer than 200,000 individuals in the United States, or a patient population greater of than 200,000 individuals in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States of that drug or biologic. ODD must be requested before submitting a BLA. After the FDA grants ODD, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has received ODD and subsequently receives the first FDA approval for a particular clinically active component for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years from the approval of the BLA, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of ODD are tax credits for certain research and a waiver of the BLA application user fee.

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 ODD. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-approval Requirements for Biologics

Drugs and biologics 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, reporting of adverse experiences with the product, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as “off-label use”) and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe approved products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, including not only by company employees but also by agents of the company or those speaking on the company’s behalf, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties, including liabilities under the False Claims Act where products carry reimbursement under federal health care programs. Promotional materials for approved biologics must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement, which may require the development of additional data or preclinical studies and clinical trials.

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

In addition, drug and biologics manufacturers and their subcontractors involved in the manufacture and distribution of approved products, including those supplying products, ingredients, and components of such products, are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our contract manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. 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 the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution. There is also a continuing, annual program fee for any marketed product. The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things:

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

From time to time, legislation is drafted, introduced, passed in Congress and signed into law that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations, guidance, and policies are often revised or reinterpreted by the agency in ways that may significantly affect the manner in which pharmaceutical products are regulated and marketed.

Biosimilars and Exclusivity

The Patent Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods for all formulations, dosage forms, and indications of the biologic. This six-month exclusivity, which runs from the end of other exclusivity protection, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and regulatory interpretation of the BPCIA remain subject to significant uncertainty.

Regulation of Combination Products in the United States

Certain products may be comprised of components, such as biologic components and device components, that would normally be regulated under different types of regulatory authorities, and by different centers at the FDA. These products are known as combination products. Specifically, under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;
- a drug, or device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration or significant change in dose; or
- any investigational drug, device or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device or biological product where both are required to achieve the intended use, indication or effect.

Under the FDCA and its implementing regulations, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The designation of a lead center generally eliminates the need to receive approvals from more than one FDA component for combination products, although it does not preclude consultations by the lead center with other components of FDA. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a biologic-device combination product is attributable to the biologic product, the FDA center responsible for premarket review of the biologic product would have primary jurisdiction for the combination product. The FDA has also established an Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office is responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

A combination product with a biologic primary mode of action generally would be reviewed and approved pursuant to FDA's biologic approval processes. In reviewing the BLA application for such a product, however, FDA reviewers in the biologics center could consult with their counterparts in the device center to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA's regulations, combination products are subject to applicable cGMP requirements for drugs, biologics and devices, including the Quality System regulations applicable to medical devices.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities of product candidates following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, which may include the Centers for Medicare & Medicaid Services, or CMS, other divisions of DHHS, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

Coverage and Reimbursement

In the United States 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. Our ability to successfully commercialize our product candidates 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. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within the DHHS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

Factors payors consider in determining reimbursement are based on whether the 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.

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

Health Care Laws and Regulations

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business that may constrain the financial arrangements and relationships through which we research, as well as sell, market and distribute any products for which we obtain marketing authorization. Such laws include, without limitation:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward 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 statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil monetary penalties;
- the federal false claims and civil monetary penalties laws, including the False Claims Act, prohibit individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program, or 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. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal physician payment transparency requirements, sometimes referred to as the “Sunshine Act” under the ACA require certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or the Children’s Health Insurance Program to report to DHHS information related to payments and other transfers of value made to physician (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed health care practitioners and teaching hospitals; as well as the ownership and investment interests of such physicians and their immediate family members;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, as well as their covered subcontractors, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- 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 may be broader in scope than their federal equivalents; some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures; and
- state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts, and analogous foreign laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations and exclusion from participation in federal and state healthcare programs, and responsible individuals may be subject to imprisonment.

Health Care Reform & Legislative Updates

Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs, and those methods are not always specifically adapted for new technologies such as gene therapy and therapies addressing rare diseases such as those we are developing. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in 2010, the ACA was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress that include aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which remain in effect through 2031. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers were further reduced starting on January 1, 2025; however, legislation has been introduced (but not passed) in the U.S. Congress that would, if enacted, reverse these payment reductions. In addition to provider payment cuts under Medicare, the American Rescue Plan Act of 2021 also eliminated the statutory Medicaid drug rebate cap, previously set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. These laws and regulations may result in additional restrictions in Medicare and other healthcare funding available for healthcare providers and may otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

The Inflation Reduction Act of 2022, or IRA, includes several provisions that may impact our business to varying degrees. This includes provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries to $2,000 starting in 2025; impose new manufacturer financial liability on certain drugs under Medicare Part D; and require companies to pay rebates to Medicare for certain drugs whose prices have increased faster than inflation. The IRA also allows DHHS to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition. For a biological product to be selected for participation in the Medicare drug price negotiation program, at least 11 years must have elapsed since the biological product was licensed by FDA for its first indication. FDA approval of future indications or changes to a formulation of a product will not delay or halt this timing. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that rare disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation that challenges the constitutionality of the IRA's drug price negotiation program provisions. The outcome of this litigation as well as the effects of the IRA on our business and the healthcare industry in general are not yet known.

Regulation in the EU

Similar to the United States, the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls. In April 2014, the EU adopted a Clinical Trials Regulation (EU) No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022. The Clinical Trials Regulation is directly applicable in all EU Member States (and so does not require national implementing legislation in each Member State), and aims at simplifying and streamlining the approval of clinical studies in the EU. For example, a single application is now made through the Clinical Trials Information System, or CTIS, for clinical trial authorization in up to 30 European Economic Area (i.e. the EU Member States plus Iceland, Liechtenstein and Norway), or EEA, countries at the same time and with a single set of documentation.

The assessment of applications for clinical trials is divided into two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States Concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State Concerned. The role of the relevant ethics committees in the assessment procedure continues to be governed by the national law of the Member States Concerned, however overall related timelines are defined by the Clinical Trials Regulation. The Clinical Trials Regulation also provides for simplified reporting procedures for clinical trial sponsors.

We have an SME status with the EMA as a small and medium-sized enterprise. This enables us to continue to have access to administrative, regulatory and financial support, including fee reductions for scientific advice and regulatory procedures.

Drug Review and Approval

In the EU, medicinal products can only be commercialized after obtaining a marketing authorization, or MA. There are two types of MAs.

- The centralized MA is issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and is valid throughout the entire territory of the EEA. The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced therapy medicinal products (gene-therapy, somatic cell-therapy or tissue-engineered medicines) and medicinal 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. We therefore consider our product candidates would fall within the mandatory scope of the centralized procedure. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the centralized procedure, the maximum timeframe for the evaluation of an MA application by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of an MA application considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion

together with supporting documentation to the European Commission, who makes the final decision to grant an MA, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MA application under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

- National MAs, which are issued by the competent authorities of the Member States of the EEA 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 EEA, this national MA can be recognized in other Member States 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 EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

As part of its marketing authorization process, the European Commission may grant MAs for certain categories of medicinal products on the basis of less complete data than is normally required, where the benefit of immediate availability of the medicine outweighs the risk inherent in the fact that additional data are still required or in the interests of public health. In such cases, it is possible for the CHMP to recommend the granting of an MA, subject to certain specific obligations to be reviewed annually, which is referred to as a conditional MA. This may apply to medicinal products for human use that fall under the jurisdiction of the EMA, including those that are aimed at the treatment, the prevention, or the medical diagnosis of seriously debilitating or life-threatening diseases.

Regulation (EC) No 1901/2006 provides that prior to obtaining an MA in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved pediatric investigation plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted: (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

Data and Marketing Exclusivity

In the EU, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity upon the grant of an MA and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA, for a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or biosimilar MA application can be submitted and authorized, and the innovator's data may be referenced, but no generic or biosimilar product can be placed on the EU market until the expiration of the market exclusivity period. The overall ten-year period will 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 currently approved therapies. Even if an innovative medicinal product gains the prescribed period of data exclusivity, another company may 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 Designation and Exclusivity

In the EU, the European Commission grants an orphan designation in respect of a product if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition and either (i) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (ii) without incentives, it is unlikely that the marketing of the medicine would generate sufficient return in the EU to justify the necessary investment in its development. In each case, there must be no satisfactory method of diagnosis, prevention or treatment of the condition which has been authorized (or, if such a method exists, the product in question would be of significant benefit to those affected by the applicable condition).

In the EU, orphan designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following the grant of an MA for the orphan product. This period may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. During the period of market exclusivity, an MA may only be granted to a "similar medicinal product" for the same therapeutic indication as an authorized orphan product if: (i) a second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the MA holder for the authorized product consents to a second medicinal product application; or (iii) the MA holder for the authorized product cannot supply enough orphan medicinal product. 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. Orphan designation must be requested before submitting an application for an MA. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the EU Member States. The holder of an MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MA applications must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conducting of additional clinical trials or post-authorization safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

Much like the Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to induce or reward improper performance generally is usually governed by the national anti-bribery laws of EU Member States, and the Bribery Act 2010 in the UK. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the EU.

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

Regulation of Combination Products

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. EU guidance has been published to help manufacturers select the right regulatory framework. In the case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (i.e. where the medicinal product and the device do not form a single product which is intended exclusively for use in the given combination and which is not reusable), the medicinal product is regulated in accordance with the aforementioned rules while the device part is regulated as a medical device and will have to comply with all the requirements set forth by Regulation 2017/745, or the Medical Devices Regulation (which became applicable on May 26, 2021 and repealed the EU Council Directive 93/42/EEC, or the Medical Devices Directive). There is a transition period until December 31, 2028 at the latest during which certificates issued under the Medical Devices Directive remain valid, to ensure that there is sufficient time for devices to be re-certified subject to certain conditions (including compliance with requirements for market surveillance and quality management systems under the Medical Devices Regulation, and engagement with notified bodies).

The characteristics of non-integral devices used for the administration of medicinal products may impact the quality, safety and efficacy profile of the medicinal products. To the extent that administration devices are co-packaged with the medicinal product or, in exceptional cases, where the use of a specific type of administration device is specifically provided for in the product information of the medicinal product, additional information may need to be provided in the MA application for the medicinal product on the characteristics of the medical device(s) that may impact on the quality, safety and/or efficacy of the medicinal product. The requirements regarding quality aspects for integral drug-device combination products, including devices that are co-packaged with medicinal products, are outlined in an EMA guideline which came into effect on January 1, 2022.

For a medical device to obtain a CE mark under the Medical Devices Regulation, the device must meet the relevant general safety and performance requirements laid down in Annex I of the Medical Devices Regulation. The most fundamental requirement is that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the performances intended by the manufacturer and be designed, manufactured, and packaged in a suitable manner. To demonstrate compliance with the general safety and performance requirements laid down in Annex I to the Medical Devices Regulation, medical device manufacturers must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. Conformity assessment procedures require an assessment of available clinical evidence, literature data for the product, and post-market experience in respect of similar products already marketed. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can self-declare the conformity of its products with the general safety and performance requirements (except for any parts which relate to sterility or metrology), a conformity assessment procedure requires the intervention of a notified body. Notified bodies are independent organizations designated by EU Member States to assess the conformity of devices before being placed on the market. If satisfied that the relevant product conforms to the relevant general safety and performance requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE mark to the device, which allows the device to be placed on the market throughout the EU.

As a general rule, demonstration of conformity of medical devices and their manufacturers with the general safety and performance requirements must be based, among other things, on the evaluation of clinical data supporting the safety and performance of the products during normal conditions of use. Specifically, a manufacturer must demonstrate that the device achieves its intended performance during normal conditions of use, that the known and foreseeable risks, and any adverse events, are minimized and acceptable when weighed against the benefits of its intended performance, and that any claims made about the performance and safety of the device are supported by suitable evidence.

All of the aforementioned EU rules are generally applicable in the EEA.

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 EU 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 EU law.

Pricing and Reimbursement

In the EU, pricing and reimbursement schemes vary widely from country to country. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so-called health technology assessments) in order to obtain reimbursement or pricing approval.

The EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many EU Member States 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 EU Member States. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States and parallel trade (arbitrage between low-priced and high-priced Member States) can further reduce prices. Special pricing and reimbursement rules may apply to orphan medicinal products. Inclusion of orphan medicinal products in reimbursement systems tend to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any medicinal product. Acceptance of any medicinal product for reimbursement may come with cost, use and often volume restrictions, which again can vary by country. In addition, results-based rules of reimbursement may apply.

European Data Collection

The collection, use, or other processing of personal data, including clinical trial data, regarding individuals in the EEA is governed by the EU General Data Protection Regulation, or GDPR, and similar processing of personal data regarding individuals in the UK, is governed by the UK General Data Protection Regulation, or UK GDPR, and the UK Data Protection Act 2018. In this document, "GDPR" refers to both the EU GDPR and the UK GDPR, unless specified otherwise. The GDPR applies to any company established in the EEA/UK and to companies established outside the EEA/UK that process personal data in connection with the offering of goods or services to, or the monitoring of the behavior of data subjects in the EEA/UK. The GDPR enhances data protection obligations for companies processing personal data, including stringent requirements relating to ensuring an appropriate legal basis applies to the processing of personal data, expanded disclosures about how personal data is used, requirements to conduct data protection impact assessments for "high risk" processing, limitations on retention of personal data, special provisions for "sensitive information" including health and genetic information of data subjects, mandatory data breach notification and "privacy by design" requirements and direct obligations on service providers acting as processors. The GDPR also imposes strict rules and restrictions on the transfer of personal data outside of the EEA/UK to countries that do not ensure an adequate level of protection, like the United States in certain circumstances. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA Member States/UK may result in fines up to 20 million euros (£17.5 million under the UK GDPR) or 4% of a company's global annual revenues for the preceding financial year, whichever is higher. 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 infringement of the GDPR. Following the UK's decision to leave the EU on January 31, 2020, the UK's data protection regime is independent from but aligned to the EU's data protection regime. However, the UK government is planning to reform its data protection law with the Data (Use and Access) Bill, which it introduced to Parliament in October 2024. These potential future changes to UK data protection laws may alter the similarities between the UK and EEA data protection regime.

Regulation in the UK

Brexit and the Regulatory Framework in the UK

The UK formally left the EU on January 31, 2020.

As a result of the Northern Ireland Protocol, following Brexit, the EMA remained responsible for approving novel medicines for supply in Northern Ireland under the EU centralized procedure, and a separate authorization was required to supply the same medicine in Great Britain (England, Wales and Scotland). On February 27, 2023, the UK government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". The Windsor Framework was approved by the EU-UL Joint Committee on March 24, 2023, and the medicines aspects of the Windsor Framework have applied since January 1, 2025. This new framework fundamentally changes the previous system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA is now responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA no longer has any role in approving medicinal products destined for Northern Ireland under the EU centralized procedure. A single UK-wide MA will be granted by the MHRA for all novel medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. In addition, the new arrangements require all medicines placed on the UK market to be labeled "UK only", indicating they are not for sale in the EU. However, although a separate authorization is now required to market medicinal products in the UK, under an international recognition procedure which was put in place by the MHRA on January 1, 2024, the MHRA may take into account decisions on the approval of a MA from the EMA (and certain other regulators) when considering an application for a UK marketing authorization.

U.S. Data Privacy and Security Laws and Regulations

We collect, store, transmit and process sensitive and confidential data and information, including health information, and personal data. As we seek to expand our business, we are, and will increasingly become, subject to numerous state, federal and foreign laws, regulations, rules and government and industry standards relating to the collection, use, retention, security, disclosure, transfer and other processing of sensitive and personal information in the jurisdictions in which we operate. The regulatory framework for data privacy, data security and data transfers worldwide is rapidly evolving, and there has been an increasing focus on privacy and data protection issues.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of health information. HIPAA, as amended by HITECH, and their implementing regulations impose obligations on covered entities, such as health plans, healthcare clearinghouses and certain healthcare providers, as well as business associates that provide services involving the use or disclosure of personal health information to or on behalf of covered entities. These obligations, such as mandatory contractual terms, relate to safeguarding the privacy and security of protected health information. Many states also have laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA. In addition, many states and foreign countries in which we operate have laws that protect the privacy and security of sensitive and personal information. Certain of these laws may be more stringent or broader in scope, or offer greater individual rights, with respect to sensitive and personal information than federal, international or other state laws, and such laws may differ from each other.

Human Capital

As of February 28, 2025, we had 106 full-time employees and three part-time employees, of which 30 have M.D. (or its equivalent), Ph.D. or J.D. degrees. Within our workforce, 87 employees are engaged in research and development and 22 are engaged in business development, finance, legal and general management and administration. 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 stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Available Information

Our Internet address is www.aurabiosciences.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Exchange Act are available through the “Investors & Media” 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, or 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. We have included our website address in this Annual Report solely as an inactive textual reference. Our filings with the SEC may be accessed through the SEC’s website 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.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully read and consider all of the risks described below, as well as the other information in this Annual Report on Form 10-K, including our consolidated financial statements and related notes thereto and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations". The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. Unless otherwise indicated, references to our business being harmed in these risk factors will include harm to our business, reputation, financial condition, results of operations and future prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock.

Risks Related to Our Financial Position, and Additional Capital Needs

We have incurred significant net losses since our inception and anticipate that we will continue to incur losses for the foreseeable future.

Investment in biotechnology product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to gain regulatory approval or fail to become commercially viable. Our net losses were $86.9 million and $76.4 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $374.2 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect our research and development expenses to increase significantly as we continue clinical development for bel-sar and continue to discover and develop additional product candidates. In addition, if we obtain regulatory approval for our product candidates, we will incur significant sales, marketing and manufacturing expenses. We incur costs, and will incur additional costs, associated with operating as a public company. As a result, we expect to continue to incur significant 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. To date, we have not generated any revenue from any product sales. Our ability to become profitable depends upon our ability to generate revenue. We have no products approved for commercial sale and, therefore, have never generated any revenue from product sales, and we do not expect to in the foreseeable future. Further, we do not anticipate generating any revenue from product sales until after we have received marketing approval for the commercial sale of a product candidate, if ever. Our ability to generate revenue and achieve profitability depends significantly on our success in achieving a number of goals, including:

- initiating and completing research regarding, and preclinical and clinical development of, bel-sar in primary choroidal melanoma and additional oncology indications, including metastases to the choroid and bladder cancer as well as any other research programs from our VDC technology platform and any future product candidates;
- obtaining marketing approval for bel-sar and any future product candidates for which we complete clinical trials;
- transferring our manufacturing process to, and developing and maintaining it with, a CDMO for bel-sar and any future product candidates, including establishing and maintaining commercially viable supply and manufacturing relationships with third parties;
- launching and commercializing bel-sar and any future product candidates for which we obtain marketing approvals, either directly or with a collaborator or distributor;
- obtaining market acceptance of bel-sar and any future product candidates as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and developing new product candidates from our VDC technology platform;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- obtaining, maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

Even if bel-sar or any future product candidates that we develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any such product candidate. Our expenses could increase beyond expectations if we are required by the FDA or comparable foreign regulatory authorities to change our manufacturing processes or assays, or to perform clinical, nonclinical, or other types of studies in addition to those that we currently anticipate.

If we are successful in obtaining regulatory approvals to market bel-sar or any future product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain marketing approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, the labels for bel-sar and any future product candidates contain significant safety warnings, regulatory authorities impose burdensome or restrictive distribution requirements, or the reasonably accepted patient population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. If we are not able to generate revenue from the sale of any approved products, we could be prevented from or significantly delayed in achieving profitability.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, obtain product approvals, diversify our offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

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

Since our inception, we have used substantial amounts of cash to fund our operations, and our expenses will increase substantially in the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development of, initiate and complete clinical trials of, and seek marketing approval for bel-sar. Identifying and developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Even if one or more of bel-sar or any future product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing and distribution activities. Our expenses could increase beyond expectations if we are required by the FDA, the EMA or other regulatory agencies to perform clinical trials or nonclinical studies in addition to those that we are currently conducting or anticipate. Other unanticipated costs may also arise. Because the design and outcome of our current and planned clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of bel-sar or any future product candidates that we develop. We also expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to continue our operations.

Based on our current operating plan, we believe that our existing cash and cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditures into the second half of 2026. Advancing the development of bel-sar and other research programs will require a significant amount of capital. Our existing cash and cash equivalents will not be sufficient to fund bel-sar through regulatory approval, and we anticipate needing to raise additional capital to complete the development and commercialization of bel-sar. Our estimate as to how long we expect our existing cash and cash equivalents to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

We will be required to obtain further funding through public or private equity financings, debt financings, collaborative agreements, licensing arrangements or other sources of financing, which may dilute our stockholders or restrict our operating activities. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize product candidates. Disruptions in financial markets due to unfavorable global economic conditions and inflationary pressures may make equity and debt financings more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. To the extent that we raise additional capital through the sale of equity or convertible preferred stock, each investor's ownership interests will be diluted, and the terms may include liquidation or other preferences that adversely affect each investor's rights as a stockholder. Debt financing may result in imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect our business. If we raise additional funds through upfront payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to our product candidates or grant licenses on terms that are not favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to commercialize bel-sar if and when approved and develop our product candidates.

Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our clinical trials, research and development programs, future commercialization efforts or other operations.

Recent volatility in capital markets may affect our ability to access new capital through sales of shares of our common stock or issuance of indebtedness.

Our operations consume substantial amounts of cash, and we intend to continue to make significant investments to support our business growth, respond to business challenges or opportunities, develop new solutions, retain or expand our current levels of personnel, improve our existing solutions, enhance our operating infrastructure, and potentially acquire complementary businesses and technologies. Our future capital requirements may be significantly different from our current estimates and will depend on many factors, including the need to:

- finance unanticipated working capital requirements;
- develop or enhance our technological infrastructure and our existing solutions;
- pursue acquisitions or other strategic relationships; and
- respond to competitive pressures.

Accordingly, we may need to pursue equity or debt financings to meet our capital needs. With uncertainty in the capital markets and other factors, such financing may not be available on terms favorable to us or at all. If we raise additional funds through further issuances of equity or convertible debt securities, our existing stockholders could suffer significant dilution, and any new equity securities we issue could have rights, preferences, and privileges superior to those of holders of our common stock. Any debt financing secured by us in the future could involve additional restrictive covenants relating to our capital-raising activities and other financial and operational matters, which may make it more difficult for us to obtain additional capital and to pursue business opportunities, including potential acquisitions. If we are unable to obtain adequate financing or financing on terms satisfactory to us, we could face significant limitations on our ability to invest in our operations and otherwise suffer harm to our businesses.

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

We do not have any committed external source of funds or other support for our development efforts and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until we can generate sufficient product or royalty revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, existing stockholder ownership interest will be diluted. In addition, any debt financing may subject us to fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also could be required to seek commercial or development partners for our lead products or any future product candidate at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves.

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

We rely on our team's expertise in drug discovery, translational research and patient-driven precision medicine to develop our product candidates. Our business depends significantly on the success of this engine and the development and commercialization of the product candidates that we discover with this engine. We have no products approved for commercial sale and do not anticipate generating any revenue from product sales in the near term, if ever. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives, including:

- successful and timely completion of preclinical and clinical development of bel-sar in small choroidal melanoma and indeterminate lesions and additional oncology indications, including but not limited to metastases to the choroid and bladder cancer, other research programs from our VDC technology platform, and any other future programs;
- establishing and maintaining relationships with CROs and clinical sites for the clinical development of bel-sar, other research programs from our VDC technology platform, and any other future programs;
- timely receipt of marketing approvals from applicable regulatory authorities for any product candidates for which we successfully complete clinical development;
- transferring our manufacturing process to, and developing or maintaining it with, a CDMO including obtaining finished products that are appropriately packaged for sale;
- establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for our product candidates, if approved;
- successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether in-house or with one or more collaborators;
- a continued acceptable safety profile following any marketing approval of our product candidates;
- commercial acceptance of our product candidates by patients, the medical community and third-party payors;
- satisfying any required post-marketing approval commitments to applicable regulatory authorities;
- identifying, assessing and developing new product candidates from our VDC technology platform;
- obtaining, maintaining and expanding patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- defending against third-party interference or infringement claims, if any;

- entering into, on favorable terms, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- obtaining coverage and adequate reimbursement by third-party payors for our product candidates;
- addressing any competing therapies and technological and market developments; and
- attracting, hiring and retaining qualified personnel.

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

Risks Related to the Discovery and Development of our Product Candidates

We are heavily dependent on the success of bel-sar, our only product candidate to date.

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures over the next several years will be devoted to development of bel-sar in multiple oncology indications, which is currently our only product candidate. Accordingly, our business currently depends heavily on the successful development, regulatory approval, and commercialization of bel-sar. We can provide no assurance that bel-sar will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of bel-sar or if bel-sar does not receive regulatory approval or fails to achieve significant market acceptance, we would be delayed by many years in our ability to achieve profitability, if ever.

The research, testing, manufacturing, safety, efficacy, recordkeeping, labeling, approval, licensure, sale, marketing, advertising, promotion and distribution of bel-sar is, and will remain, subject to comprehensive regulation by the FDA and foreign regulatory authorities. Failure to obtain regulatory approval for bel-sar in the United States, Europe and other major markets around the world will prevent us from commercializing and marketing bel-sar in such jurisdictions.

Even if we were to successfully obtain approval from the FDA and foreign regulatory authorities for bel-sar, any approval might contain significant limitations related to use, including limitations on the stage or type of cancer bel-sar is approved to treat, as well as restrictions for specified age groups, warnings, precautions or contraindications, or requirement for a risk evaluation and mitigation strategy, or REMS. Any such limitations or restrictions could similarly impact any supplemental marketing approvals we may obtain for bel-sar. Furthermore, even if we obtain regulatory approval for bel-sar, we will still need to develop a commercial infrastructure or develop relationships with collaborators to commercialize, establish a commercially viable pricing structure and obtain coverage and adequate reimbursement from third-party payors, including government healthcare programs. If we, or any future collaborators, are unable to successfully commercialize bel-sar, we may not be able to generate sufficient revenue to continue our business.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for bel-sar, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Before we can commercialize any of our product candidates, we must obtain marketing approval. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction and it is possible that none of our product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. We utilize third-party CROs and/or regulatory consultants to assist us in the regulatory approval process globally and expect to continue to do so in the future. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities and clinical sites by the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining regulatory approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted IND, Premarket Approval, or PMA, or biologics license application, or BLA, or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Because the activity of bel-sar in ocular melanoma requires a drug delivery device and activation by a laser, the regulatory complexity of the product candidate is greater than for products that do not utilize a device, which creates uncertainties in the requirements for regulatory approval. Our 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 with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve our manufacturing processes or facilities or those 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 drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process, as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

Our novel VDC product candidates are based on a technology that we are in the process of developing. We expect the novel nature of such product candidates to create further challenges in obtaining regulatory approval. As a result, our ability to develop product candidates and obtain regulatory approval may be significantly impacted.

The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop based on the completed clinical trials. Additionally, the conduct of Advisory Committee meetings may be disrupted or delayed and the impact that may have on the overall timing of regulatory approvals is uncertain.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

We have initiated but not yet completed a pivotal clinical trial nor have we commercialized any pharmaceutical products, which may make it difficult to evaluate our future prospects.

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA, the EMA, or other regulatory agencies to market bel-sar or any future product candidate. Carrying out later-stage clinical trials is a complicated process. Our operations to date have been limited to financing and staffing our company, developing our technology and conducting preclinical research and Phase 1 and Phase 2 clinical trials for our product candidates, primarily related to our bel-sar program in small choroidal melanoma and indeterminate lesions. Although we have an ongoing global Phase 3 trial in small choroidal melanomas and indeterminate lesions, we have not yet demonstrated an ability to successfully complete pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. In order to complete later stage or pivotal trials, we are expanding our clinical operations, CMC and regulatory capabilities, and we may be unable to recruit and train qualified personnel or sign a contract with a global clinical research organization to conduct such trials on our behalf. Consequently, we may be unable to successfully and efficiently design, execute and complete necessary clinical trials in a way that leads to approval of bel-sar or future product candidates. We may require more time to enroll patients and incur greater costs than our competitors and may not succeed in obtaining global regulatory approvals of product candidates that we develop. Furthermore, we may conduct a pivotal trial based on an adaptive design, which could increase the time spent on or costs associated with this trial. We have transferred our manufacturing process to our intended external CDMO commercial manufacturer, but transfers to additional CDMOs may occur in the future. Further, some modifications to our manufacturing process may be needed to ensure manufacturability and ability to scale-up the process to commercial batch sizes and to meet worldwide regulatory standards for commercial manufacture. We intend to perform an analytical comparability assessment between the current clinical process and the intended commercial process, however, if this analytical process comparability assessment is unsuccessful, clinical comparability or other studies may be required, which may result in delayed regulatory approval. We do not anticipate a change in formulation. However, failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by clinical-stage biopharmaceutical companies such as ours. Any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

If we fail to develop additional product candidates, or obtain additional indications of our first product candidate, our commercial opportunity could be limited.

We expect to focus our resources on the development of bel-sar in the near term. Developing, obtaining marketing approval for, and commercializing any future product candidates will require substantial additional funding and will be subject to the risks of failure inherent in drug product development. We cannot assure you that we will be able to successfully advance any future product candidates through the development process.

Even if we obtain approval from the FDA or comparable foreign regulatory authorities to market any future product candidates for any indication, we cannot assure you that any such product candidates will be successfully commercialized, widely accepted in the marketplace, or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize additional product candidates, our commercial opportunity may be limited and our business, financial condition, results of operations, stock price and prospects may be materially harmed.

Bel-sar is a biologic that requires the use of multiple medical devices, which may result in additional regulatory risks.

Bel-sar is a novel biologic for which the intended use in ocular oncology requires delivery to the suprachoroidal space, or SCS, and activation by a laser. For ocular oncology indications, we use Clearside Biomedical Inc.'s SCS Microinjector®, or the SCS Microinjector, to deliver bel-sar into the SCS. In the United States, we plan to submit a single BLA for the review and approval of this combination of bel-sar with the SCS Microinjector and the laser(s) in our initial target indication of small choroidal melanoma and indeterminate lesions, but subsequent indications and delivery systems may require different or additional applications for marketing authorization. The SCS Microinjector was approved by FDA in October 2021 as a constituent of the drug/device combination product XIPERE® (triamcinolone acetonide injectable suspension). There may be additional regulatory risks for biologic-device combination products. We may experience delays in obtaining regulatory approval of bel-sar given the increased complexity of the review process when approval of the product and a medical device is sought under a single BLA. In the United States, each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a drug, biologic or device. Devices are subject to the FDA design control device requirements which comprise among other things, design verification, design validation, and testing to assess performance, cleaning, and robustness. In the European Union, or EU, medical devices must be authorized under the EU's Medical Devices Regulation, which requires compliance with the general safety and performance requirements set forth in such legislation. Delays in or failure of the studies conducted by us, or failure of our company, our collaborators, if any, or our third-party providers or suppliers to maintain compliance with regulatory requirements could result in increased development costs, delays in or failure to obtain regulatory approval, and associated delays in bel-sar reaching the market.

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

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, may be altered along the way in an effort to optimize processes and results. Such changes to a product candidate carry the risk that they will not achieve the intended objectives of optimizing the performance of the candidate. Any such changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay or prevent completion of clinical trials, require conducting bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay or prevent approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities, or as needed to provide appropriate statistical power for a given trial. For example, the EMA required additional testing to support drug substance characterization which led to a later than anticipated authorization to commence enrolling patients in our Phase 3 clinical trial under the EU Clinical Trial Regulation process.

In addition, our competitors may in the future commence clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may choose instead to enroll in clinical trials of our competitors. Additionally, the process of finding patients may prove costly. We also may not be able to identify, recruit or enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidates under study, the availability and efficacy of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective

patients, and the patient referral practices of physicians. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. Our lead indication of early-stage choroidal melanoma is a rare disease and as such clinical trial recruitment estimates may be inaccurate and such recruitment may take longer than expected.

Patient enrollment may be affected by other factors, including:

- the severity of the disease under investigation;
- clinicians' and patients' awareness of, and perceptions as to the potential advantages and risks of bel-sar in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- the efforts to obtain and maintain patient consents and facilitate timely enrollment in clinical trials;
- the ability to monitor patients adequately during and after treatment;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion;
- competing studies or trials with similar eligibility criteria;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- reporting of the preliminary results of any of our clinical trials; and
- factors we may not be able to control that may limit patients, principal investigators or staff or clinical site availability.

We are conducting a clinical trial outside the United States, and we may in the future conduct additional clinical trials for current or future product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are currently conducting a Phase 3 clinical trial and have, or anticipate to have, sites in the United States as well as in some or all of the following countries, among others: Ireland, the UK, Canada, Australia, Austria, Italy, Greece, South Korea, Israel, Germany, France, Spain, Denmark, Sweden, Belgium, Finland, and the Czech Republic. We also may in the future choose to conduct one or more additional clinical trials outside the United States, including in Europe. The acceptance of data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and the U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to Good Clinical Practices, or GCP, regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

Even if we receive marketing approval for our current or future product candidates in the United States, we may never receive regulatory approval to market our current or future product candidates outside of the United States.

We plan to seek regulatory approval of our current or future product candidates outside of the United States. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction.

For example, even if the FDA grants marketing approval of a product candidate, we may not obtain approvals in other jurisdictions, and comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. However, a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the regulatory

approval process in others. Approval procedures vary among countries and can involve additional product candidate testing and administrative review periods different from those in the United States. The time required to obtain approvals in other countries might differ substantially from that required to obtain the FDA approval. The marketing approval processes in other countries generally implicate all of the risks detailed above regarding the FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries.

Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fail to comply with regulatory requirements in international markets or fail to receive applicable marketing approvals, it would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects.

The results of preclinical studies and early clinical trials may not be predictive of future results.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials. Bel-sar and any other product candidates we may develop may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. For example, bel-sar may not be effective at slowing or arresting tumor growth or may not preserve visual acuity in later stage trials. Even if bel-sar successfully slows or completely arrests tumor growth, this may not result in a reduction in the risk of metastasis. Additionally, any positive results generated in our ongoing clinical trials and preclinical studies would not ensure that we will achieve similar results in larger, pivotal clinical trials or in clinical trials of bel-sar in broader patient populations. 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, and we cannot be certain that we will not face similar setbacks. 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. Furthermore, the failure of any product candidate to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of that product candidate in other indications or patient populations or any other product candidates then under development and/or cause the FDA or other regulatory authorities to require additional testing before approving such product candidate or any other product candidates.

Interim, "top-line," and preliminary or early data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, early, interim or top-line data from our clinical trials. These interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or early results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between interim data and final data could materially affect our business, financial condition, results of operations and growth prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and our company in general. Further, additional disclosure of interim data by us or by our potential competitors in the future could result in volatility in the price of our common stock. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available

information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or top-line data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our product candidates may be harmed, which could materially affect our business, financial condition, results of operations and growth prospects.

Additionally, we may continue to utilize "open-label" trial designs or open-label extensions to our clinical trials in the future. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial or extension may not be predictive of future clinical trial results with bel-sar or any future product candidates when studied in a controlled environment with a placebo or active control.

Bel-sar or any future product candidates may cause or reveal significant adverse events, toxicities or other undesirable side effects which may delay or prevent marketing approval. In addition, if we obtain approval for any of our product candidates, significant adverse events, toxicities or other undesirable side effects may be identified during post-marketing surveillance, which could result in regulatory action or negatively affect our ability to market the product.

Adverse events or other undesirable side effects caused by or associated with treatment by bel-sar or our future product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, the EMA or other comparable foreign regulatory authorities. Although bel-sar has been evaluated in clinical trials, unexpected side effects may still arise in our ongoing or any future clinical trials. These side effects have included pigmentary changes around the tumor margin and vision loss.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were not observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale, pivotal clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product or require additional warnings on the label;
- additional clinical trials or post-approval studies;
- we may be required to create a REMS plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- regulatory authorities may require additional warnings or limitations in the labeling, such as a contraindication, limitation of use, or a boxed warning, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be subject to regulatory investigations and government enforcement actions; and
- our reputation may suffer.

Moreover, if bel-sar or any of our future product candidates is associated with undesirable or unexpected side effects in clinical trials, we may elect to abandon or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the product candidate, even if it is approved.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could materially affect our business, financial condition, results of operations, and growth prospects.

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

We may experience delays in initiating or completing our preclinical studies or clinical trials, including as a result of delays in obtaining, or failure to obtain, the FDA's clearance to initiate clinical trials under future INDs. Additionally, we cannot be certain that preclinical studies or clinical trials for our product candidates will not require redesign, will enroll an adequate number of patients on time, or will be completed on schedule, if at all. We may experience numerous unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent our ability to receive regulatory approval or commercialize our product candidates, including:

- we may receive feedback from regulatory authorities that require us to modify the design or implementation of our preclinical studies or clinical trials or to delay or terminate a clinical trial;
- regulators or institutional review board, or IRBs, or ethics committees may delay or may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- preclinical studies or clinical trials of our product candidates may fail to show safety or efficacy or otherwise produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, or we may decide to abandon product research or development programs;
- preclinical studies or clinical trials of our product candidates may not produce differentiated or clinically significant results across tumor types or indications;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls, be unable to provide us with sufficient product supply to conduct or complete preclinical studies or clinical trials, fail to meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators or IRBs or ethics committees may require us or our investigators to, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our clinical trials are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our product candidates; and
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination or clinical hold due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, adverse findings upon an inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA may disagree with our clinical trial design or our interpretation of data from clinical trials or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

Moreover, principal investigators for our trials involving bel-sar or any 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 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 the interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site, and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of regulatory approval of one or more of our product candidates.

Our product development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our future clinical trials will begin as planned, or whether any of our current or future clinical trials will need to be restructured or will be completed on schedule, if at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may significantly harm our business, operating results, financial condition and prospects.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expenses. Additionally, our product candidates, if approved, could be subject to post-marketing commitments/requirements, marketing and labeling restrictions, and even recall or market withdrawal if unanticipated safety issues are discovered following approval. In addition, we may be subject to penalties or other enforcement action if we fail to comply with regulatory requirements.

If the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, import, export, adverse event reporting, storage, advertising, promotion, monitoring, and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and listing, compliance with applicable product tracking and tracing requirements, as well as continued compliance with current Good Manufacturing Practices, or cGMPs, and GCPs for any clinical trials that we conduct post-approval. Additionally, under the Food and Drug Omnibus Reform Act of 2022, or FDORA, sponsors of approved drugs and biologics must provide six months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing studies, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. The FDA may also require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Later discovery of previously unknown problems with a product, including adverse events 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 the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;

- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the inclusion of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- clinical trial holds;
- fines, warning letters or other regulatory enforcement action;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of products; 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. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we do not market our medicines for their approved indications, 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. 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 and state consumer protection laws. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

The FDA's and other regulatory authorities' policies and interpretations may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements, interpretations or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability. Moreover, 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 FDA's regulations, policies, and decisions may become subject to increasing legal challenges, delays, and/or changes.

We may be unable to obtain ODD for additional indications, or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. ODD must be requested before submitting an NDA or BLA. In the United States, ODD 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 ODD, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. ODD does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product that has ODD subsequently receives the first FDA approval for a particular active ingredient 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 product for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for

which the drug was designated. As a result, even if our current product candidates and any future product candidates receive orphan exclusivity, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

We have obtained orphan designation for bel-sar for the treatment of uveal melanoma from the FDA and EMA, and we may seek additional ODDs for bel-sar or some or all of our future product candidates in orphan indications in which there is a medically plausible basis for the use of these products. Even if we obtain ODD, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

The FDA may reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Similarly, in the EU, the European Commission grants an orphan designation in respect of a product after receiving the opinion of the EMA's Committee for Orphan Medicinal Products on a designation application. Orphan designation in the EU is granted to products where the sponsor can establish that (1) such product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (i) such condition affects no more than five in 10,000 persons in the EU when the application is made; or (ii) without incentives, it is unlikely that the marketing of the product would generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition that has been authorized in the EU, or if such a method exists, the product in question would be of significant benefit to those affected by that condition. In the EU, orphan designation entitles a party to a number of incentives, such as protocol assistance and scientific advice specifically for designated orphan medicines, and potential fee reductions depending on the status of the sponsor. Generally, if a product with an orphan designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a ten-year period of marketing exclusivity, which precludes the EMA from approving another marketing authorization application for a similar medicinal product in the same indication for that time period, except in limited circumstances. The EU exclusivity period can be reduced to six years if, at the end of the fifth year, a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable such that market exclusivity is no longer justified. The European Commission introduced a legislative proposal in April 2023 that, if implemented, could reduce the current ten-year marketing exclusivity period in the EU for certain orphan medicines.

A breakthrough therapy designation or Fast Track designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development, regulatory review or approval process, and each designation does not increase the likelihood that any of our product candidates will receive regulatory approval in the United States.

We may seek breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates 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. Products designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. 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. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We have obtained Fast Track designation for bel-sar for the treatment of choroidal melanoma, for the treatment of metastases to the choroid and for the treatment of NMIBC, and we may seek additional Fast Track designation for other product candidates we may develop. If a drug or biologic is intended for the treatment of a serious or life-threatening condition and the drug or biologic demonstrates the potential to address unmet medical needs for this condition, the 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 withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures.

Accelerated approval by the FDA, even if granted for bel-sar or any other future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive regulatory approval.

We may seek accelerated approval of our current or future product candidates using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate 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, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA requires that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials, and the FDA is permitted to require, as appropriate, that such studies be underway prior to approval or within a specified period after the date of approval. Sponsors must also update FDA on the status of these studies, and under FDORA, the FDA has increased authority to withdraw approval of a drug granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. In addition, the FDA currently requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate FDA approval.

The FDA's agreement to a Special Protocol Assessment, or SPA, with respect to the study design of our global Phase 3 trial of bel-sar for the treatment of early-stage choroidal melanoma does not guarantee any particular outcome from regulatory review, including ultimate approval, and may not lead to a successful review or approval process.

We obtained agreement from the FDA on the design and planned analysis of our global Phase 3 trial of bel-sar for the treatment of early-stage choroidal melanoma through an SPA. An SPA agreement documents FDA's agreement that the design and planned analysis of a study can adequately address objectives in support of a regulatory submission. However, final determinations for marketing application approval are made after complete review of a marketing application and are based on the entire data in the application.

The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs and biologics by allowing the FDA to evaluate the proposed design and size of certain clinical or animal studies, including clinical trials that are intended to form the primary basis for determining a product candidate's efficacy. The FDA ultimately assesses whether specific elements of the protocol design of the trial, such as entry criteria, dose selection, endpoints and/or planned analyses, are acceptable to support a regulatory submission.

Although the FDA may agree to an SPA, an SPA agreement does not guarantee approval of a product. Even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor company fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts.

In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding by the FDA review division, except under the circumstances described above,

if the FDA and the sponsor agree in writing to modify the protocol. Generally, such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

Moreover, if the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval of bel-sar for the treatment of small choroidal melanoma and indeterminate lesions.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and expect to continue to do so, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, central reading centers, medical institutions and clinical investigators, to conduct some aspects of our research, preclinical testing and clinical trials. We are using a clinical CRO for the pivotal trial for bel-sar for the treatment of early-stage choroidal melanoma. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, our product development activities would be delayed.

Our reliance on these third parties for research and development activities reduces our control over these activities, but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial, as well as the applicable legal, regulatory and scientific standards. 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, reproducible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA may require us to perform additional clinical trials before approving our marketing applications. We are also required to register ongoing clinical trials and to post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. Due to the rarity of ocular melanomas, we may engage clinical trial sites that have little experience in the conduct of clinical trials under GCPs. Even though we train the clinical trial sites, monitor the activities, and perform quality audits to assess and ensure compliance, we cannot ensure such compliance.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting clinical trials or other biological product development activities that could harm our competitive position. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

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

We currently rely on third-party CDMOs for the production of clinical supply of bel-sar and may continue to rely on CDMOs for the production of commercial supply of bel-sar, if approved. This reliance on CDMOs increases the risk that we will not have sufficient quantities of such materials, product candidates, or any therapies that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

We currently do not have any manufacturing facilities and have no plans to build our own clinical or commercial scale manufacturing capabilities. Instead, we expect to rely on third parties for the manufacture of our product candidates and related raw materials for future preclinical and clinical development, as well as for commercial

manufacture if any of our product candidates receive marketing approval. We are currently reliant on a single source for each of our regulatory starting materials, drug substance and drug product manufacturing for bel-sar.

We or our third-party suppliers or manufacturers may encounter shortages in the raw materials or active pharmaceutical ingredient, or API, necessary to produce bel-sar and future product candidates we may develop in the quantities needed for our clinical trials or, if bel-sar or any future product candidates we may develop are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or APIs, including shortages caused by the purchase of such raw materials or API, by our competitors or others. Even if raw materials or API are available, we may be unable to obtain sufficient quantities at an acceptable cost or quality. The failure by us or our third-party suppliers or manufacturers to obtain the raw materials or API necessary to manufacture sufficient quantities of bel-sar or any future product candidates we may develop could delay, prevent or impair our development efforts and may have a material adverse effect on our business. To date, we have only encountered minor delays in our manufacturing process due to a supply chain constraint with one of our vendors.

Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture clinical or commercial supply of our product candidates ourselves. The facilities used by third-party manufacturers to manufacture bel-sar or any future product candidates must be authorized by the FDA pursuant to inspections that will be conducted after we submit a BLA to the FDA. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements for manufacture of drug products and other laws and regulations. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and maintain regulatory approval for their manufacturing facilities. Some of our contract manufacturers may not have produced a commercially-approved product and, therefore, may not have obtained the requisite FDA approvals to do so. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

Finding new CDMOs or third-party suppliers involves additional cost and requires our management's time and focus. In addition, there is typically a transition period when a new CDMO commences work. Although we generally have not, and do not intend to, begin a clinical trial unless we believe we have on hand, or will be able to obtain, a sufficient supply of our product candidates to complete the clinical trial, any significant delay in the supply of our product candidates or the raw materials needed to produce our product candidates, could considerably delay conducting our clinical trials and potential regulatory approval of our product candidates. Additionally, any changes implemented by a new CDMO could delay completion of clinical trials, require the conduct of bridging clinical trials or studies, require the repetition of one or more clinical trials, increase clinical trial costs, delay approval of bel-sar and future product candidates and jeopardize our ability to commence product sales and generate revenue.

As part of their manufacture of our product candidates, our CDMOs and third-party suppliers are expected to comply with and respect the intellectual property and proprietary rights of others. If a CDMO or third-party supplier fails to acquire the proper licenses or otherwise infringes, misappropriates or otherwise violates the intellectual property or proprietary rights of others in the course of providing services to us, we may have to find alternative CDMOs or third-party suppliers or defend against applicable claims, either of which would significantly impact our ability to develop, obtain regulatory approval for or commercialize 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, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. In addition, we may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms.

Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- failure of third-party manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of the manufacturing agreement by the third-party manufacturers;

- failure to manufacture our product according to our specifications;
- lack of qualified backup suppliers for those components or materials that are currently purchased from a sole or single source supplier;
- failure to manufacture our product according to our schedule or at all;
- production difficulties caused by unforeseen events that may delay the availability of one or more of the necessary raw materials or delay the manufacture of bel-sar or any future product candidates for use in clinical trials or for commercial supply;
- supply or service disruptions or increased costs that are beyond our control;
- misappropriation of our proprietary information, including our trade secrets and know-how; and
- termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Bel-sar and any other product candidates that we may develop may compete with other product candidates and products for access to manufacturing facilities. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time-consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of our product candidates. If our current third-party manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or on terms acceptable to us. Our current and anticipated future dependence upon others for the manufacture of bel-sar or any other future product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Risks Related to Commercialization

If bel-sar or any future product candidates do not achieve broad market acceptance, the revenue that we generate from their sales may be limited, and we may never become profitable.

We have never commercialized a product candidate for any indication. Even if bel-sar and any future product candidates are approved by the appropriate regulatory authorities for marketing and sale, they may not gain acceptance among physicians, patients, third-party payors, and others in the medical community. If any product candidates for which we obtain regulatory approval do not gain an adequate level of market acceptance, we may not generate significant revenue and may not become profitable or may be significantly delayed in achieving profitability. Market acceptance of bel-sar and any future product candidates by the medical community, patients and third-party payors will depend on a number of factors, some of which are beyond our control. For example, physicians are often reluctant to switch their patients, and patients may be reluctant to switch, from existing therapies even when new and potentially more effective or safer treatments enter the market. If public perception is influenced by claims that the use of VDCs is unsafe, whether related to our or our competitors' products, our products may not be accepted by the general public or the medical community. In addition, training clinicians to properly use bel-sar or any future product candidate that requires a similar laser and microinjector may create reluctance by clinicians to adopt our products, potentially adversely affecting our future sales and marketing efforts. Furthermore, such training increases our costs to generate sales associated with any such product. Future adverse events in targeted oncology or the biopharmaceutical industry could also result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approvals of our product candidates. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost effective as compared with competing treatments.

Efforts to educate the medical community and third-party payors on the benefits of bel-sar and any future product candidates may require significant resources and may not be successful. If bel-sar or any future product candidates are approved but do not achieve an adequate level of market acceptance, we could be prevented from or significantly delayed in achieving profitability. The degree of market acceptance of any of bel-sar and any future product candidates will depend on a number of factors, including:

- the efficacy of bel-sar and our VLP technology, and any future product candidates;
- the prevalence and severity of adverse events associated with bel-sar and any future product candidates or those products with which they may be co-administered;

- the clinical indications for which bel-sar are approved and the approved claims that we may make for the products;
- limitations or warnings contained in the product's FDA-approved labeling or those of comparable foreign regulatory authorities, including potential limitations or warnings for bel-sar and any future product candidates that may be more restrictive than other competitive products;
- changes in the SoC for the targeted indications for bel-sar and any future product candidates, which could reduce the marketing impact of any claims that we could make following FDA approval or approval by comparable foreign regulatory authorities, if obtained;
- the relative convenience and ease of administration of bel-sar and any future product candidates and any products with which they are co-administered;
- the cost of treatment compared with the economic and clinical benefit of alternative treatments or therapies;
- the availability of adequate coverage or reimbursement by third-party payors, including government healthcare programs such as Medicare and Medicaid and other healthcare payors;
- the price concessions required by third-party payors to obtain coverage;
- the perception of physicians, patients, third-party payors and others in the medical community of the relative safety, efficacy, convenience, effect on quality of life and cost effectiveness of bel-sar compared to those of other available treatments;
- the willingness of patients to pay out-of-pocket in the absence of adequate coverage and reimbursement;
- the extent and strength of our marketing and distribution of bel-sar and any future product candidates;
- the safety, efficacy, and other potential advantages over, and availability of, alternative treatments already used or that may later be approved;
- distribution and use restrictions imposed by the FDA or comparable foreign regulatory authorities with respect to bel-sar and any future product candidates or to which we agree as part of a REMS or voluntary risk management plan;
- the timing of market introduction of bel-sar and any future product candidates, as well as competitive products;
- our ability to offer bel-sar and any future product candidates for sale at competitive prices;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the extent and strength of our third-party manufacturer and supplier support;
- the publicity concerning our bel-sar or competing products and treatments;
- the actions of companies that market any products with which bel-sar and any future product candidates may be co-administered;
- the approval of other new products;
- adverse publicity about bel-sar and any future product candidates or any products with which they are co-administered, or favorable publicity about competitive products; and
- potential product liability claims.

We currently have no marketing and sales organization and have no experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to generate product revenue.

We have never commercialized a product candidate and we currently have no sales, marketing or distribution capabilities and have no experience in marketing products. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring the rights to our product candidate and undertaking preclinical studies and clinical trials of our product candidate. We intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. We may not be successful in transitioning from a company with a development focus to a company capable of supporting commercial activities.

In addition to establishing internal sales, marketing and distribution capabilities, we will pursue collaborative arrangements regarding the sales and marketing of our products, however, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. Further, if we enter into arrangements with third parties to perform sales and marketing services, our product revenues, if any, may be lower than if we were to market and sell any products that we develop ourselves. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

Furthermore, developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our product candidate. We may not be able to build an effective sales and marketing organization in the United States, the EU or other key global markets. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidate, we may have difficulties generating revenue from them.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

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

The biopharmaceutical industry is characterized by intense competition and rapid innovation. While we are not aware of anyone currently developing a treatment for early-stage choroidal melanoma, in the future our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results than us. There are multiple companies that have drugs in clinical development for the treatment of NMIBC, such as Johnson & Johnson, UroGen Pharma Ltd., CG Oncology, Inc., ImmunityBio, Inc. and Ferring Pharmaceuticals. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our potential competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly as they develop novel approaches to treating disease indications that our product candidates are also focused on treating. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel therapeutics or to in-license novel therapeutics that could make the product candidates that we develop obsolete. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaboration partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products, which may reduce or eliminate our commercial opportunity. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety, tolerability, reliability, convenience of use, price and reimbursement.

Even if we obtain regulatory approval of our product candidates, the availability and price of our potential future competitors' products could limit the demand and the price we are able to charge for our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances. For additional information regarding our competition, see the section of our Annual Report on Form 10-K for the year ended December 31, 2024 titled "Business—Competition."

Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

In the United States 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. Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. For more information, see the section of our Annual Report on Form 10-K for the year ended December 31, 2024 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 and the amount of reimbursement for particular medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid and Veterans Affairs, or VA, hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our product candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

If the market opportunity for bel-sar is smaller than we estimate or if any regulatory approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

The incidence and prevalence for target patient populations of bel-sar and any future product candidates has not been established with precision. Bel-sar is a VDC product candidate being developed for the first line treatment of early-stage choroidal melanoma. Our projections of both the number of people who have choroidal melanoma, as well as additional ocular oncology and bladder cancer indications, are based on our estimates.

The total addressable market opportunity will ultimately depend upon, among other things, the patient criteria included in the final label, the indications for which bel-sar is approved for sale, acceptance by the medical community and patient access, product pricing and reimbursement. The number of patients with choroidal melanoma, metastases to the choroid, and bladder cancer for which bel-sar may be approved as treatment may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. Bel-sar is our only product candidate and therefore our business is dependent on the market opportunity for our product.

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

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. For more information, see the section of our Annual Report on Form 10-K for the year ended December 31, 2024 titled "Business—Government Regulation—Health Care Laws and Regulations."

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many states in the United States have adopted laws similar to the federal Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. State and foreign laws, including for example the General Data Protection Regulation, or GDPR, 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 the Health Insurance Portability and Accountability Act, or HIPAA, thus complicating compliance efforts. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, individual imprisonment, reputational harm, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. Further, defending against any such actions can be costly and time consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, our ability to operate our business and our results of operations could be adversely affected.

Current and future healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted and/or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay regulatory approval of our current or future product candidates or any future product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell a product for which we obtain regulatory approval. Changes in laws, regulations, statutes or the interpretation of existing laws and regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. For more information, see the section of our Annual Report on Form 10-K for the year ended December 31, 2024 titled "Business—Government Regulation—Health Care Reform & Legislative Updates."

In the United States, there have been, and continue to be, a significant number of legislative initiatives to contain healthcare costs. The United States has also sought to implement legislation at the state level, and individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. 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. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our current or future product candidates or additional pricing pressures. In particular any policy changes through CMS as well as local state Medicaid programs could have a significant impact on our business.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our current or future product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement approval for a product;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

Risks Related to Our Intellectual Property

Our ability to compete may decline if we do not adequately protect our proprietary rights, and our proprietary rights do not necessarily address all potential threats to our competitive advantage.

Our commercial success depends upon obtaining and maintaining proprietary rights to our intellectual property estate, including rights relating to our technology platform using HPV-derived VLPs to target tumors and VDCs like bel-sar, as well as successfully defending these rights against third-party challenges and successfully enforcing these rights to prevent third-party infringement. We will only be able to protect bel-sar or a future product candidate derived from our platform from unauthorized use by third parties to the extent that valid and enforceable patents cover it. Our ability to maintain patent protection for bel-sar or a future product candidate is uncertain due to a number of factors, including that:

- others may design around our patent claims to produce competitive technologies, products or methods that fall outside of the scope of our patents;
- we may not obtain patent protection in all jurisdictions that may eventually provide us a significant business opportunity; and
- any patents issued to us may be successfully challenged by third parties.

Even with our patents covering bel-sar, we may still not be able to make use or sell bel-sar or a future product candidate because of the patent rights of others. Others may have filed patent applications covering compositions, products or methods that are similar or identical to ours, which could materially affect our ability to successfully commercialize bel-sar or a future product candidate.

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 United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited.

Obtaining and maintaining a patent portfolio entails significant expense, including periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and patent applications. These expenditures can be at numerous stages of prosecuting patent applications and over the lifetime of maintaining and enforcing issued patents. We may or may not choose to pursue or maintain protection for particular intellectual property in our portfolio. If we choose to forgo patent protection or to allow a patent application or patent to lapse purposefully or inadvertently, our competitive position could suffer. Furthermore, we employ reputable law firms and other professionals to help us comply with the various procedural, documentary, fee payment and other similar provisions we are subject to and, in many cases, an inadvertent lapse 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 failure to make certain payments or noncompliance with certain requirements in the patent process can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Legal action that may be required to enforce our patent rights can be expensive and may involve the diversion of significant management time. There can be no assurance that we will have sufficient financial or other resources to file and pursue infringement claims, which typically last for years before they are concluded. In addition, these legal actions could be unsuccessful and result in the invalidation of our patents, a finding that they are unenforceable or a requirement that we enter into a licensing agreement with or pay monies to a third party for use of technology covered by our patents. We may or may not choose to pursue litigation or other actions against those that have infringed on our patents, or have used them without authorization, due to the associated expense and time commitment of monitoring these activities. If we fail to successfully protect or enforce our intellectual property rights, our competitive position could suffer, which could harm our results of operations.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of bel-sar or any future product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize bel-sar or any future product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. If we are unable to obtain such licenses on commercially reasonable terms, our business could be harmed.

The growth of our business may depend in part on our ability to acquire, in-license or use third-party proprietary rights. We may be unable to acquire or in-license any such proprietary rights from third parties that we identify as necessary or important to our business operations. In addition, we may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. Were that to happen, we may need to cease use of the compositions or methods covered by those third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on those intellectual property rights, which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, which means that our competitors may also receive access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

We rely on intellectual property licensed from third parties. We face risks with respect to such reliance, including the risk that, if we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business. Our existing license agreements impose on us various diligence, milestone payment, royalty and other obligations. If we fail to comply with any of our obligations under these agreements, or we are subject to a bankruptcy, our licensors may have the right to terminate the license, in which event we would not be able to market any products covered by the license.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted and related obligations under the license agreement and other interpretation-related issues;
- our licensor's right to license or sublicense patent and other rights to us, and whether and the extent to which the right is retained by a third party;
- whether and the extent to which our technology infringes 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 technology in relation to our development and commercialization of bel-sar or any future 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.

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.

In addition, disputes may arise regarding the payment of the royalties due to licensors in connection with our exploitation of the rights we license from them. Licensors may contest the basis of royalties we retained and claim that we are obligated to make payments under a broader basis. Such disputes may be costly to resolve and may divert management's attention away from day-to-day activities. In addition to the costs of any litigation we may face, any legal action against us could increase our payment obligations under the respective agreement and require us to pay interest and potentially damages to such licensors. If disputes over intellectual property that we have licensed from third parties prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we or our collaborators may be unable to successfully manufacture and commercialize bel-sar or a future product candidate.

If we fail to comply with our obligations under the license agreements, our licensors may have the right to terminate these agreements, in which event we might not be able to manufacture or market bel-sar or a future product candidate. Termination of these agreements or reduction or elimination of our rights under these agreements 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 or technology.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation with respect to bel-sar or a future product candidate, thereby potentially extending the term of marketing exclusivity for such product, our business may be harmed.

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of the FDA marketing approval of our product candidates, one or more of our owned, co-owned, or in-licensed U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA-approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. In the EU, bel-sar or a future product candidate may be eligible for term extensions based on similar legislation. In either jurisdiction, 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. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

Patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.

The patent positions of biopharmaceutical and biotechnology companies and other actors in our fields of business can be highly uncertain and typically involve complex scientific, legal and factual analyses. In particular, the interpretation and breadth of claims allowed in some patents covering biopharmaceutical compositions may be uncertain and difficult to determine and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The standards of the U.S. Patent and Trademark Office, or the USPTO, and its foreign counterparts are sometimes uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. The U.S. patents and patent applications may also be subject to interference or derivation proceedings, and the U.S. patents may be subject to reexamination proceedings, post-grant review and/or *inter partes* review in the USPTO. International patents may also be subject to opposition or comparable proceedings in the corresponding international patent office, which could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such interference, derivation, reexamination, post-grant review, *inter partes* review and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

Furthermore, even if not challenged, our patents and patent applications may not prevent others from designing their products to avoid being covered by our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to bel-sar or a future product candidate is threatened, it could dissuade companies from collaborating with us to develop, and could threaten our or their ability to successfully commercialize, bel-sar or a future product candidate.

In addition, changes in, or different interpretations of, patent laws in the United States and other countries may permit others to use our discoveries or to develop and commercialize our technology without providing any compensation to us and may limit the scope of patent protection that we are able to obtain. The laws of some countries do not protect intellectual property rights to the same extent as the U.S. laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights.

Third parties may assert claims against us alleging infringement of their patents and proprietary rights, or we may need to become involved in lawsuits to defend or enforce our patents, either of which could result in substantial costs or loss of productivity, delay or prevent the development and commercialization of product candidates, prohibit our use of proprietary technology or sale of potential products or put our patents and other proprietary rights at risk.

Our commercial success depends upon our ability to develop, manufacture, market and sell bel-sar or a future product candidate without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. Litigation relating to infringement or misappropriation of patent and other intellectual property rights in the biotechnology industry is common, including patent infringement lawsuits, interferences, oppositions, reexamination proceedings, post-grant review, and/or *inter partes* review before the USPTO and corresponding international patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. As a result of any patent infringement claims, or in order to avoid any potential infringement claims, we may choose to seek, or be required to seek, a license from the third-party, which may require payment of substantial royalties or fees, or require us to grant a cross-license under our intellectual property rights. These licenses may not be available on reasonable terms or at all. Even if a license can be obtained on reasonable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we could be prevented from commercializing bel-sar or a future product candidate, or forced to modify bel-sar or a future product candidate, or to cease some aspect of our business operations, which could harm our business significantly. We might also be forced to redesign or modify our technology or product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible. Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Further, if a patent infringement suit is brought against us or our third-party service providers, our development, manufacturing or sales activities relating to bel-sar or a future product candidate that is the subject of the suit may be delayed or terminated. In addition, defending such claims may cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages if we are found to be infringing a third-party's patent rights. These damages potentially could include increased damages and attorneys' fees if we are found to have infringed such rights willfully. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. In addition, if the breadth or strength of protection provided by the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We may in the future be subject to third-party claims and similar adversarial proceedings or litigation in other jurisdictions regarding our infringement of the patent rights of third parties. Even if such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to further develop or commercialize bel-sar or a future product candidate unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable.

If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering our technology or a product candidate, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and Europe, defendant counterclaims alleging invalidity or unenforceability are common. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, but that an adverse third party may identify and submit in support of such assertions of invalidity. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part of the patent protection on bel-sar or a future product candidate.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world, and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on bel-sar or a future product candidate in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

We have and have applied for patents in those countries where we intend to make, have made, use, offer for sale or sell products and where we assess the risk of infringement to justify the cost of seeking patent protection. Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and may export otherwise infringing products to territories where we have patent protection, but where our ability to enforce our patent rights is not as strong as in the United States. These products may compete with any products that we may develop, and our patents or other intellectual property rights may not be effective or sufficient to prevent such competition.

The laws of some other countries do not protect intellectual property rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we chose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. In addition, the legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biopharmaceuticals or biotechnologies. As a result, many companies have encountered significant difficulties in protecting and defending intellectual property rights in certain jurisdictions outside the United States. Such issues may make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, subject our patents to the risk of being invalidated or interpreted narrowly, subject our patent applications to the risk of not issuing or 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 to us, if any, may not be commercially meaningful, while the damages and other remedies we may be ordered to pay such third parties may be significant. 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.

If we or our licensors are unable to protect the confidentiality of the proprietary information related to our product or process, our business and competitive position would be harmed.

We and our licensors rely on confidentiality agreements to protect unpatented know-how, technology and other proprietary information related to our product and process, to maintain our competitive position. For example, our licensor Rakuten (previously LI-COR) maintains its manufacture of IRDye 700DX® dye molecules (used in bel-sar) as a trade secret. Trade secrets and know-how can be difficult to protect. In particular, the trade secrets and know-how in connection with our development programs and other proprietary technology we may develop may over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology and the movement of personnel with scientific positions in academic and industry.

We seek to protect our proprietary information, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated proprietary information is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or are unwilling to protect trade secrets.

We may be subject to claims that third parties have an ownership interest in our trade secrets. For example, we may have disputes arise from conflicting obligations of our employees, consultants or others who are involved in developing bel-sar. Litigation may be necessary to defend against these and other claims challenging ownership of our trade secrets. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable trade secret rights, such as exclusive ownership of, or right to use, trade secrets that are important to our therapeutic programs and other proprietary technologies we may develop. Such an outcome could have a materially 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 our management and other employees.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our proprietary information. Competitors could purchase our products and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our proprietary information 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 technology or information to compete with us. If any of our proprietary information 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 data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached or subject to unauthorized access and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any cybersecurity incident or breach. In addition, our confidential information may otherwise become known or be independently discovered by competitors, in which case we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to our Business and Industry

If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to pursue our business strategy will be impaired, could result in loss of markets or market share and could make us less competitive.

Our ability to compete in the highly competitive biopharmaceutical industries depends upon our ability to attract, manage, motivate and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel. The loss of the services of any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements for these individuals could harm our business. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and 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.

Competition for skilled personnel in our industry is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms, in a timely manner or at all. In particular, we have experienced a very competitive hiring environment in the Boston area, where we are headquartered. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided equity incentive awards that vest over time. The value to employees of restricted stock awards and stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams are at-will employees and may terminate their employment with us on short notice. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees. Given the stage of our programs and our plans to expand operations, our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior personnel across our organization.

Inadequate funding, substantial changes in leadership, personnel, policies or priorities of, or other disruptions at federal governmental agencies, including from government shut downs, layoffs of federal agency employees or other disruptions to these agencies' operations, funding or staffing, could hinder their ability to hire and retain key leadership and other personnel, prevent, delay, or hinder the research, development or commercialization of new products and services 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, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Currently, federal agencies in the United States are operating under a continuing resolution that is set to expire on September 30, 2025.

Disruptions in staffing, funding or operations at the FDA, SEC, NIH, USPTO and other government agencies, including a potential or actual government shutdown or any changes and/or additional policies or regulations relating to federal agencies as a result of the new U.S. presidential administration, may also prevent, delay or hinder the research, development or commercialization of new products, including review and/or approval of new products by necessary government agencies, any of which would adversely affect our business. For example, over the last several years, the U.S. government has shut down at times and certain federal agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, including as a result of reaching the debt ceiling, it could significantly impact the ability of federal agencies to perform normal business functions on which the operation of our business may rely, including the FDA's ability to timely review and process our regulatory submissions, any of which could have a material adverse effect on our business. Further, future government shutdowns or other disruption of the operations of federal agencies could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

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

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims

that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

Changes in tax laws or in their implementation or interpretation may adversely affect us or our investors.

The rules dealing with the U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many changes have been made and changes are likely to continue to occur in the future. For example, under Section 174 of the Code, in taxable years beginning after December 31, 2021, expenses that are incurred for research and development in the United States will be capitalized and amortized, which may have an adverse effect on our cash flow.

It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

Our internal information technology systems, or those of our third-party CROs, contractors, consultants or others who process sensitive information on our behalf, may fail or suffer cybersecurity incidents or breaches, loss or leakage of data and other compromises, any of which could result in a material disruption of our product candidates' development programs, compromise sensitive information related to our business or prevent us from accessing such information, expose us to liability or otherwise adversely affect our business.

In the ordinary course of our business, we may collect, store and transmit confidential information, including intellectual property, proprietary business information and personal information (including health information). We have established safeguards to do so in a secure manner in an effort to maintain the confidentiality, integrity and availability of such information. We also have outsourced certain of our operations to third parties, and as a result, we manage a number of third parties who have access to our information. Despite the implementation of security measures, our internal computer systems and infrastructure, and those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access and misuse, cyberattacks by sophisticated nation-state and nation-state supported actors or by malicious third parties (including the deployment of harmful malware (such as malicious code, viruses and worms), natural disasters, global pandemics, fire, terrorism, war and telecommunication and electrical failures, fraudulent activity, as well as cybersecurity incidents or breaches from inadvertent or intentional actions (such as error or theft) by our employees, contractors, consultants, business partners, and/or other third parties, phishing attacks, ransomware, denial-of-service attacks, social engineering schemes (including phishing attacks) and other means that affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure as well as lead to unauthorized access, disclosure, misuse or acquisition of information. We, and our service providers, have from time to time and may in the future continue to experience threats and cybersecurity incidents relating to our and our third-party vendors' information systems. Cyberattacks generally are increasing in their frequency, sophistication and intensity. The techniques used to sabotage or to obtain unauthorized access to our information technology systems or those upon whom we rely on to process our information change frequently, and we may be unable to anticipate such techniques or implement adequate preventative measures or to stop or to adequately address cybersecurity incidents or breaches in all instances. The recovery systems, security protocols, network protection mechanisms and other security measures that we have integrated into our information technology systems, which are designed to protect against, detect and minimize cybersecurity incidents or breaches, may not be adequate to prevent or detect or adequately address service interruption, system failure or data loss.

Significant disruptions of our information technology systems or cybersecurity incidents could adversely affect our business operations and/or result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information including health information), and could result in financial, legal, business and reputational harm to us. If such disruptions 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, 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. Further, as a result of increased hybrid work, a significant number of our employees and partners are working remotely, which increases the risk of a cybersecurity incident or breach or other data and cybersecurity issues. To the extent that any disruption or cybersecurity incident or breach results in a loss of, or damage to, our data or applications, or inappropriate disclosure or misuse of or access to confidential or proprietary information, we could incur liability and the further development of our future product candidates could be delayed.

We may also be required to comply with laws, regulations, rules, industry standards, and other legal obligations that require us to maintain the security of personal data. We may also have contractual and other legal obligations to notify collaborators, our clinical trial participants, or other relevant stakeholders of cybersecurity incidents and breaches. Failure to prevent or mitigate cyberattacks could result in unauthorized access to data, including personal data. Most jurisdictions have enacted laws requiring companies to notify individuals, regulatory authorities, and others of cybersecurity incidents or breaches involving certain types of data. Such disclosures are costly, could lead to negative publicity, may cause our collaborators or other relevant stakeholders to lose confidence in the effectiveness of our security measures and require us to expend significant capital and other resources to respond to and/or alleviate problems caused by the actual or perceived cybersecurity incident or breach. In addition, the costs to respond to a cybersecurity event or to mitigate any identified security vulnerabilities could be significant, including costs for remediating the effects of such an event, paying a ransom, restoring data from backups, and conducting data analysis to determine what data may have been affected by the cybersecurity incident or breach. In addition, our efforts to contain or remediate a cybersecurity incident or any vulnerability exploited to cause an incident may be unsuccessful, and efforts and any related failures to contain or remediate them could result in interruptions, delays, harm to our reputation, and increases to our insurance coverage.

In addition, litigation resulting from cybersecurity incidents or breaches may adversely affect our business. Unauthorized access to our information technology systems or infrastructure could result in litigation with our collaborators, our clinical trial participants, or other relevant stakeholders. These proceedings could force us to spend money in defense or settlement, divert management's time and attention, increase our costs of doing business, or adversely affect our reputation. We could be required to fundamentally change our business activities and practices in response to such litigation, which could have an adverse effect on our business. If a cybersecurity incident or breach were to occur and the confidentiality, integrity or availability of our data or the data of our collaborators were disrupted, we could incur significant liability, which could negatively affect our business and damage our reputation.

Furthermore, we may not have adequate insurance coverage or otherwise to protect us from, or adequately mitigate, liabilities or damages. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage and coverage for errors and omissions will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

We are, or may become, subject to stringent and changing privacy and information security laws, regulations, standards, policies and contractual obligations related to data privacy and security. Our actual or perceived failure to comply with such data privacy and security obligations could lead to government enforcement actions (which could include civil or criminal fines or penalties), a disruption of our clinical trials or commercialization of our products, private litigation, changes to our business practices, increased costs of operations, and adverse publicity that could otherwise negatively affect our operating results and business. Compliance or the failure to comply with such obligations could increase the costs of our products, could limit their use or adoption, and could otherwise negatively affect our operating results and business.

Regulation of data (including personal and clinical trial data) is evolving, as federal, state, and foreign governments continue to adopt new, or modify existing, laws and regulations addressing data privacy and security,

and the collection, processing, storage, transfer, and use of data. These new or proposed laws and regulations are subject to differing interpretations and may be inconsistent among jurisdictions, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data. Moreover, we are subject to the terms of our privacy and security policies, representations, certifications, standards, publications, contracts and other obligations to third parties related to data privacy, security and processing. These and other requirements could require us or our collaborators to incur additional costs to achieve compliance, limit our competitiveness, necessitate the acceptance of more onerous obligations in our contracts, restrict our ability to use, store, transfer, and process data, impact our or our collaborators' ability to process or use data in order to support the provision of our products, affect our or our collaborators' ability to offer our products in certain locations, cause regulators to reject, limit or disrupt our clinical trial activities, result in increased expenses, reduce overall demand for our products, and make it more difficult to meet expectations of relevant stakeholders.

We and any potential collaborators may be subject to federal, state and foreign data protection laws and regulations including, without limitation, laws that regulate personal data such as health data. For example, in the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state personal information laws (e.g., the California Consumer Privacy Act of 2018, or CCPA), state data breach notification laws, state health information privacy laws and federal and state consumer protection laws and regulations (e.g., Section 5 of the Federal Trade Commission Act), govern the collection, use, disclosure and protection of health-related and other personal data. These laws and regulations could apply to our operations, the operations of our collaborators, or other relevant stakeholders upon whom we depend. In addition, we may obtain personal data (including health information) from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA. Additionally, we could be subject to 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, the CCPA established a comprehensive privacy framework for covered businesses by creating an expanded definition of personal information, providing data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. The law also provides California residents with the ability to limit use of certain sensitive information, establishes restrictions on the retention of personal data, and established a new state regulatory agency, the California Privacy Protection Agency, to implement and enforce the legislation. Although there are limited exemptions for protected health information covered under HIPAA and clinical trial data, the CCPA may increase our compliance costs and potential liability.

Similar comprehensive consumer privacy laws have been passed in numerous other states and a number of other states have proposed new privacy laws. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. In addition, laws in all 50 U.S. states require businesses to provide notice to individuals if certain of their personal information has been disclosed as a result of a qualifying data breach or cybersecurity incident. There are also states that are specifically regulating health information. For example, Washington state recently enacted a health privacy law that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain specific types of information. For example, a small number of states have passed laws that regulate biometric data specifically. These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. State laws are changing rapidly and there is discussion in the U.S. Congress of a new comprehensive federal data privacy law to which we may likely become subject, if enacted. These laws demonstrate our vulnerability to the evolving regulatory environment related to personal data. As we expand our operations, these and similar laws may increase our compliance costs and potential liability.

Foreign data protection laws, such as, without limitation, the EU GDPR, the EU member state implementing legislation, and the UK GDPR, may also apply to health-related and other personal data that we process, including, without limitation, personal data relating to clinical trial participants. The GDPR imposes strict obligations on the ability to process health-related and other personal data, including in relation to security (which requires the adoption of administrative, physical and technical safeguards designed to protect such information), collection, use and transfer of personal data. These obligations include, without limitation, several transparency requirements relating to communications with data subjects regarding the processing of their personal data, ensuring an appropriate legal basis or conditions applies to the processing of personal data, limitations on the retention of personal data, increased requirements pertaining to health data, notification of data processing obligations or security incidents to the competent national data protection authorities and/or data subjects, the security and confidentiality of the personal data, various rights that data subjects may exercise with respect to their personal data, and strict rules and restrictions on the international transfer of personal data.

The GDPR imposes strict rules on the transfer of personal data out of the EEA and UK to other regions outside the EEA/UK, or third countries, that have not been deemed to offer "adequate" privacy protections by the competent data protection authorities, including the United States in certain circumstances, unless a derogation exists or adequate international transfer safeguards (for example, the European Commission approved Standard Contractual Clauses, or the EU SCCs, and the UK International Data Transfer Agreement/Addendum, or the UK IDTA) are put in place. Where relying on the EU SCCs or UK IDTA for data transfers, we may also be required to carry out transfer impact assessments on the transfers made pursuant to the EU SCCs and UK IDTA, on a case-by-case basis, to ensure the law in the recipient country provides "essentially equivalent" protections to safeguard the transferred personal data as provided in the EEA and UK, and may be required to adopt supplementary measures if this standard is not met. Further, the EU and United States have adopted its adequacy decision for the EU-U.S. Data Privacy Framework, or the Framework, which entered into force on July 11, 2023. This Framework provides that the protection of personal data transferred between the EU and the United States is comparable to that offered in the EU. This provides a further avenue to ensuring transfers to the United States are carried out in line with GDPR. There has been an extension to the Framework to cover UK transfers to the United States. The Framework could be challenged like its predecessor frameworks. The international transfer obligations under the EEA and UK data protection regimes will require significant effort and cost, and may result in us needing to make strategic considerations around where EEA and UK personal data is located and which service providers we can utilize for the processing of EEA and UK personal data. Any inability to process or transfer personal data from the EEA to the United States in compliance with data protection laws may impede our ability to conduct trials and may adversely affect our business and financial position.

Although the UK is regarded as one of the third countries under the EU GDPR, the European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EEA member states to the UK without additional safeguards. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK Government has introduced a Data (Use and Access) Bill, or the UK Bill, into the UK legislative process. The aim of the UK Bill is to reform the UK's data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime. In addition, EEA Member States have adopted national laws to implement the GDPR that may partially deviate from the GDPR. Further, the competent authorities in the EEA Member States interpret GDPR obligations slightly differently from country to country (particularly in relation to the processing of health data) and therefore we do not expect to operate in a uniform legal landscape in the EEA. The potential of the respective provisions and enforcement of the EU GDPR and UK GDPR further diverging in the future creates additional regulatory challenges and uncertainties for us. This lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, complexity and cost to our handling of personal data and our privacy and data security compliance programs and could require us to implement different compliance measures for the UK and the EEA.

The increase of foreign privacy and security legal frameworks with which we must comply, increases our compliance burdens and exposure to substantial fines and penalties for non-compliance. For example, under the GDPR, entities that violate the GDPR can face fines of up to the greater of 20 million euros (£17.5 million under UK GDPR) or 4% of their worldwide annual turnover, or revenue. Additionally, regulators could prohibit our use of personal data subject to the GDPR. 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 infringement of the GDPR. The GDPR has increased our responsibility and potential liability in relation to personal data that we process, requiring us to put in place additional mechanisms to comply with the GDPR and other foreign data protection requirements.

We may also publish privacy policies and other documentation regarding our collection, processing, use and disclosure of personal data and/or other confidential information. Although we endeavor to comply with our published policies and documentation, we may at times fail to do so or may be perceived to have failed to do so. Moreover, despite our efforts, we may not be successful in achieving compliance if our employees or contractors fail to comply with our published policies and documentation. Such failures can subject us to potential foreign, local, state and federal action if they are found to be deceptive, unfair, or misrepresentative of our actual practices.

Additionally in the EU, the NIS 2 Directive (NIS 2) is replacing the cybersecurity legal framework under the current NIS framework, aiming to ensure a high level of cybersecurity in the region. NIS 2 brings new medium and large organizations providing services in the EU within scope of the legal framework. It extends to additional sectors and expands the list of in-scope healthcare organizations, including to certain providers engaged in research and development of medicinal products. The new regime imposes direct obligations on management in respect of an in-scope organization's compliance with NIS 2, requires covered organizations to put in place certain cyber risk management measures, strengthens incident reporting requirements and provides supervisory authorities with greater oversight. The majority of obligations will come into force when national legislation implementing NIS 2 becomes effective in the relevant EU Member State. EU Member States had until 17 October 2024 to transpose NIS 2 into national legislation, although many countries have still not completed the transposition. As such, the cybersecurity regulatory landscape in the EU is currently fragmented and uncertain. To the extent we are subject to NIS 2, we will require additional investment of our resources in compliance programs and will potentially come under greater regulatory scrutiny. Under NIS 2 companies may be subject to administrative fines of up to the higher amount of €10 million or 2% of worldwide turnover.

Regulators and legislators in the United States are increasingly scrutinizing and restricting certain personal data transfers and transactions involving foreign countries. For example, Executive Order 14117 of February 28, 2024, Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government-Related Data by Countries of Concern as implemented by Department of Justice regulations issued in December 2024, prohibits data brokerage transactions involving certain sensitive personal data categories, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict certain investment agreements, employment agreements and vendor agreements involving such data and countries of concern, absent specified cybersecurity controls. Actual or alleged violations of these regulations may be punishable by criminal and/or civil sanctions, and may result in exclusion from participation in federal and state programs.

Compliance with U.S. federal and state as well as foreign data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and/or divert resources from other initiatives and projects. Failure, or perceived failure, to comply with federal, state and foreign data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties, fines or penalties), private litigation, a diversion of management attention, adverse publicity and negative effects on our operating results and business. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages if we fail to comply with applicable data protection laws, privacy policies or data protection obligations related to information security, cybersecurity incidents or data breaches. Moreover, clinical trial participants or patients about whom we or our collaborators obtain information, as well as the providers who share this information with us, may limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, contracts or privacy notices or breached other obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business. Compliance with data protection laws may be time consuming, require additional resources and could result in increased expenses, reduce overall demand for our products and make it more difficult to meet expectations of or commitments to our relevant stakeholders. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Issues in the development and use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. We may integrate generative artificial intelligence tools into our systems for specific use cases reviewed by legal and information security. In addition, our vendors may incorporate generative artificial intelligence tools into their offerings without disclosing this use to us, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If we, our vendors, or our third-party partners experience an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. We also expect to see increasing government and supranational regulation related to artificial intelligence use and ethics, which may also significantly increase the burden and cost of research, development and compliance in this area. For example, the EU's Artificial Intelligence Act, or the AI Act, the world's first comprehensive AI law, is entered into force in Spring 2024 and, with some exceptions, become effective 24 months thereafter. This legislation imposes significant obligations on providers and deployers of high risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems.

Likewise, in the United States, several states, including Colorado and California, passed laws that will take effect in 2026, to regulate various uses of artificial intelligence, including to make consequential decisions. In addition, various federal regulators have issued guidance and focused enforcement efforts on the use of AI in regulated sectors. The FDA, for example, issued guidance on the use of artificial intelligence in medical devices, requiring detailed risk management and review processes to obtain approvals. If we develop or use AI systems governed by these laws or regulations, we will need to meet higher standards of data quality, transparency, monitoring and human oversight, and we would need to adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements, with the potential for significant enforcement or litigation in the event of any perceived non-compliance. If we develop or use AI systems that are governed by the AI Act, it may necessitate ensuring higher standards of data quality, transparency, and human oversight, as well as adhering to specific and potentially burdensome and costly ethical, accountability, and administrative requirements. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information, and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

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

Our operations, and those of our contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, pandemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Any future acquisitions, in-licensing or strategic partnerships may increase our capital requirements, dilute our stockholders, divert our management's attention, cause us to incur debt or assume contingent liabilities and subject us to other risks.

We may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;
- the issuance of our equity securities which would result in dilution to our stockholders;
- assimilation of operations, intellectual property, products and product candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product candidates and initiatives in pursuing such an acquisition or strategic partnership;
- spend substantial operational, financial and management resources in integrating new businesses, technologies and products;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology and/or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, we may incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

We or the third parties upon whom we depend on may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities on which we rely, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. For example, following Hurricane Maria, shortages in production and delays in a number of medical supplies produced in Puerto Rico resulted, and any similar interruption due to a natural disaster affecting us or any of our third-party manufacturers could materially delay our operations.

We expect to significantly expand our organization, including building sales and marketing capability and creating additional infrastructure to support our operations as a public company, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of sales and marketing and finance and accounting. 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 our limited experience in managing 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 or stretch our management and business development resources in a way that we may not anticipate. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any current or future product candidates that we may develop.

We will face an inherent risk of product liability exposure related to the testing of our current or future product candidates in human clinical trials and will face an even greater risk if we commercially sell any current or future product candidates that we may develop. Claims could also be asserted under the state consumer production acts. If we cannot successfully defend ourselves against claims that our current or future product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any current or future product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- a diversion of management's time and resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- a decline in our stock price; and
- the inability to commercialize any current or future product candidates that we may develop.

While we maintain product liability insurance, we anticipate that we will need to increase our insurance coverage as we conduct additional clinical trials and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain product liability insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Our employees and independent contractors, including principal investigators, consultants, commercial collaborators, service providers and other vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.

We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, any future commercial collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; the U.S. federal and state fraud and abuse laws, data privacy and security laws and other similar non-United States laws; or laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third-parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to 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 and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other United States federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, imprisonment,

other sanctions, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Our Common Stock

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

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 the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

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

Based on the beneficial ownership of our common stock as of December 31, 2024, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 52.6% of our outstanding common stock. As a result, these stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, amendment of our organizational documents, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity over a three year period), the corporation's ability to use its pre-change net operating loss, or NOL, carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. Our gross operating losses and tax credits may also be impaired or restricted under state law. As of December 31, 2024, we had federal gross operating loss carryforwards of approximately $209.8 million, state gross operating loss carryforwards of $183.6 million, and foreign gross operating loss carryforwards of $0.7 million. Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating the U.S. federal and state taxable income. As a result, the amount of the gross operating loss and tax credit carryforwards presented in our financial statements could be limited and may expire unutilized. Under current law, unused U.S. federal gross operating loss carryforwards generated in taxable years beginning after December 31, 2017 are not subject to expiration and may be carried forward indefinitely. For taxable years beginning after December 31, 2020, however, the deductibility of such U.S. federal NOLs is limited to 80% of our taxable income in such taxable years.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

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

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

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

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

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

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

Our amended and restated bylaws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, or our amended and restated certificate of incorporation or our amended and amended and restated bylaws (including the interpretation, validity or enforceability thereof) or (iv) any action asserting a claim that is governed by the internal affairs doctrine, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws will further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or 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 capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the U.S. federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, these forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of 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 are "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 United States 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.

If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could harm our business.

Anti-takeover provisions in our amended and restated certificate of incorporation and amended and restated bylaws and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management and, therefore, decrease the trading price of our common stock.

Our tenth amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors, or Board, that our stockholders might consider favorable. Some of these provisions include:

- a Board divided into three classes serving staggered three-year terms, such that not all members of the Board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of the stockholders may be called only by the Board acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office, and special meetings of stockholders may not be called by any other person or persons;
- advance notice requirements for stockholder proposals and nominations for election to our Board;
- a requirement that no member of our Board may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds (2/3) of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than a majority of all outstanding shares of our voting stock to amend any bylaws by stockholder action and not less than two-thirds (2/3) of all outstanding shares of our voting stock to amend specific provisions of our certificate of incorporation; and
- the authority of the Board to issue preferred stock on terms determined by the Board without stockholder approval, which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our tenth amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our Board or initiate actions that are opposed by the then-current Board and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our Board could cause the market price of our common stock to decline.

Future sales and issuances of our common stock or rights to acquire shares of our common stock, could result in additional dilution to the ownership of our stockholders and cause the market price of our common stock to decline significantly.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could be granted rights superior to our existing stockholders. In March 2024, we filed a registration statement on Form S-3 relating to the registration of our common stock, preferred stock, debt securities, warrants and units or any combination thereof. Concurrently with the filing of such registration statement, we filed an "at-the-market" offering prospectus supplement, which provides for the offering, issuance and sale by us of shares of our common stock from time to time for aggregate gross proceeds of up to $75 million in sales deemed to be "at-the-market offerings" as defined by the Securities Act. Any sale or issuance of securities pursuant to this registration statement or otherwise may result in dilution to our stockholders and may cause the market price of our stock to decline. Furthermore, new investors purchasing securities that we may issue and sell in the future could obtain rights superior to the rights of our existing stockholders.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. As of December 31, 2024, we have 49,998,279 shares of common stock outstanding. Significant portions of these shares are held by a small number of stockholders, including persons who were our stockholders prior to our IPO. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock. Moreover, certain shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also registered or intend to register all shares of common stock that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. In addition, our directors, executive officers and certain affiliates may establish programmed selling plans under Rule 10b5-1 of the Exchange Act for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

General Risk Factors

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for violations.

Among other matters, the U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase in time. We plan to engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or non-performance by financial institutions or transactional counterparties, could adversely affect our company's current and projected business operations and its financial condition and results of operations.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the

financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems.

Inflation and rapid increases in interest rates have led to a decline in the trading value of previously issued government securities with interest rates below current market interest rates. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $25 billion of loans to financial institutions secured by certain of such government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, widespread demands for customer withdrawals or other liquidity needs of financial institutions for immediately liquidity may exceed the capacity of such program. There is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion.

Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect our company, the financial institutions with which we have credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. These factors could involve financial institutions or financial services industry companies with which we have financial or business relationships, but could also include factors involving financial markets or the financial services industry generally.

The results of events or concerns that involve one or more of these factors could include a variety of material and adverse impacts on our current and projected business operations and our financial condition and results of operations. These could include, but may not be limited to, the following:

- delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- loss of access to revolving existing credit facilities or other working capital sources and/or the inability to refund, roll over or extend the maturity of, or enter into new credit facilities or other working capital resources;
- potential or actual breach of contractual obligations that require us to maintain letters of credit or other credit support arrangements;
- potential or actual breach of financial covenants in our credit agreements or credit arrangements;
- potential or actual cross-defaults in other credit agreements, credit arrangements or operating or financing agreements; or
- termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by our customers or suppliers, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. For example, a customer may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy, or a supplier may determine that it will no longer deal with us as a customer. In addition, a customer or supplier could be adversely affected by any of the liquidity or other risks that are described above as factors that

could result in material adverse impacts on our company, including but not limited to delayed access or loss of access to uninsured deposits or loss of the ability to draw on existing credit facilities involving a troubled or failed financial institution. Any customer or supplier bankruptcy or insolvency, or the failure of any customer to make payments when due, or any breach or default by a customer or supplier, or the loss of any significant supplier relationships, could result in material losses to us and may have material adverse impacts on our business.

Our employees, independent contractors, consultants, academic collaborators, partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, academic collaborators, partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with the laws of the FDA, the EMA and comparable foreign regulatory authorities, provide true, complete and accurate information to the FDA, the EMA and comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain the FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by our employees, independent contractors, consultants, academic collaborators, partners and vendors, and the precautions we take to detect and prevent such activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of civil, criminal and administrative penalties, damages, monetary fines, imprisonment, disgorgement, possible exclusion from participation in government healthcare programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings and the curtailment of our operations.

We are an "emerging growth company" and a "smaller reporting company" and we cannot be certain if the reduced reporting requirements applicable to "emerging growth companies" and "smaller reporting companies" will make our common stock less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act. For as long as we continue to be an "emerging growth company," we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (1) not being required to comply with the independent auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Section 404, (2) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (3) exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not approved previously. In addition, as an "emerging growth company," we are only required to provide two years of audited financial statements and two years of selected financial data in our periodic reports.

We will remain an "emerging growth company" until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the closing 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," which requires the market value of our common stock that is held by non-affiliates to exceed $700.0 million as of the prior June 30, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Even after we no longer qualify as an "emerging growth company," we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the independent auditor attestation requirements of Section 404 and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may 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 share price may be more volatile.

Under the JOBS Act, "emerging growth companies" can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to take advantage of the benefits of this extended transition period. Our financial statements may therefore not be comparable to those of companies that comply with such new or revised accounting standards. Until the date that we are no longer an "emerging growth company" or affirmatively and irrevocably opt out of the exemption provided by Section 7(a)(2)(B) of the Securities Act, upon issuance of a new or revised accounting standard that applies to our financial statements and that has a different effective date for public and private companies, we will disclose the date on which adoption is required for non-emerging growth companies and the date on which we will adopt the recently issued accounting standard.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We may continue to be a "smaller reporting company" until (i) the market value of our stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million as of the prior June 30. If we are a "smaller reporting company" at the time we cease to be an "emerging growth company," we may continue to rely on exemptions from certain disclosure requirements that are available to "smaller reporting companies." Specifically, as a "smaller reporting company" we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, "smaller reporting companies" have reduced disclosure obligations regarding executive compensation.

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

The trading price of our common stock is highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. As a result of this volatility, you may not be able to sell your common stock at or above the price you paid for your common stock. The market price for our common stock may be influenced by many factors, including the other risks described in the section of this Annual Report titled "Risk Factors" and the following:

- results of preclinical studies and results or enrollment of clinical trials of bel-sar or our future product candidates, or those of our potential future competitors or our existing or future collaborators;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our product candidates;
- the success of future competitive products or technologies;
- introductions and announcements of new products by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our products, clinical trials, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, products or product candidates;
- developments concerning any future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- market conditions in the pharmaceutical and biotechnology sectors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for bel-sar or our future product candidates and products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;

- speculation in the press or investment community;
- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- natural disasters, pandemics and other calamities;
- acts of war or periods of widespread civil unrest, including the increasingly volatile global economic conditions resulting from the Russia-Ukraine conflict and the conflict in the Middle East; and
- general economic, industry, and market conditions, including inflationary pressures.

In addition, the stock market in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme price and volume fluctuations that have been often unrelated or disproportionate to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

In the past, securities class action litigation has often been brought against public companies following declines in the market price of their securities. This risk is especially relevant for biopharmaceutical companies, which have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and our resources, which could harm our business.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management devotes substantial time to compliance initiatives.

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act and rules implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our Board, our Board committees or as executive officers. The increased costs may require us to reduce costs in other areas of our business or increase the prices of our products once commercialized. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an "emerging growth company," we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. In addition, for as long as we are a "smaller reporting company" with less than $100 million in annual revenue, we would be exempt from the requirement to obtain an external audit on the effectiveness of internal control over financial reporting provided in Section 404(b) of the of the Sarbanes-Oxley Act of 2002. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In additional, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

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

We are subject to the periodic reporting requirements of the Exchange Act. We have designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC.

However, 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 will be 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 due to error or fraud may occur and not be detected.

Global economic uncertainty and unfavorable global economic conditions caused by political instability, changes in trade agreements and conflicts, such as the Russia-Ukraine conflict and the conflict in the Middle East, could adversely affect our business, financial condition, results of operations or prospects.

Our business, financial condition, results of operations or prospects could be adversely affected by unstable economic and political conditions within the United States and foreign jurisdictions, including as a result of an economic downturn and geopolitical events, such as changes in U.S. federal policy that affect the geopolitical landscape. Changes to policy implemented by the U.S. Congress, the Trump administration or any new administration have impacted and may in the future impact, among other things, the U.S. and global economy, international trade relations, unemployment, immigration, healthcare, taxation, the U.S. regulatory environment, inflation and other areas. For example, during the prior Trump administration, increased tariffs were implemented on goods imported into the United States, particularly from China, Canada, and Mexico. On February 1, 2025, the United States imposed a 25% tariff on imports from Canada and Mexico, which were subsequently suspended for a period of one month, and a 10% additional tariff on imports from China. Historically, tariffs have led to increased trade and political tensions, between not only the United States and China, but also between the United States and other countries in the international community. In response to tariffs, other countries have implemented retaliatory tariffs on U.S. goods. 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. Until we know what policy changes are made, whether those policy changes are challenged and subsequently upheld by the court system and how those changes impact our business and the business of our competitors over the long term, we will not know if, overall, we will benefit from them or be negatively affected by them.

In addition, the current military conflict between Russia and Ukraine and the armed conflict in Israel and the Gaza Strip could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions that may be initiated by nations including the United States, the EU or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and/or our supply chain, our CROs, CDMOs and other third parties with which we conduct business. A severe or prolonged economic downturn or political unrest could result in a variety of risks to our business, including but not limited to weakened demand for our product candidates 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, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current political and economic climate and financial market conditions could adversely impact our business.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management and Strategy

We have implemented cybersecurity risk management procedures, in accordance with our risk profile and business size, that are designed to identify, assess, and mitigate risks from current and emerging cybersecurity threats. Our cybersecurity procedures, which are informed by the National Institute of Standards and Technology cybersecurity framework, are supported by a third-party managed services provider that assists us in managing our information technology systems.

Our cybersecurity procedures are comprised of a variety of tools designed to protect our data and information technology systems, including but not limited to endpoint protection and network security measures, that are supported by our third-party service providers. We also have a process to require our employees to undergo cybersecurity awareness training. Further, we have a process to review risks to our company in connection with certain third-party providers and vendors, as appropriate.

To date, we have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition; however, like other companies in our industry, we and our third-party information technology service providers and vendors have from time to time experienced threats that could affect our information or systems. For more information, see, "*Risk Factors*," in this Annual Report on Form 10-K.

Cybersecurity Governance

Our cybersecurity program is managed and directed by our Head of Information Technology, or IT, who has nearly thirty years of experience in information technology and information systems management. Our Head of IT reports to our Chief Legal Officer and Secretary. Our Cybersecurity Governance Team, which is made up of representatives from across the organization, is responsible for oversight of cybersecurity risks and addressing potential cybersecurity risks to business programs, employees, clients, vendors and partners.

Our Board has delegated oversight of our cybersecurity risk management program to our Audit Committee, per the Audit Committee charter. Our Head of IT provides periodic updates to the Audit Committee regarding our cybersecurity risk management program, including information about cybersecurity risk management governance, as well as status updates on plans intended to enhance the overall cybersecurity posture of our company, as applicable. In the event of a cybersecurity incident, we have established a process for escalation to the Audit Committee as well as our Board, as appropriate.

Item 2. Properties.

Our corporate headquarters are located in Boston, Massachusetts, where we lease and occupy approximately 29,836 square feet of office and laboratory space at 80 Guest Street, Boston, MA 02135. The current term of our Boston lease expires in August 2032.

We believe that our facilities are adequate for our current needs and for the foreseeable future. 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 subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of December 31, 2024, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

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 has been listed on the Nasdaq Global Market since November 3, 2021. Our common stock trades under the symbol "AURA". Prior to this time, there was no public market for our common stock.

Holders of Record

As of March 19, 2025, we had approximately 53 stockholders of record for our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid cash dividends on our capital stock. We anticipate that we will retain all available funds and any future earnings, if any, for use in the operation of our business and do not anticipate paying cash dividends in the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Use of Proceeds from Initial Public Offering

None.

Stock Performance Graph

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange act, and are not required to provide a performance graph.

Recent Sales of Unregistered Equity Securities

None.

Issuer Purchaser of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Item 6. [Reserved]

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

The following discussion and analysis should be read in conjunction with the audited consolidated financial statements and related notes included elsewhere in this Annual Report. This discussion and analysis and other parts of this Annual Report contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under Part I, Item 1A, "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. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biotechnology company developing precision therapies to treat solid tumors designed to preserve organ function. Our lead candidate bel-sar is in late-stage clinical development for the treatment of patients with primary choroidal melanoma and is also in clinical development for other ocular oncology indications and bladder cancer.

There is significant unmet need for novel treatments for patients with choroidal melanoma, given the limitations of the current standard of care, or SoC, and patient reluctance to undergo radiotherapy in the form of either plaque brachytherapy or proton beam therapy, both highly-invasive therapies that result in significant vision loss, and potential legal blindness in the treated eye. Enucleation, or surgical removal of the affected eye, is another treatment option for patients with choroidal melanoma, in which patients lose all vision without the possibility of vision restoration. We are evaluating the safety and efficacy of bel-sar as a potential vision-sparing therapy in our ongoing global Phase 3 CoMpass trial for the first-line treatment of adult patients with small choroidal melanoma and indeterminate lesions, or early-stage choroidal melanoma. Moreover, we intend to assess the safety and efficacy of bel-sar in treating a range of other solid tumors, beginning with metastases of the choroid and bladder cancer where bel-sar is in clinical development. We believe bel-sar, if approved, has the potential to change the current treatment paradigm for patients with ocular and urologic cancers and other solid tumors.

Bel-sar has shown clinical benefit and has been generally well-tolerated in clinical trials to date. In a Phase 2 study (ClinicalTrials.gov ID: NCT04417530) evaluating suprachoroidal administration of bel-sar for the first-line treatment of early-stage choroidal melanoma, patients were closely monitored over a twelve-month follow-up period to assess tumor control, visual acuity preservation, and tumor growth rate. A total of 22 patients were enrolled in the study. Bel-sar achieved an 80% tumor control rate (n=8/10) among Phase 3-eligible patients who received the therapeutic regimen, with complete cessation of growth following treatment among responders (post-treatment average growth rate of 0.011 mm/yr among responders compared to 0.351 mm/yr prior to study entry; $p<0.0001$). Visual acuity preservation was achieved in 90% of these ten patients. Importantly, 80% of these ten patients were at high risk for vision loss with tumors close to the fovea or optic disc, highlighting the potential for vision preservation with this novel class of drugs. The safety profile of bel-sar was highly favorable in all participants regardless of dose. We believe the Phase 2 results are a significant achievement considering the typically poor prognosis associated with choroidal melanoma, a rare and life-threatening ocular cancer, where there are no approved vision-preserving therapies to date. We believe bel-sar has the possibility to transform the field of ocular oncology beyond choroidal melanoma and we plan to expand clinical development in two additional indications: metastases to the choroid and cancers of the ocular surface. We have initiated a Phase 2 clinical trial in metastases to the choroid and have activated sites with patients in prescreening. We also plan to continue to advance our preclinical work designed to be IND-enabling in cancers of the ocular surface.

VDCs are a novel class of drugs with a dual mechanism of action that promote cancer cell death by both the delivery of the cytotoxic payload to generate acute necrosis and activation of a secondary immune mediated response. Bel-sar, our lead VDC candidate, consists of modified capsid proteins of the human papilloma virus, or HPV, conjugated to hundreds of light-activated molecules.

Light activation of bel-sar is designed to result in precise tumor cell killing with minimal damage to surrounding healthy tissues. In the absence of bel-sar activation or binding to the tumor cell membrane, there is no cytotoxic effect. Multiple light activations, following a single dose of bel-sar, increase antitumor activity because of the reoxygenation of the tumor and the photostability of bel-sar. Finally, acute necrosis triggers immunogenic cell death leading to the generation of an adaptive, long-term antitumor immune response. The tumor targeting specificity of

VDCs is driven by the selective binding of the VLPs to a subset of modified tumor associated glycosaminoglycans, or GAGs, that are part of the heparan sulphate chain of heparan sulfate proteoglycans or HSPGs, expressed on the tumor cell membrane. This targeting mechanism enables the delivery of multiple types of cytotoxic payloads directly to a wide range of solid tumors.

Beyond ocular cancers, bel-sar is in early-stage clinical development in bladder cancer. Bladder cancer is the ninth most common cancer worldwide and it is diagnosed early as non-muscle invasive bladder cancer, or NMIBC, with a prevalence of approximately 80,000 cases per year in the United States. Despite the early diagnosis, patients with NMIBC have a high risk of recurrence and progression with current SoC treatments. In March 2025, we announced positive data from our Phase 1 trial in NMIBC (NCT05483868).

We were incorporated as a Delaware corporation in 2009 and our headquarters are located in Boston, Massachusetts. Since our inception, we have focused our efforts on identifying and developing potential product candidates, conducting preclinical studies and clinical trials, organizing and staffing our company, business planning, establishing our intellectual property portfolio, raising capital, conducting discovery, research and development activities and providing general and administrative support for these operations. We do not have any product candidates approved for sale and have not generated any revenue to date. We have funded our operations primarily through the sale of convertible preferred stock, common stock, and warrants. From inception through December 31, 2024, we have raised an aggregate of approximately $419.9 million of gross proceeds primarily from private placements of our equity and convertible preferred stock as well as through the issuance of our common stock. On November 9, 2023, we issued and sold 11,000,000 shares of common stock at a price to the public of $9.00 per share for aggregate gross proceeds of $99.0 million, or the 2023 Follow-On Offering. We received approximately $92.6 million in net proceeds from the 2023 Follow-On Offering after deducting underwriting discounts and commissions and offering expenses. On December 5, 2022, we issued and sold 7,705,000 shares of common stock, including the full exercise of the underwriters' option to purchase additional shares at a price to the public of $12.00 per share, for aggregate gross proceeds of $92.5 million, or the 2022 Follow-On Offering. We received approximately $86.7 million in net proceeds from the 2022 Follow-On Offering after deducting underwriting discounts, commissions and offering expenses. On November 1, 2022, we filed a shelf registration statement on Form S-3, or the 2022 Shelf, with the SEC in relation to the registration of up to an aggregate offering price of $250.0 million of common stock, preferred stock, debt securities, warrants and units or any combination thereof. We also simultaneously entered into an Open Market Sale Agreement℠, or the Sales Agreement, with Jefferies LLC, or the Sales Agent, to provide for the offering, issuance and sale by us of up to an aggregate of $75.0 million of its common stock from time to time in "at-the-market" offerings, or the ATM, under the 2022 Shelf and subject to the limitations thereof. In connection with the 2023 Follow-On Offering, on November 6, 2023, we delivered written notice to Jefferies that we were suspending and terminating the prospectus related to the shares issuable in the ATM pursuant to the terms of the Sales Agreement. During the year ended December 31, 2023, we issued a total of 261,807 shares of common stock at an average price of $12.49 for aggregate gross proceeds of $3.3 million under the ATM. On March 27, 2024, we filed a new shelf registration statement on Form S-3, or the 2024 Shelf, with the SEC in relation to the registration of up to an aggregate offering price of $350.0 million of common stock, preferred stock, debt securities, warrants and units or any combination thereof, which superseded the 2022 Shelf. The 2024 Shelf included a prospectus supplement to provide for offerings in the ATM under the Sales Agreement. We did not issue any shares of common stock during the year ended December 31, 2024 under the ATM.

We have incurred significant operating losses in every year since our inception in 2009 and have not generated any revenue. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our ability to generate product revenue sufficient to achieve profitability will depend on the successful development and commercialization of one or more of our product candidates. Our net losses were $86.9 million and $76.4 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $374.2 million. In addition, our losses from operations may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

We anticipate that our expenses and capital requirements will increase substantially in connection with our ongoing activities, particularly as we advance the preclinical studies and clinical trials of our product candidates. In addition, we incur additional costs associated with operating as a public company. We expect that our expenses and capital requirements will increase substantially if and as we:

- conduct our current and future clinical trials of bel-sar;
- progress the preclinical and clinical development of new indications;

- establish our manufacturing capability, including developing our CDMO relationships;
- seek to identify and develop additional product candidates;
- seek regulatory approval of our current and future product candidates;
- expand our operational, financial, and management systems and increase personnel, including personnel to support our preclinical and clinical development, manufacturing and commercialization efforts;
- maintain, expand and protect our intellectual property portfolio; and
- incur additional legal, accounting, or other expenses in operating our business, including the additional costs associated with operating as a public company.

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, collaborations or other strategic transactions. 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.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain marketing approval for our product candidates. The lengthy process of securing marketing approvals for new drugs requires the expenditure of substantial resources. Any delay or failure to obtain regulatory approvals would materially adversely affect the development efforts of our product candidates and our business overall. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2024, we had cash and cash equivalents and marketable securities of $151.1 million. We believe that our existing cash and cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into the second half of 2026. 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. See “*Liquidity and Capital Resources*” below.

Components of Our Results of Operations

Revenue

Since inception, we have not generated any revenue and do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for one or more of our product candidates are successful and result in regulatory approval, or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements. We cannot predict if, and when, or to what extent, we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts and the development of our bel-sar program, and include:

- employee-related expenses, including salaries, benefits and stock-based compensation expense for employees engaged in research and development functions;
- fees paid to consultants for services directly related to our product development and regulatory efforts;
- expenses associated with conducting preclinical studies and clinical trials performed by ourselves, outside vendors or academic collaborators;
- expenses incurred under agreements with contract research organizations, or CROs, as well as consultants that conduct and provide supplies for our preclinical studies and clinical trials;

- the cost of manufacturing bel-sar, including the potential cost of CDMOs that manufacture product for use in our preclinical studies and clinical trials and perform analytical testing, scale-up and other services in connection with our development activities;
- costs associated with preclinical activities and clinical development activities;
- costs associated with our intellectual property portfolio;
- costs related to compliance with regulatory requirements; and
- allocated expenses for utilities and other facility-related costs.

We expense research and development costs as incurred. Costs for external development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses. We allocate our direct external research and development costs across the entire bel-sar program. Preclinical expenses consist of external research and development costs associated with activities to support our current and future clinical programs, but are not allocated by specific indications due to the overlap of the potential benefit of those efforts across the entire bel-sar program.

Research and development activities are central to our business. We expect that our research and development expenses will increase for the foreseeable future as we continue clinical development for bel-sar and continue to discover and develop additional product candidates. If any of our product candidates enter into later stages of clinical development, they will generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive and finance functions. General and administrative expenses also include professional fees for legal, accounting, auditing, tax and consulting services; travel expenses; and facility-related expenses, which include allocated expenses for rent and maintenance of facilities and other operating costs not included in research and development.

We expect that our general and administrative expenses will increase in the near-term as we continue to build a team to support our administrative, accounting and finance, communications, legal and business development efforts. We expect to incur increased expenses associated with our growth, including costs of accounting, audit, legal, regulatory and tax compliance services; director and officer insurance costs; and investor and public relations costs.

Other Income (Expense)

Our other income (expense) consists of accretion, interest income and realized gains and losses on marketable securities, interest income on our invested cash balances, and gains and losses on disposals of equipment.

Income Tax Provision, Net

For the year ended December 31, 2024, we recorded a $0.1 million income tax provision related to current state income taxes. Since our inception, we have not recorded any U.S. federal or state tax benefits for our net operating loss carryforwards or research and development tax credits due to the realizability of future taxable income to utilize these tax attributes. As of December 31, 2024, we had accumulated federal, state, and foreign net operating loss carryforwards of approximately $209.8 million, $183.6 million, and $0.7 million, respectively, which may be available to offset future taxable income before applicable expiration periods. As of December 31, 2024, we had federal and state research and development credit carryforwards of $11.3 million and $2.9 million, respectively, which may be available to offset future income tax liabilities before applicable expiration periods. We have recorded a full valuation allowance against the tax benefits, as the determination of the realization of the deferred tax assets was not determined to be more likely than not.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023:

	Year Ended December 31,		
	2024	2023	Change
	(in thousands)		
Operating expenses:			
Research and development	$ 73,302	$ 65,232	$ 8,070
General and administrative	22,814	19,759	3,055
Total operating expenses	96,116	84,991	11,125
Loss from operations	(96,116)	(84,991)	(11,125)
Other income (expense):			
Interest income, including amortization and accretion income	9,429	8,588	841
Gain on disposal of property and equipment	—	208	(208)
Other expense	(120)	(76)	(44)
Total other income	9,309	8,720	589
Loss before income taxes	(86,807)	(76,271)	(10,536)
Income tax provision, net	(112)	(137)	25
Net loss	$ (86,919)	$ (76,408)	$ (10,511)

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2024 and 2023:

	Year Ended December 31,		
	2024	2023	Change
	(in thousands)		
Preclinical	$ 1,651	$ 805	$ 846
Clinical trials	22,512	17,310	5,202
Manufacturing development	15,977	12,992	2,985
Personnel/overhead expenses	33,162	34,125	(963)
Total research and development expenses	$ 73,302	$ 65,232	$ 8,070

Research and development expenses increased to $73.3 million for the year ended December 31, 2024, from $65.2 million for the year ended December 31, 2023, primarily due to ongoing clinical and CRO costs associated with the progression of our Phase 3 global trial, and manufacturing and development costs for bel-sar.

General and Administrative Expenses

General and administrative expenses increased to $22.8 million for the year ended December 31, 2024, from $19.8 million for the year ended December 31, 2023, primarily driven by personnel expenses, as well as increases in general corporate expenses related to the global growth of our company.

Liquidity and Capital Resources

To date we have funded our operations primarily through the sale of convertible preferred stock, warrants and common stock. Through December 31, 2024, we have raised an aggregate of approximately $419.9 million of gross proceeds primarily from private placements of our equity and convertible preferred stock and warrants, as well as through the issuance of our common stock. On November 9, 2023, we issued and sold 11,000,000 shares of common stock at a price to the public of $9.00 per share for aggregate gross proceeds of $99.0 million in the 2023 Follow-On Offering. We received approximately $92.6 million in net proceeds from the 2023 Follow-On Offering after deducting underwriting discounts and commissions and offering expenses. On December 5, 2022, we issued and sold 7,705,000 shares of common stock, including the full exercise of the underwriters' option to purchase additional shares at a price to the public of $12.00 per share for aggregate gross proceeds of $92.5 million in the 2022 Follow-On Offering. We received approximately $86.7 million in net proceeds from the 2022 Follow-On Offering after deducting underwriting discounts, commissions and offering expenses. On November 1, 2022, we filed the 2022 Shelf with the SEC in relation to the registration of up to an aggregate offering price of $250.0 million of common stock, preferred stock, debt securities, warrants and units or any combination thereof. We also simultaneously entered into the Sales Agreement with the Sales Agent to provide for the offering, issuance and sale by us of up to an aggregate of $75.0 million of our common stock from time to time in the ATM under the 2022 Shelf and subject to the limitations thereof. In connection with the 2023 Follow-On Offering, on November 6, 2023, we delivered written notice to Jefferies that we were suspending and terminating the prospectus related to the shares issuable in the ATM pursuant to the terms of the Sales Agreement. During the year ended December 31, 2023, we issued a total of 261,807 shares of common stock at an average price of $12.49 for aggregate gross proceeds of $3.3 million under the ATM. On March 27, 2024, we filed a new shelf registration statement on Form S-3, or the 2024 Shelf, with the SEC in relation to the registration of up to an aggregate offering price of $350.0 million of common stock, preferred stock, debt securities, warrants and units or any combination thereof, which superseded the 2022 Shelf. The 2024 Shelf included a prospectus supplement to provide for offerings in the ATM under the Sales Agreement. We did not issue any shares of common stock during the year ended December 31, 2024 under the ATM.

The following table summarizes our cash flows for each of the periods presented:

	Year Ended December 31,	
	2024	2023
	(in thousands)	
Net cash used in operating activities	$ (79,805)	$ (63,847)
Net cash provided by (used in) investing activities	68,821	(113,963)
Net cash provided by financing activities	1,595	97,290
Net decrease in cash, cash equivalents, and restricted cash	$ (9,389)	$ (80,520)

Operating Activities

During the year ended December 31, 2024, net cash used in operating activities was $79.8 million, primarily due to our net loss of $86.9 million and an increase in clinical and CRO prepaid expenses and other assets for belsar, partially offset by an increase in stock-based compensation expense.

During the year ended December 31, 2023, net cash used in operating activities was $63.8 million, primarily due to our net loss of $76.4 million, partially offset by an increase in accrued clinical and CRO expenses for belsar.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2024 was $68.8 million, primarily due to maturities of marketable securities, partially offset by purchases of marketable securities and property and equipment.

Net cash used in investing activities for the year ended December 31, 2023 was $114.0 million, primarily due to purchases of marketable securities and property and equipment, partially offset by proceeds from maturities of marketable securities.

Financing Activities

During the year ended December 31, 2024, net cash provided by financing activities was $1.6 million from proceeds from stock option exercises and ESPP purchases.

During the year ended December 31, 2023, net cash provided by financing activities was $97.3 million from the net proceeds from the 2023 Follow-On Offering, ATM draw-downs, and proceeds from stock option exercises and ESPP purchases.

Funding Requirements

Our plan of operation is to continue implementing our business strategy, continue research and development of bel-sar and any other product candidates we may acquire or develop and continue to expand our research pipeline and our internal research and development capabilities. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our current and future product candidates. In addition, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or terminate our research and development programs or future commercialization efforts. Our future capital requirements will depend on many factors, including:

- the scope, timing, progress, costs, and results of discovery, preclinical development, and clinical trials for our current and future product candidates;
- the number of clinical trials required for regulatory approval of our current and future product candidates;
- the costs, timing, and outcome of regulatory review of any of our current and future product candidates;
- the cost of manufacturing clinical and commercial supplies of our current and future product candidates;
- the costs and timing of future commercialization activities, including 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, including any claims by third parties that we are infringing upon their intellectual property rights;
- our ability to maintain existing, and establish new, strategic collaborations, licensing, or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty, or other payments due under any such agreement;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- expenses to attract, hire and retain, skilled personnel;
- the costs of operating as a public company;
- if our product candidates are approved, our ability to establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payors;
- the effect of competing technological and market developments;
- the extent to which we acquire or invest in businesses, products, and technologies; and
- unfavorable global economic conditions, which may exacerbate the magnitude of the factors discussed above.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. As of December 31, 2024, we had cash, cash equivalents, and marketable securities of $151.1 million. Based on our research and development plans, we believe that our existing cash, cash equivalents, and marketable securities will be sufficient to fund our operations into the second half of 2026. 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.

Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations from the sale of additional equity or debt financings, or other capital which comes in the form of strategic collaborations, licensing, or other arrangements. In the event that additional financing is required, we may not be able to raise it on terms acceptable to us, or at all. If we raise additional funds through the issuance of equity or convertible preferred stock, it may result in dilution to our existing stockholders. Debt financing or preferred equity financing, if available, may result in increased fixed payment obligations, and the existence of securities with rights

that may be senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations.

If we raise funds through strategic collaboration, licensing or other arrangements, we may relinquish significant rights or grant licenses on terms that are not favorable to us. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Material Cash Requirements

The following table summarizes our contractual obligations and commitments as of December 31, 2024.

		Payments Due by Period			
	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
			(in thousands)		
Operating lease commitments	$ 27,653	$ 3,306	6,913	7,327	10,107
Total	$ 27,653	$ 3,306	$ 6,913	$ 7,327	$ 10,107

(1) Amounts in the table above reflect payments due for our lease of office and lab space in Boston, MA, that expires in August 2032.

On May 16, 2022, we entered into an office and laboratory lease in Boston, MA with an initial 10-year term and one renewal option to extend the lease for an additional seven years. The lease commenced on August 1, 2022.

Except as disclosed in the table above, we have no long-term debt or finance leases and no material non-cancelable purchase commitments with service providers, as we have generally contracted on a cancelable, purchase-order basis. We enter into contracts in the normal course of business with equipment and reagent vendors, CROs, CDMOs and other third parties for clinical trials, preclinical research studies and testing and manufacturing services. These contracts are cancelable by us upon prior notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation. We have also acquired exclusive and non-exclusive rights to use, research, develop and offer for sale certain products and patents under license agreements. The license agreements obligate us to make payments to the licensors for license fees, milestones, license maintenance fees and royalties. These payments are not included in the preceding table as the amount and timing of such payments are not known.

Critical Accounting Policies and Significant Judgments and Estimates

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

While our significant accounting policies are described in greater detail in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Research and Development Costs

We expense all costs in performing research and development activities in the periods in which they are incurred. Research and development expenses include salaries and benefits, stock-based compensation expense, lab supplies and facility costs, as well as fees paid to nonemployees and entities that conduct certain research and development activities on our behalf and expenses incurred in connection with license agreements. Non-refundable advance payments for goods or services that will be used for rendered or future research and development activities are deferred and amortized over the period that the goods are delivered, or the related services are performed, subject to an assessment of recoverability.

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We account for our stock-based compensation as expense in the consolidated statements of operations and comprehensive loss based on the awards' grant date fair values. We account for forfeitures as they occur by reversing any expense recognized for unvested awards.

For grants of restricted stock units, we base the fair value on the stock price as of the date of grant. We estimate the fair value of options granted using the Black-Scholes option pricing model. The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to us, including stage of product development and life science industry focus. We use the simplified method as allowed by the SEC, Staff Accounting Bulletin, or SAB, No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and have no current plans to pay any dividends on our common stock. The fair value of stock-based payments is recognized as expense over the requisite service period which is generally the vesting period.

Recent Accounting Pronouncements

See Note 2 in our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our consolidated financial statements. Other than as disclosed in our consolidated financial statements, we do not expect that any recently issued accounting standards will have a material impact on our consolidated financial statements or will otherwise apply to our operations.

Emerging Growth Company and Smaller Reporting Company Status

The JOBS Act permits that an "emerging growth company" may take advantage of the extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to use the extended transition period under the JOBS Act. Accordingly, our consolidated financial statements may not be comparable to the financial statements of public companies that comply with such new or revised accounting standards. The JOBS Act also exempts us from having to provide an auditor attestation of internal control over financial reporting under Sarbanes-Oxley Act Section 404(b).

We will remain an "emerging growth company" until the earliest of: the last day of the fiscal year in which we have more than $1.235 billion in annual revenue; the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; the issuance, in any three-year period, by us of more than $1.0 billion in non-convertible debt securities; or the last day of the fiscal year ending after the fifth anniversary of our IPO.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million.

If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we will not be required to obtain a separate attestation of internal control over financial reporting, or ICFR, from an outside auditor.

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

Under SEC rules and regulations, as a smaller reporting company, we are not required to provide the information required by this item.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear beginning on page F-1 of this Annual Report for the year ended December 31, 2024.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures.

We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of December 31, 2024, our management, under the supervision of our Chief Executive Officer and Senior Vice President, Finance (Interim Principal Financial Officer and Interim Principal Accounting Officer), performed an evaluation of the effectiveness of our disclosure controls and procedures. Based on this evaluation, our Chief Executive Officer and Senior Vice President, Finance (Interim Principal Financial Officer and Interim Principal Accounting Officer) concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2024.

Management’s Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining an adequate system of internal control over financial reporting, as defined in the Exchange Act Rule 13a-15(f). Management conducted an assessment of our internal control over financial reporting based on the framework established in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework. Based on the assessment, management concluded that, as of December 31, 2024, our internal control over financial reporting was effective.

This Annual Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting as required by Section 404(c) of the Sarbanes Oxley Act of 2002. Because we qualify as an emerging growth company under the JOBS Act, management's report was not subject to attestation by our independent registered public accounting firm.

Limitations on Effectiveness of Controls and Procedures

Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Due to the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within our company have been detected. Because of these limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become ineffective because of changes in conditions or that the degree of compliance with established policies or procedures may deteriorate.

Our management, with the participation of our Chief Executive Officer and Senior Vice President, Finance (Interim Principal Financial Officer and Interim Principal Accounting Officer), has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), as of the end of the period covered by this Annual Report. Based on such evaluation, our Chief Executive Officer and Senior Vice President, Finance (Interim Principal Financial Officer and Interim Principal Accounting Officer) have concluded that as of December 31, 2024, our disclosure controls and procedures were effective to provide reasonable assurance that the information required to be disclosed by us in this Annual Report was (a) reported within the time periods specified by the SEC rules and regulations, and (b) communicated to our management, including our Chief Executive Officer and Senior Vice President, Finance (Interim Principal Financial Officer and Interim Principal Accounting Officer), to allow timely decisions regarding any required disclosure.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the year ended December 31, 2024, that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our independent registered public accounting firm will not be required to opine on our internal control over financial reporting until we are no longer an emerging growth company.

Item 9B. Other Information.

(a) None.

(b) Insider Trading Arrangements.

None of our directors or “officers,” as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, adopted or terminated a Rule 10b5-1 trading plan or arrangement or a non-Rule 10b5-1 trading plan or arrangement, as defined in Item 408(c) of Regulation S-K, during the fiscal quarter covered by this report.

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

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2024.

Item 11. Executive Compensation.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2024.

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

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2024.

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

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2024.

Item 14. Principal Accounting Fees and Services.

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2024.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) 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 on Form 10-K, incorporated into this Item by reference.

(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the financial statements or the notes thereto.

(3) Exhibits:

Exhibit Number	Description
3.1	Tenth Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect, as amended by the Certificate of Amendment, dated June 20, 2024 (incorporated by reference to Exhibit 3.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-40971) filed on August 8, 2024).
3.2	Amended and Restated Bylaws of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.2 of the Registrant's Annual Report on Form 10-K (File No. 001-40971) filed on March 23, 2022).
4.1*	Description of Securities.
4.2	Fifth Amended and Restated Investors' Rights Agreement (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 8, 2021).
10.1#	2009 Amended and Restated Stock Option and Restricted Stock Plan, and form of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-8 (File No. 333-260589) filed on October 29, 2021).
10.2#	2018 Equity 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 (File No. 333-260156) filed on October 25, 2021).
10.3#	2021 Stock Option and Incentive Plan, and form of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-8, as amended (File No. 333-260589) filed on October 29, 2021).
10.4#	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 25, 2021).
10.5#	Amended and Restated Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-40971) filed on August 8, 2024).
10.6#	Senior Executive Cash Bonus Plan (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 25, 2021).
10.7#	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 25, 2021).
10.8#	Employment Agreement between the Registrant and Elisabet de los Pinos, dated January 1, 2015, as amended on October 13, 2017 (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 25, 2021).
10.9#*^	Employment Offer Letter between the Registrant and Amy Elazzouzi, dated August 19, 2015.
10.10#^	Employment Offer Letter between the Registrant and Conor Kilroy, dated March 12, 2024 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-40971) filed on May 9, 2024).
10.11†	Exclusive Patent License Agreement with the National Institutes of Health, dated September 3, 2013 as amended (incorporated by reference to Exhibit 10.11 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 8, 2021).

10.12†	Exclusive License and Supply Agreement with Rakuten Medical, Inc. (successor-in-interest to LI-COR, Inc.), dated January 31, 2014, as amended (incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 8, 2021).
10.13†	License Agreement with Clearside Biomedical, Inc., dated July 3, 2019 (incorporated by reference to Exhibit 10.13 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 8, 2021).
10.14*%	First Amendment to License Agreement with Clearside Biomedical, Inc., dated February 23, 2022.
10.15	Lease Agreement, between the Registrant and Ice Box, LLC, dated as of May 16, 2022 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-40971) filed on August 11, 2022).
10.16#	Employment Offer Letter, dated August 9, 2023, by and between Jill Hopkins and the Registrant (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-40971) filed on November 9, 2023).
10.17#	Employment Offer Letter, dated August 10, 2023, by and between Mark Plavsic and the Registrant (incorporated by reference to Exhibit 10.17 of the Registrant's Annual Report on Form 10-K (File No. 001-40971) filed on March 27, 2024.
10.18#	Resignation and Consulting Agreement, dated September 25, 2024, by and between Julie Feder and the Registrant (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-40971) filed on November 12, 2024).
10.19#(1)	Transition and Release Agreement, dated September 25, 2024, by and between Julie Feder and the Registrant (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-40971) filed on November 12, 2024).
10.20#	Executive Severance Plan, and form of participation agreement thereunder (incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-40971) filed on November 12, 2024).
19.1*	Amended and Restated Insider Trading Policy.
21.1*	List of Subsidiaries of Registrant.
23.1*	Consent of Ernst & Young, 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 Interim 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 97.1 of the Registrant's Annual Report on Form 10-K (File No. 001-40971) filed on March 27, 2024.
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

* Filed herewith.

**These certifications are furnished to the SEC pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 and are deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, nor shall they be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such filing.

# Indicates a management contract or any compensatory plan, contract or arrangement.

† Confidential treatment has been granted for portions of this Exhibit pursuant to Rule 406 promulgated under the Securities Act of 1933, as amended.

% Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K under the Securities Act of 1933, as amended, because they are both (i) not material and (ii) the type that the Registrant treats as private or confidential. A copy of the omitted portions will be furnished to the SEC upon its request.

^ Certain information in this document (indicated by asterisks) has been excluded pursuant to Regulation S-K, Item 601(a)(6).

(1) Certain schedules and exhibits have been excluded pursuant to Regulation S-K Item 601(a)(5). The Company agrees to furnish supplementally a copy of any omitted schedule or exhibit to the SEC upon its request.

Item 16. Form 10-K Summary

Not applicable.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Aura Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Aura Biosciences, Inc. (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2024, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2016.

Boston, Massachusetts

March 24, 2025

Aura Biosciences, Inc.

Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 31,693	$ 41,063
Marketable securities	119,401	185,087
Restricted cash and deposits	—	19
Prepaid expenses and other current assets	9,529	5,625
Total current assets	160,623	231,794
Restricted cash and deposits, net of current portion	768	768
Right-of-use assets - operating lease	17,379	18,854
Other long-term assets	518	509
Property and equipment, net	3,215	3,150
Total Assets	$ 182,503	$ 255,075
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	2,304	1,787
Short-term operating lease liability	3,149	2,687
Accrued expenses and other current liabilities	9,460	7,883
Total current liabilities	14,913	12,357
Long-term operating lease liability	15,620	16,870
Total Liabilities	30,533	29,227
Commitments and Contingencies (Note 12)		
Stockholders' Equity:		
Common stock, $0.00001 par value, 150,000,000 authorized at December 31, 2024 and December 31, 2023, and 49,998,279 and 49,350,788 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	—	—
Additional paid-in capital	525,934	512,617
Accumulated deficit	(374,227)	(287,308)
Accumulated other comprehensive income	263	539
Total Stockholders' Equity	151,970	225,848
Total Liabilities and Stockholders' Equity	$ 182,503	$ 255,075

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

Aura Biosciences, Inc.

Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,	
	2024	**2023**
Operating Expenses:		
Research and development	$ 73,302	$ 65,232
General and administrative	22,814	19,759
Total operating expenses	96,116	84,991
Total operating loss	(96,116)	(84,991)
Other income (expense):		
Interest income, including amortization and accretion income	9,429	8,588
Gain on disposal of property and equipment	—	208
Other expense	(120)	(76)
Total other income	9,309	8,720
Loss before income taxes	(86,807)	(76,271)
Income tax provision, net	(112)	(137)
Net loss	(86,919)	(76,408)
Net loss per common share—basic and diluted	(1.75)	(1.93)
Weighted average common stock outstanding—basic and diluted	49,650,480	39,620,036
Comprehensive loss:		
Net loss	$ (86,919)	$ (76,408)
Other comprehensive items:		
Unrealized (loss) gain on marketable securities	(271)	611
Other	(5)	—
Total other comprehensive (loss) income	(276)	611
Total comprehensive loss	$ (87,195)	$ (75,797)

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

Aura Biosciences, Inc.

Consolidated Statements of Stockholders' Equity
(in thousands, except share data)

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income Amount	Equity
Balance, December 31, 2023	49,350,788	$—	$512,617	$(287,308)	$539	225,848
Stock-based compensation expense	—	—	11,722	—	—	11,722
Employee Stock Purchase Plan Issuance	24,477	—	177	—	—	177
Vesting of restricted stock	310,245	—	—	—	—	—
Stock option exercises	312,769	—	1,418	—	—	1,418
Unrealized loss on marketable securities	—	—	—	—	(271)	(271)
Other	—	—	—	—	(5)	(5)
Net loss	—	—	—	(86,919)	—	(86,919)
Balance, December 31, 2024	49,998,279	—	525,934	(374,227)	263	151,970

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss) Amount	Equity
Balance, December 31, 2022	37,771,918	$—	$406,555	$(210,900)	$(72)	195,583
Issuance of common stock - follow-on offering, net of issuance costs of $444	11,000,000	—	92,616	—	—	92,616
Issuance of common stock under ATM facility, net of issuance costs	261,807	—	3,170	—	—	3,170
Stock-based compensation expense	—	—	8,772	—	—	8,772
Employee Stock Purchase Plan Issuance	14,911	—	128	—	—	128
Vesting of restricted stock	43,162	—	—	—	—	—
Stock option exercises	258,990	—	1,376	—	—	1,376
Unrealized gain on marketable securities	—	—	—	—	611	611
Net loss	—	—	—	(76,408)	—	(76,408)
Balance, December 31, 2023	49,350,788	—	512,617	(287,308)	539	225,848

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

Aura Biosciences, Inc.

Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2024	**2023**
Cash flows from operating activities:		
Net loss	$ (86,919)	$ (76,408)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	1,223	1,295
Accretion on marketable securities	(4,659)	(3,992)
Other	(5)	—
Stock-based compensation expense	11,722	8,772
Gain on disposal of property and equipment	—	208
Non-cash lease expense	1,475	1,837
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(3,904)	3,579
Other long-term assets	(9)	(86)
Accounts payable	482	(1,040)
Accrued expenses and other liabilities	1,577	3,310
Operating lease liabilities	(788)	(1,322)
Net cash used in operating activities	(79,805)	(63,847)
Cash flows from investing activities:		
Purchases of property and equipment	(1,253)	(709)
Purchases of marketable securities	(59,103)	(233,651)
Proceeds from sale of marketable securities	(5)	—
Maturities of marketable securities	129,182	120,397
Net cash provided by (used in) investing activities	68,821	(113,963)
Cash flows from financing activities:		
Proceeds from exercise of stock options	1,418	1,376
Proceeds from issuance of common stock under ATM facility, net of issuance costs	—	3,170
Proceeds from follow-on issuance of common stock	—	92,616
Proceeds from ESPP purchases	177	128
Net cash provided by financing activities	1,595	97,290
Net decrease in cash, cash equivalents and restricted cash	(9,389)	(80,520)
Cash, cash equivalents and restricted cash at beginning of period	41,850	122,370
Cash, cash equivalents and restricted cash at end of period	$ 32,461	$ 41,850
Supplemental disclosure of cash flow information:		
Purchases of property and equipment in accounts payable and accrued expenses and other liabilities	$ 35	$ 94
Initial measurement of right-of-use assets and lease liabilities	—	20
Disposal of equipment	—	1,333

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statements of cash flows (in thousands):

	December 31,	
	2024	**2023**
Cash and cash equivalents, end of period	$ 31,693	$ 41,063
Short-term restricted cash, end of period	—	19
Long-term restricted cash, end of period	768	768
Cash, cash equivalents and restricted cash at end of period	$ 32,461	$ 41,850

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

1. Description of Business

Aura Biosciences, Inc., or the Company or Aura, is a clinical-stage biotechnology company developing precision therapies to treat solid tumors designed to preserve organ function. Within these consolidated financial statements, unless the context otherwise requires, references to the Company or Aura refer to Aura Biosciences, Inc. and its subsidiaries on a consolidated basis. The Company's proprietary platform is designed to enable the targeting of a broad range of solid tumors using Virus-Like Particles, that can be conjugated with drugs or loaded with nucleic acids to create Virus-Like Drug Conjugates, or VDCs. VDCs are a novel class of drugs with a dual mechanism of action that promote cancer cell death by both the delivery of the cytotoxic payload to generate acute necrosis and activation of a secondary immune mediated response. The Company's initial focus is in ocular and urologic oncology, both areas of high unmet medical need where local targeted therapies may enable early intervention. The Company is evaluating the safety and efficacy of its lead candidate, bel-sar, as a potential vision-sparing therapy in an ongoing global Phase 3 CoMpass trial for the first-line treatment of adult patients with small choroidal melanoma and indeterminate lesions, or early-stage choroidal melanoma. Bel-sar is also in Phase 2 clinical development for metastases to the choroid, is being explored for cancers of the ocular surface and is in Phase 1 clinical development in bladder cancer. The Company envisions the potential for development of bel-sar in additional therapeutic areas. Aura's headquarters are located in Boston, Massachusetts.

The Company's operations to date have consisted primarily of conducting research and development and raising capital.

The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, the successful development and commercialization of products, fluctuations in operating results and financial risks, need for additional financing or alternative means of financial support or both to fund its current operating plan, protection of proprietary technology and patent risks, compliance with government regulations, dependence on key personnel, collaborative partners, contract development and manufacturing organizations and other third-parties, competition, customer demand, management of growth, and the effectiveness of marketing by the Company.

Liquidity

Through December 31, 2024, the Company has funded its operations primarily with proceeds from the initial and additional closings of its convertible preferred stock financings, and through its initial public offering, or IPO, follow-on offering and at-the-market offering, or ATM. On November 1, 2022, the Company filed a shelf registration statement on Form S-3, or the 2022 Shelf, with the Securities and Exchange Commission, or SEC, in relation to the registration of up to an aggregate offering price of $250.0 million of common stock, preferred stock, debt securities, warrants and units or any combination thereof. The Company also simultaneously entered into the Open Market Sale Agreement℠, or Sales Agreement, with Jefferies LLC, or the Sales Agent, to provide for the offering, issuance and sale by the Company of up to an aggregate of $75.0 million of common stock from time to time in the ATM under the 2022 Shelf and subject to the limitations thereof. On November 9, 2023, the Company issued and sold 11,000,000 shares of common stock at a price to the public of $9.00 per share for aggregate gross proceeds of $99.0 million, or the 2023 Follow-On Offering. The Company received approximately $92.6 million in net proceeds from the 2023 Follow-On Offering after deducting underwriting discounts and commissions and offering expenses. In connection with the 2023 Follow-On Offering, on November 6, 2023, the Company delivered written notice to Jefferies that the Company was suspending and terminating the prospectus related to the shares issuable in the ATM pursuant to the terms of the Sales Agreement. On March 27, 2024, the Company filed a new shelf registration statement on Form S-3, or the 2024 Shelf, with the SEC in relation to the registration of up to an aggregate offering price of $350.0 million of common stock, preferred stock, debt securities, warrants and units or any combination thereof, which superseded the 2022 Shelf. The 2024 Shelf included a prospectus supplement to provide for offerings in the ATM under the Sales Agreement. The Company issued no shares of common stock during the year ended December 31, 2024 under the ATM.

As of the issuance date of these consolidated financial statements for the year ended December 31, 2024, the Company expects that its cash and cash equivalents and marketable securities will be sufficient to fund its operating expenses and capital expenditure requirements through at least 12 months from the issuance of these consolidated financial statements. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The consolidated financial statements include those accounts of the Company and its subsidiaries after elimination of all intercompany accounts and transactions.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. Significant items subject to such estimates and assumptions include the fair value of stock-based compensation and accrued research and development costs. Management bases its estimates on historical experience and on various other market-specific relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Segment Information

Operating segments are defined as components of an entity about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the development of oncology targeted therapies for a range of cancer indications with high unmet need.

Cash and Restricted Cash

Cash consists of standard checking accounts. As of December 31, 2024, the restricted cash account is comprised of a $0.8 million security deposit held by the lessor for the Company’s operating lease.

Cash Equivalents

Cash equivalents are highly liquid investments with an original maturity of 90 days or less at the date of purchase and consist of time deposits and investments in money market funds that invest in U.S. Treasury obligations and government funds with commercial banks and financial institutions.

Marketable Securities

All marketable securities have original maturities greater than 90 days. The Company has classified its investments with maturities beyond one year as short-term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. The Company considers its investment portfolio of marketable securities to be available-for-sale. Accordingly, these investments are recorded at fair value. When the fair value is below the amortized cost of the asset, an estimate of expected credit losses is made. The credit-related impairment amount is recognized in loss; the remaining impairment amount and unrealized gains or losses are reported as a component of accumulated other comprehensive income in stockholders' equity. Credit losses are recognized through the use of an allowance for credit losses account and subsequent improvements in expected credit losses are recognized as a reversal of an amount in the allowance for credit losses account. If the Company has the intent to sell the security or it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis, the allowance for the credit loss is written-off and the excess of the amortized cost basis of the asset over its fair value is recorded in the consolidated statements of operations and comprehensive loss. Regardless of the Company's intent to sell a security, it performs additional analysis on all securities with unrealized losses to evaluate losses associated with the creditworthiness of the security. Credit losses are identified where the Company does not expect to receive cash flows sufficient to recover the amortized cost basis of a security. Unrealized gains and losses are reported as a component of accumulated other comprehensive income in stockholders' equity. Amortization and accretion of premiums and discounts are recorded in other income (expense) within the consolidated statements of operations and comprehensive loss. Realized gains or losses are included in interest income or interest expense, respectively. If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence such as industry, financial inputs, and capital markets data to evaluate the extent to which the decline is other than temporary and, if so, marks the investment to market on the Company's consolidated statement of operations and comprehensive loss.

Fair Value Measurements

Accounting Standards Codification 820, Fair Value Measurement, or ASC 820, establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs).

Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1—Inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2—Inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.
- Level 3—Inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety 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 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. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist primarily of cash and cash equivalents. The Company maintains its cash in bank deposit accounts which, at times, may exceed federally insured limits. The Company has not experienced any losses in such accounts. The Company believes it is not exposed to any significant credit risk on cash.

Property and Equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful life of the assets. Costs for property and equipment not yet placed into service are capitalized as assets under construction and depreciated in accordance with the aforementioned policy once placed into service. Upon retirement or disposal of property and equipment, the cost and related accumulated depreciation are removed from the consolidated balance sheet and any gain or loss is reflected in the consolidated statements of operations and comprehensive loss. Repair and maintenance expenditures are charged to expense as incurred.

The estimated useful lives of the Company's property and equipment are as follows:

	Estimated Useful Life
Leasehold improvements	The shorter of the life of the leasehold improvement or the remaining term of the lease
IT equipment	3 years
Laboratory equipment	5 years

Impairment of Long-Lived Assets

The Company reviews all long-lived assets for impairment whenever events or circumstances indicate the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by comparison of the carrying value of the assets to the future undiscounted net cash flows expected to be generated by the asset. If such asset is considered to be unrecoverable, the impairment recognized is measured by the difference between the estimated fair value of the asset and its carrying value. The Company did not recognize any impairments of long-lived assets during the years ended December 31, 2024 or 2023.

Research and Development

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits, facilities costs, depreciation, third-party license fees, and external costs of outside vendors engaged to conduct preclinical development activities and clinical trials as well as to manufacture research and development materials. The Company accrues costs for clinical trial activities and contract manufacturers based upon estimates of the services received and related expenses incurred that have yet to be invoiced by the contract research organizations, clinical study sites, contract manufacturers, laboratories, consultants, or other vendors that perform the activities.

Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred. Such amounts are expensed as the goods are delivered or the related services are performed or until it is no longer expected that the goods will be delivered, or the services rendered.

Costs incurred in obtaining technology licenses are recognized as research and development expense as incurred if the technology licensed has not reached technological feasibility and has no alternative future uses.

Patent and Trademark Costs

All patents and trademark related costs incurred in connection with filing and prosecuting patent and trademark applications are expensed as incurred due to uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Leases

Effective January 1, 2021, the Company accounts for leases in accordance with ASU No. 2016-02, Leases (Topic 842), or ASC 842. At contract inception, the Company determines if an arrangement is or contains a lease. A lease conveys the right to control the use of an identified asset for a period of time in exchange for consideration. If determined to be or contain a lease, the lease is assessed for classification as either an operating or finance lease at the lease commencement date, defined as the date on which the leased asset is made available for use by the Company, based on the economic characteristics of the lease. For each lease with a term greater than twelve months, the Company records a right-of-use asset and lease liability.

A right-of-use asset represents the economic benefit conveyed to the Company by the right to use the underlying asset over the lease term. A lease liability represents the obligation to make lease payments arising from the lease. The Company elected the practical expedient to not separate lease and non-lease components for all classes of underlying assets and therefore measures each lease payment as the total of the fixed lease and associated non-lease components. Lease liabilities are measured at lease commencement and calculated as the present value of the future lease payments in the contract using the rate implicit in the contract, when available. If an implicit rate is not readily determinable, the Company uses an incremental borrowing rate measured as the rate at which the Company could borrow, on a fully collateralized basis, a commensurate loan in the same currency over a period consistent with the lease term at the commencement date. Right-of-use assets are measured as the lease liability plus initial direct costs and prepaid lease payments, less lease incentives granted by the lessor. The lease term is measured as the noncancelable period in the contract, adjusted for any options to extend or terminate when it is reasonably certain the Company will extend the lease term via such options based on an assessment of economic factors present as of the lease commencement date. The Company elected the practical expedient to not recognize leases with a lease term of twelve months or less.

Components of a lease are split into three categories: lease components, non-lease components, and non-components. The fixed and in-substance fixed contract consideration (including any consideration related to non-components) are allocated, based on the respective relative fair values, to the lease components and non-lease components. The Company has elected to account for lease and non-lease components together as a single lease component for all underlying assets and allocate all of the contract consideration to the lease component only.

The Company's operating leases are presented in the consolidated balance sheets as operating lease right-of-use assets, classified as noncurrent assets, and operating lease liabilities, classified as current and noncurrent liabilities. Operating lease expense is recognized on a straight-line basis over the lease term. Variable costs associated with a lease, such as maintenance and utilities, are not included in the measurement of the lease liabilities and right-of-use assets but rather are expensed when the events determining the amount of variable consideration to be paid have occurred.

Income Taxes

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the Company's consolidated financial statements and/or tax returns. Deferred tax assets and liabilities are based upon the differences between the financial statement carrying amounts and the tax bases of existing assets and liabilities and for loss and credit carryforwards using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that some portion or all the deferred tax asset will not be realized.

The Company provides reserves related to uncertain tax positions when management determines the related tax benefit is not more likely than not to be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as the consideration of the available facts and circumstances. The Company has no reserves related to uncertain tax positions as of December 31, 2024 and 2023.

Interest and penalty charges, if any, related to uncertain tax positions would be classified as income tax expense in the accompanying consolidated statements of operations and comprehensive loss. As of December 31, 2024 and 2023, the Company had no accrued interest related to uncertain tax positions.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process preferred stock or common stock financings as deferred offering costs until such financings are consummated. After the closing of the IPO, follow-on offering and the ATM draw downs, these costs were recorded in stockholders' equity as a reduction of additional paid-in capital generated as a result of the financings.

Stock-Based Compensation

The Company recognizes stock-based compensation expense for all stock-based awards based on their grant date fair value.

The Company recognizes stock-based compensation expense over the requisite service period, which is generally the vesting period of the award. For awards that include performance-based vesting conditions, expense is recognized using the accelerated attribution method when the performance condition is deemed to be probable of being satisfied. The Company accounts for forfeitures as they occur. The Company determines the fair value of restricted stock awards in reference to the fair value of its common stock less any applicable purchase price.

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 the Company's expected dividend yield. The Company determines the volatility for awards granted based on an analysis of reported data for a group of guideline companies that have issued options with substantially similar terms. The expected volatility has been determined using a weighted average of the historical volatility measures of this group of guideline companies. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options granted to employees has been determined utilizing the "simplified" method, using the midpoint between the vesting date and the contractual 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. The Company has not paid, and does not anticipate paying, cash dividends on its common stock; therefore, the expected dividend yield is assumed to be zero.

The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's cash compensation costs are classified.

Net Loss per Share

Net loss per share attributable to common stockholders is computed by using the two-class method, which is an earnings allocation formula that determines net loss per share for the holders of the Company's common stock and participating securities. All series of preferred stock contain participation rights in any dividend declared or accumulated by the Company and are deemed to be participating securities. Income available to common stockholders and participating convertible preferred stock is allocated to each share on an as-converted basis as if all of the earnings for the period had been distributed. The participating securities do not include a contractual obligation to share in losses of the Company and are not included in the calculation of net loss per share in the periods that have a net loss.

Diluted net loss per share is computed using the if-converted method. The Company allocates earnings first to preferred stockholders based on dividend rights and then to common and preferred stockholders based on ownership interests. The weighted-average amount of common stock included in the computation of diluted loss gives effect to all potentially dilutive common equivalent shares, including outstanding stock options, warrants, and convertible preferred stock. Common stock equivalent shares are excluded from the computation of diluted loss per share if their effect is antidilutive.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources.

Recently Adopted Accounting Pronouncements

In November 2023, the FASB issued ASU No. 2023-07, “Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosure.” The ASU updates reportable segment disclosure requirements, primarily through requiring enhanced disclosures about significant segment expenses and information used to assess segment performance. The amendments do not change how segments are determined, aggregated, or how thresholds are applied to determine reportable segments. The Company adopted ASU No. 2023-07 during the year ended December 31, 2024 and the standard did not have a material impact on its results of operations. The Company's reporting segments disclosure is included within the consolidated financial statements at Note 15 "Segment Reporting".

Accounting Pronouncements Not Yet Adopted

In November 2024, the FASB issued ASU No. 2024-03, "Disaggregation of Income Statement Expenses (Subtopic 220-40)." The ASU requires public entities to disaggregate, in a tabular presentation, certain income statement expenses into different categories, such as purchases of inventory, employee compensation, depreciation, and intangible asset amortization. The guidance is effective for fiscal years beginning after December 15, 2026, with early adoption permitted, and may be applied retrospectively. The Company is currently evaluating the impact of adopting the new ASU on our consolidated financial statements and related disclosures.

Other accounting standards that have been issued or proposed by FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company’s consolidated financial statements upon adoption.

3. Fair Value of Assets and Liabilities

The following table presents information about the Company’s financial assets and liabilities measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values as of December 31, 2024 and 2023 (in thousands):

Description	December 31, 2024	Quoted prices active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant other observable inputs (Level 3)
Financial assets				
Cash equivalents:				
Money market funds	30,845	$ 30,845	$ —	$ —
Marketable securities:				
U.S. Government agencies	119,401	—	119,401	—
Total financial assets	$ 150,246	$ 30,845	$ 119,401	$ —

Description	December 31, 2023	Quoted prices active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant other observable inputs (Level 3)
Financial assets				
Cash equivalents:				
Money market funds	$ 40,551	$ 40,551	$ —	$ —
Marketable securities:				
Commercial paper	9,137	—	9,137	—
Corporate bonds	6,187	—	6,187	—
U.S. Government agencies	166,002	—	166,002	—
Yankee bonds	2,982	—	2,982	—
Asset-backed securities	779	—	779	—
Total financial assets	$ 225,638	$ 40,551	$ 185,087	$ —

There have been no transfers between levels for the years ended December 31, 2024 and 2023.

4. Property and Equipment, Net

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

	December 31, 2024	December 31, 2023
Assets under construction	$ 272	$ 391
IT equipment	451	289
Leasehold improvements	471	—
Lab equipment	8,007	7,506
	$ 9,201	$ 8,186
Less—accumulated depreciation	(5,986)	(5,036)
Property and equipment, net	$ 3,215	$ 3,150

Depreciation expense was $1.2 million and $1.3 million for the years ended December 31, 2024 and 2023, respectively.

5. Prepaid Expenses and Other Current Assets

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

	December 31, 2024	December 31, 2023
Prepaid insurance	$ 1,696	$ 1,817
Prepaid research and development expenses	6,007	1,399
Other	1,826	2,409
Prepaid expenses and other current assets	$ 9,529	$ 5,625

6. Marketable Securities

Marketable securities consisted of the following (in thousands):

	December 31, 2024			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
U.S. Government agencies	119,130	297	(26)	$ 119,401
Total	$ 119,130	$ 297	$ (26)	$ 119,401

	December 31, 2023			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Commercial paper	$ 9,144	$ —	$ (7)	$ 9,137
Corporate bonds	6,186	3	(2)	$ 6,187
U.S. Government agencies	165,453	563	(14)	$ 166,002
Yankee bonds	2,985	—	(3)	$ 2,982
Asset-backed securities	780	—	(1)	$ 779
Total	$ 184,548	$ 566	$ (27)	$ 185,087

As of December 31, 2024 and December 31, 2023, the unrealized losses on the Company's investments in U.S. government agencies securities, Yankee bonds, and asset-backed securities were caused by interest rate increases. The current credit ratings are all within the guidelines of the investment policy of the Company and the Company does not expect the issuers to settle any security at a price less than the amortized cost basis of the investment. The Company does not intend to sell the investments, and it is not probable that the Company will be required to sell the investments before recovery of their amortized cost basis.

As of December 31, 2024, one marketable security with a contractual maturity of one year or less was in an unrealized loss position totaling $0.03 million, and all marketable securities held by the Company had remaining contractual maturities of one year or less.

As of December 31, 2023, 13 marketable securities with contractual maturities of one year or less were in an unrealized loss position totaling $0.03 million. All marketable securities held by the Company had remaining contractual maturities of one year or less, except for asset-backed securities and U.S. government agencies securities with a fair value of $58.7 million that had maturities of one to two years.

There were no impairments of the Company's marketable securities measured and carried at fair value during the years ended December 31, 2024 and 2023.

7. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2024	December 31, 2023
Accrued research and development expenses	$ 3,386	$ 3,445
Accrued compensation	5,456	3,503
Other	618	935
Accrued expenses and other current liabilities	$ 9,460	$ 7,883

8. Stockholders' Equity

The Company had 150,000,000 authorized shares of common stock, par value $0.00001 per share, of which 49,998,279 and 49,350,788 shares were issued and outstanding at December 31, 2024 and December 31, 2023, respectively.

In addition, the Company had 10,000,000 authorized shares of preferred stock, par value $0.00001 per share, all of which shares of preferred stock are undesignated. No authorized shares of preferred stock were issued and outstanding at December 31, 2024 and December 31, 2023.

Financings

On March 27, 2024, the Company filed the 2024 Shelf with the SEC in relation to the registration of up to an aggregate offering price of $350.0 million of common stock, preferred stock, debt securities, warrants and units or any combination thereof, which superseded the 2022 Shelf. The 2024 Shelf included a prospectus supplement to provide for offerings in the ATM under the Sales Agreement. The Company issued no shares of common stock during the year ended December 31, 2024 under the ATM.

On November 9, 2023, the Company issued and sold 11,000,000 shares of common stock at a price to the public of $9.00 per share for aggregate gross proceeds of $99.0 million in the 2023 Follow-On Offering. The Company received approximately $92.6 million in net proceeds from the 2023 Follow-On Offering after deducting underwriting discounts and commissions and offering expenses.

On November 1, 2022, the Company filed the 2022 Shelf with the SEC in relation to the registration of up to an aggregate offering price of $250.0 million of common stock, preferred stock, debt securities, warrants and units or any combination thereof. The Company also simultaneously entered into the Sales Agreement with the Sales Agent to provide for the offering, issuance and sale by the Company of up to an aggregate of $75.0 million of common stock from time to time in the ATM under the 2022 Shelf and subject to the limitations thereof. The Company issued 261,807 shares of common stock at an average price of $12.49 for aggregate gross proceeds of $3.3 million during the year ended December 31, 2023 under the ATM.

9. Stock-Based Compensation

2018 Stock Option and Incentive Plan

On December 12, 2018, the Company adopted the Aura Biosciences, Inc. 2018 Equity Incentive Plan, or the 2018 Plan. The 2018 Plan will expire in 2028. Under the 2018 Plan, Aura may grant incentive stock options, non-qualified stock options, restricted and unrestricted stock awards and stock rights. The Board of Directors, or the Board, has determined not to make any further awards under the 2018 Plan as of November 2, 2021. However, the 2018 Plan will continue to govern outstanding equity awards granted thereunder.

2021 Stock Option and Incentive Plan

The 2021 Stock Option and Incentive Plan, or the 2021 Plan, was adopted by the Board on October 7, 2021, approved by the Company's stockholders on October 22, 2021 and became effective on November 1, 2021. The 2021 Plan permits the granting of several award types, including restricted stock units and both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the United States Internal Revenue Code, or the Code, and options that do not so qualify. The number of shares initially reserved for issuance under the 2021 Plan was 3,352,166, which increased on January 1, 2022 and will continue to increase each January 1 thereafter, by 5% of the outstanding number of shares of common stock on the immediately preceding December 31 or such lesser number of shares as determined by the Company's compensation committee. The maximum number of shares of common stock that may be issued in the form of incentive stock options shall not exceed the initial limit, cumulatively increased on January 1, 2022 and on each January 1 thereafter by the lesser of the annual increase for such year or 3,352,166 shares of common stock. On January 1, 2024, the shares reserved for issuance was increased to 9,414,162 shares. With the transfer of shares to the 2021 Plan in connection with the termination or expiration of awards under the 2018 Plan, together with shares otherwise available under the 2021 Plan, at December 31, 2024 there were 4,164,754 shares available for grants under the 2021 Plan.

2021 Employee Stock Purchase Plan

The 2021 Employee Stock Purchase Plan, or the ESPP, was adopted by the Board on October 7, 2021, approved by the Company's stockholders on October 22, 2021 and became effective on November 1, 2021. A total of 335,217 shares of common stock were initially reserved for issuance under this plan, which increased on January 1, 2022 and will continue to increase each January 1 thereafter through January 1, 2031, by the least of (i) 335,217 shares of common stock, (ii) 1% of the outstanding number of shares of common stock on the immediately preceding December 31 or (iii) such lesser number of shares of common stock as determined by the administrator of the ESPP. On January 1, 2024, the shares reserved for issuance was increased to 1,282,856 shares. The purchase price of the shares under the ESPP are at 85% of the lower of the fair market value of the Company's common stock on the first trading day of the offering period or on the purchase date. As of December 31, 2024, 1,258,379 shares were available to be issued under the ESPP. The Company recognized $0.1 million share-based compensation expense related to the ESPP for the years ended December 31, 2024 and 2023.

Stock Options

The Board is authorized to administer the 2021 Plan. In accordance with the provisions of the 2021 Plan, the Board determines the terms of Aura options and other awards issued pursuant thereto, including the following:

- which employees, directors and consultants shall be granted awards;
- the number of shares of common stock subject to options and other awards;

- the exercise price of each option, which generally shall not be less than fair market value of the common stock on the date of grant;
- the termination or cancellation provisions applicable to options;
- the terms and conditions of other awards, including conditions for repurchase, termination or cancellation, issue price and repurchase price; and
- all other terms and conditions upon which each award may be granted in accordance with the 2021 Plan.

In addition, the Board may award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. The Board or any committee to which the Board delegates authority may, with the consent of the affected plan participants, re-price or otherwise amend outstanding awards consistent with the terms of the 2021 Plan.

The following table summarizes stock option activity under the 2018 Plan and 2021 Plan for the year ended December 31, 2024:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2023	5,030,351	$ 8.46	7.54	$ 10,353
Granted	1,650,730	7.94		
Exercised	(312,769)	4.53		
Cancelled/Forfeited	(845,959)	10.78		
Outstanding at December 31, 2024	5,522,353	$ 8.17	6.91	$ 8,068
Exercisable at December 31, 2024	3,244,171	$ 7.73	5.62	$ 7,119

The weighted-average grant date fair value of stock options granted during the years ended December 31, 2024 and 2023 was $5.99 and $7.50 per share, respectively. The total intrinsic value of options exercised was $1.5 million and $1.5 million for the years ended December 31, 2024 and 2023, respectively.

The fair value of the stock options issued as of December 31, 2024 and 2023 was measured with the following weighted-average assumptions:

	Year Ended December 31,	
	2024	2023
Risk-free interest rate	3.93%	3.94%
Expected term (years)	6.03	6.04
Expected volatility of the underlying stock	88.63%	86.15%
Expected dividend rate	—%	—%

Restricted Stock Units

The Company has granted restricted stock units with service-based vesting conditions. Unvested restricted stock units may not be sold or transferred by the holder.

A summary of the restricted stock unit activity during the year ended December 31, 2024 is as follows:

	Restricted Stock Units	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2023	1,093,402	$ 10.27
Granted	1,159,205	8.04
Vested/Released	(310,245)	10.36
Forfeited	(353,320)	9.67
Unvested at December 31, 2024	1,589,042	$ 8.76

As a result of the 2021 Plan, the Company granted restricted stock units which vest in increments of 25% annually over a period of four years. During the year ended December 31, 2024, 310,245 restricted stock units vested with a fair value of $3.2 million.

Stock-based Compensation Expense

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

	Year Ended December 31,	
	2024	2023
Research and development	$ 5,696	$ 3,929
General and administrative	6,026	4,843
Total	$ 11,722	$ 8,772

As of December 31, 2024, there was $13.1 million of unrecognized compensation expense related to stock options, which is expected to be recognized over a weighted-average period of 2.53 years.

As of December 31, 2024, there was $11.3 million of unrecognized compensation expense related to restricted stock units, which is expected to be recognized over a weighted-average period of 2.83 years.

10. Common Stock Warrants

In February 2015 and May 2015, the Company issued warrants to purchase 1,650,098 and 887,536 shares of Series B convertible preferred stock, respectively, at an exercise price of $1.24235 per share, or the Series B Warrants. Each Series B Warrant was immediately exercisable and expires ten years from the original date of issuance. Pursuant to FASB ASC Topic 480, Distinguishing Liabilities from Equity, the Series B Warrants were classified as a liability and were re-measured to fair value at each balance sheet date. A total of 173,827 of the Series B Warrants were outstanding and were converted into warrants to purchase 12,686 shares of common stock with an exercise price of $17.03 upon the completion of the IPO in November 2021. As a result, the 12,686 common stock warrants were converted into equity instruments and remain outstanding as of December 31, 2024.

11. Compensation

In January 2012, the Company adopted the Aura Biosciences 401(k) Profit Sharing Plan and Trust, or the 401(k) Plan, for its employees, which is designed to be qualified under Section 401(k) of the Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. The Company makes matching contributions of 100% of the first 6% of employee contributions. The Company made matching contributions in the amount of $0.9 million and $0.7 million for the years ended December 31, 2024 and 2023, respectively.

12. Commitments and Contingencies

Lease Commitments

The Company has historically entered into lease arrangements for its facilities. The Company has one operating lease for its office and laboratory facility with required future minimum payments as of December 31, 2024.

On May 16, 2022, the Company entered into an office and laboratory lease in Boston, MA with an initial 10-year term and one renewal option to extend the lease for an additional seven years which has not been deemed probable of being exercised by the Company as of December 31, 2024. The lease commenced on August 1, 2022, and estimated payments due under the initial term totaled $35.2 million. The lease requires a letter of credit totaling $0.8 million which is classified as long-term restricted cash and deposits on the consolidated balance sheets. The landlord will reimburse the Company up to $0.5 million for certain costs related to expansion of the laboratory space. As of December 31, 2024, the Company has completed the expansion and has incurred and been fully reimbursed for $0.5 million of expenses.

The following table contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company's leases for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Lease Costs		
Operating lease costs	3,509	3,517
Variable lease costs	1,193	883
Short-term lease costs	—	7
Total lease costs	$ 4,702	$ 4,407
Cash paid for amounts included in the measurement of lease liabilities—operating leases	$ 2,822	$ 3,002
Weighted-average remaining lease term—operating leases (years)	7.59	8.59
Weighted-average discount rate—operating leases	10.71%	10.71%

The following table reconciles the future minimum commitments to the Company's operating lease liabilities at December 31, 2024 (in thousands):

	Operating lease payments as of December 31, 2024
2025	3,306
2026	3,405
2027	3,508
2028	3,611
2029	3,716
Thereafter	10,107
Total lease payments	27,653
Less: interest	(8,884)
Total lease liabilities at December 31, 2024	18,769
Less: current portion of lease liabilities	3,149
Lease liabilities, net of current portion	$ 15,620

License Agreements

The Company has entered into the following key agreements that relate to the core technology under development:

Rakuten License and Supply Agreement

In May 2024, the Company received notice from LI-COR, Inc., or LI-COR, that as of April 16, 2024, LI-COR assigned, and Rakuten Medical, Inc., or Rakuten, assumed, the 2014 Exclusive Agreement and the 2014 Non-Exclusive Agreement (each described below), each originally entered into by and between the Company and LI-COR. The 2014 Exclusive Agreement and 2014 Non-Exclusive Agreement were not otherwise modified by this assignment and assumption and remain in effect.

2014 Exclusive Agreement

In January 2014, the Company entered into an Exclusive License and Supply Agreement, or the 2014 Exclusive Agreement, with LI-COR for the license of IRDye 700DX and related licensed patent (now expired) for the treatment and diagnosis of ocular cancers in humans, as amended in January 2016, July 2017, April 2018 and April 2019. The 2014 Exclusive Agreement required a one-time upfront license issue fee of $0.1 million and aggregate milestone payments of up to $0.2 million upon certain regulatory and development milestones. The Company is also required to pay Rakuten low-single digit royalties on net sales. The term of the 2014 Exclusive Agreement expires on a country-by-country basis, until the longer of (i) ten years from the first commercial sale of a licensed product in such country and (ii) the last to expire valid claim in such country.

The Company recognized no expenses related to this agreement and related amendments for the years ended December 31, 2024 and 2023, respectively.

2014 Non-Exclusive Agreement

In December 2014, the Company entered into a Non-Exclusive License Agreement, or the 2014 Non-Exclusive Agreement, with LI-COR for the supply of IRDye 700DX to the Company for the treatment and diagnosis of non-ocular solid tumor cancers in humans. Under the 2014 Non-Exclusive Agreement, the Company paid a license issue fee of $0.03 million on the effective date. The Company must also pay Rakuten a non-refundable, non-creditable fee of $0.03 million per each licensed product upon pre-IND designation, as defined of such licensed product, aggregate milestone payments of up to $0.3 million upon certain regulatory and development milestones; and during the term, the Company must pay Rakuten a low-single digit percentage royalty on net sales. Rakuten receives 10% of all sublicensee income within 30 days of the Company's receipt from the sublicensee. The 2014 Non-Exclusive Agreement also required the Company to make certain payments upon the achievement of specified development and commercial milestones of up to $0.4 million in aggregate. During the years ended December 31, 2024 and 2023, the Company recognized no milestones related to this agreement.

Life Technologies Corporation License Agreement

In December 2014, the Company entered into a non-exclusive, perpetual license agreement with Life Technologies Corporation, or Life Technologies, which allows for five licensed products. Under this agreement the Company is required to pay an initial license fee of $0.1 million for each product. An annual development fee of $0.1 million is due within a year from payment of the initial license fee and due annually or earlier of (i) payment of a commercialization fee or (ii) all development work is terminated. The commercialization fee is a one-time, non-refundable, non-creditable fee of $0.3 million due upon receipt of approval of a licensed product. In the event of a change of control, there will be a change of control fee of $0.2 million.

In January 2022, the Company entered into the First Amendment to the non-exclusive, perpetual license agreement with Life Technologies for use of the license in an additional indication. The cost of this amendment was a one-time fee of $0.05 million. During the years ended December 31, 2024 and 2023, the Company did not recognize any expenses related to this agreement.

Effective in September 2022, the Company entered into a new non-exclusive, perpetual license agreement with Life Technologies for licensed products. Under this agreement, the Company is required to pay an initial license fee of $0.4 million for the first licensed product and $0.5 million for each additional licensed product. In addition, the agreement allows the Company the right to sublicense which would lead to a $0.2 million payment for each sublicense per licensed product and a $0.03 million payment for use of the cell line document package. In the event of a change of control, there will be a change of control fee of $0.5 million. During the years ended December 31, 2024 and 2023, the Company recognized $0.5 million and $0 million of expenses related to this agreement, respectively.

National Institute of Health (NIH)-Collaboration Research and Development Agreement

In July 2011, the Company entered into a Collaboration Research and Development Agreement, or the CRADA, with Dr. John Schiller at the NIH, for a period of two years with the rights to an exclusive license to all technology generated within the collaboration. Under this agreement, the Company is required to make annual payments of $0.03 million to fund the research activities, the first payment of which was paid within 30 days of the effective date. Subsequent payments are due within 30 days of the anniversary of the effective date. This agreement was previously amended in 2012, 2013, 2014, 2015, 2016, 2018, and 2020. During the years ended December 31, 2024 and 2023, the Company paid no research collaboration fees related to this agreement.

An eighth amendment was effective in September 2022, requiring payment of $0.04 million within 30 days of November 1, 2022, and payment of another $0.03 million within 30 days of the 12th anniversary of the CRADA, which was in August 2023. This eighth amendment extended the term of the CRADA to September 30, 2024. During the years ended December 31, 2024 and 2023, the Company recognized $0 million and $0.03 million of expenses related to this agreement, respectively.

A ninth amendment was effective in September 2024, requiring payment of $0.06 million within 30 days of November 30, 2024, and payment of another $0.05 million within 30 days of September 30, 2025. This ninth amendment extended the term of the CRADA to September 30, 2026. During the year ended December 31, 2024, the Company recognized $0.1 million of expenses related to this agreement.

National Institute of Health (NIH)-Exclusive Patent License Agreement

In September 2013, the Company entered into an exclusive patent license agreement, or the NIH Exclusive License Agreement, with the NIH, that required the Company to pay a license issue royalty of $0.1 million and reimburse the NIH for any patent expenses incurred. Under the agreement, the Company is required to make low single-digit percentage royalty payments based on specified levels of annual net sales of licensed products subject to certain specified reductions. The Company is required to make development and regulatory milestone payments of up to $0.7 million in aggregate and sales milestone payments up to $0.6 million in the aggregate. The Company is also required to pay NIH a mid-single to low teen-digit percentage of any sublicensing revenue the Company receives. Additionally, the Company's payment obligations to the NIH are subject to an annual minimum royalty payment of low five figures. The Company recognized $0.03 million and $0.2 million for patent licensing fees for the years ended December 31, 2024 and 2023, respectively.

In 2015, 2018 and 2019, the Company amended its exclusive patent license to include updates on the status of the commercial development and update/expand the list of licensed patents and patent applications. Each of those amendments required a $0.03 million payment that the Company paid.

Inserm-Transfert License Agreement

In November 2009, the Company entered into an exclusive, royalty-bearing patent license agreement with Inserm-Transfert of France. The agreement expires on a country-by-country basis based on the last to expire of any patent encompassed within the scope of the patent rights or 10 years from the date of the first commercial sales by the Company, whichever is later. The IND filing milestone of €0.01 million was accrued in 2016 and paid in 2017 by the Company. The milestones for the successful Phase I, II and III clinical trials are based on receiving a final report and achieving the primary endpoints defined in that trial, and the milestones for Phases I and II have been achieved as of December 31, 2024. Upon the sublicense by the Company of a product for which royalties are payable under the agreement, low- to mid-single-digit royalty payments would be due by the Company. The non-milestone payments in this agreement are subject to an anti-stacking clause. The Company recognized $0.1 million and $0 million in expenses related to this agreement for the years ended December 31, 2024 and 2023, respectively.

Clearside License Agreement

In July 2019, the Company entered into an exclusive license agreement, or the Clearside License Agreement, with Clearside Biomedical, Inc., or Clearside, for the license of Clearside's Suprachoroidal Microneedle Technology for use in the treatment of indeterminate lesions and choroidal tumors. Upon execution of the Clearside License Agreement, the Company paid Clearside an upfront payment of $0.1 million which was expensed as incurred. Under the Clearside License Agreement, the Company is required to pay milestones up to $21.0 million in the aggregate upon the achievement of specified regulatory and development milestones, and upon the achievement of certain commercial sales milestones. The Company is also required to pay low to mid-single digit royalties on net sales. If the Company sublicenses a product for which royalties are payable, then the Company is required to pay the greater of 20% received or low single digit royalties on net sales.

The Clearside License Agreement expires on a country-by-country basis upon the later of the last to expire patent or ten years from the date of the first commercial sale of a product.

The Company recognized $0 million and $1.0 million of expenses related to this agreement and related amendments for the years ended December 31, 2024 and 2023, respectively.

13. Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is the same as basic net loss per share for the periods presented since the effects of potentially dilutive securities are antidilutive given the net loss of the Company.

The Company has calculated basic and diluted net loss per share for the years ended December 31, 2024 and 2023 as follows (in thousands, except share and per share data):

	Year Ended December 31,	
	2024	2023
Numerator:		
Net loss	$ (86,919)	$ (76,408)
Denominator:		
Weighted-average common stock outstanding—basic and diluted	49,650,480	39,620,036
Net loss per common share—basic and diluted	$ (1.75)	$ (1.93)

The following potentially dilutive securities were excluded from the computation of the diluted net loss per share for the periods presented because their effect would have been antidilutive:

	Year Ended December 31,	
	2024	2023
Stock options to purchase common stock	5,522,353	5,030,351
Restricted stock units that vest into common stock	1,589,042	1,093,402
Warrants to purchase common stock	12,686	12,686
Total potential dilutive shares	7,124,081	6,136,439

14. Income Taxes

For the years ended December 31, 2024 and 2023, the loss before income taxes consisted of the following:

	2024	2023
Domestic	$ (86,185)	$ (76,191)
Foreign	(622)	(80)
Total	$ (86,807)	$ (76,271)

The Company has recorded a $0.1 million tax provision for the periods presented due to the current state income taxes and the losses incurred and the need for a full valuation allowance on net deferred tax assets. The difference between the income tax provision at the U.S. federal statutory rate and the recorded provision is primarily due to the valuation allowance recorded on all deferred tax assets.

The Company's income tax provision, net consisted of the following:

	2024	2023
Components of income tax provision:		
Current:		
Federal	$ —	$ —
State	112	137
Foreign	—	—
Total Current	112	137
Deferred:		
Federal	—	—
State	—	—
Foreign	—	—
Total Deferred	—	—
Total Income Tax Provision	$ 112	$ 137

A reconciliation of the federal statutory income tax rate to the Company's effective tax rate as of December 31, 2024 and 2023 is as follows:

	2024	2023
Income tax provision at statutory rate	21.0%	21.0%
State taxes, net of federal benefit	4.6%	6.6%
Federal tax credits	3.6%	2.3%
Permanent items	(1.6)%	(1.0)%
Other	(0.1)%	(0.1)%
Decrease in valuation reserve	(27.5)%	(28.8)%
Total	0.0%	0.0%

Temporary differences that give rise to significant deferred tax assets (liabilities) as of December 31, 2024 and 2023 are as follows (in thousands):

	2024	2023
Deferred tax assets:		
Net operating loss carryforwards	$ 55,826	$ 45,999
Stock-based compensation expense	2,450	2,110
Capitalized research and development expenses	32,422	22,068
Tax credit carryforwards	13,582	10,007
Accrued expenses and other current liabilities	1,025	1,018
Lease liability	4,903	5,282
Other	938	766
Total deferred tax assets	111,146	87,250
Deferred tax liabilities:		
Right-of-use assets	(4,540)	(5,092)
Depreciable assets	(312)	(225)
Prepaid expenses and other current assets	(443)	—
Valuation allowance	(105,851)	(81,933)
Net deferred tax assets	$ —	$ —

As of December 31, 2024, the Company had accumulated federal net operating loss carryforwards of approximately $209.8 million which may be available to offset future taxable income, of which $44.2 million begin to expire in 2029 and go through 2037 and $165.6 million do not expire. The Company had accumulated state net operating loss carryforwards of $183.6 million, which may be available to offset future taxable income and begin to expire in 2030, except for $1.2 million of state net operating losses, or NOLs, that do not expire. The Company had accumulated foreign net operating loss carryforwards of $0.7 million, which may be available to offset future taxable income and do not expire. As of December 31, 2024, the Company had federal and state research and development credit carryforwards of $11.3 million and $2.9 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2029 and 2028, respectively.

The Company's ability to use its operating loss carryforwards and tax credit carryforwards to offset taxable income is subject to restrictions under Sections 382 and 383 of the Code. Under the Code provisions, certain substantial changes in the Company's ownership, including the sale of the Company or significant changes in ownership due to sales of equity, have limited and may limit in the future, the amount of net operating loss carryforwards which could be used annually to offset future taxable income. The Company has not yet completed an analysis of ownership changes. The Company may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside the Company's control. As a result, the Company's ability to use our pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to the Company. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. All federal NOLs generated post tax reform have an indefinite life, are not subject to carryback provisions, and limited to 80% of taxable income in any year.

The Company has not conducted a study of its research and development credit carryforwards. A study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts will be presented as an uncertain tax position. A full valuation allowance has been recorded against the Company's research and development credit carryforwards and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheets or statements of operations and comprehensive loss at this time, if an adjustment were required.

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are principally comprised of NOL carryforwards and tax credit carryforwards. Management has determined that it is more likely than not that the Company will not realize the benefits of its deferred tax assets, and as a result, a valuation allowance of $105.9 million has been recorded at December 31, 2024. The increase in the valuation allowance of $23.9 million during the year ended December 31, 2024 was primarily due to the increase in net operating losses generated by the Company and capitalized R&D expenses related to the Section 174 requirements.

As of December 31, 2024 and 2023, the Company had no unrecognized tax benefits. Interest and penalty charges, if any, related to income taxes would be classified as a component of the income tax provision in the consolidated statements of operations and comprehensive loss. The Company does not expect any significant change in its uncertain tax positions in the next twelve months.

The Company files income tax returns in the United States federal tax jurisdiction and several state tax jurisdictions as well as in the Netherlands and Germany for its foreign subsidiaries. Since the Company is in a loss carryforward position, it is generally subject to examination by federal and state tax authorities for all tax years in which a loss carryforward is available.

With respect to the income of its foreign subsidiaries, the Company asserts the position that the undistributed earnings of its foreign subsidiaries are permanently invested in each jurisdiction. As a result, no additional income taxes have been provided on the possible repatriation of these earnings to the parent company. The Company does not have any unremitted earnings as of December 31, 2024.

15. Segment Reporting

Segment reporting is prepared on the same basis that the Company's Chief Executive Officer, who is its chief operating decision maker, or CODM, manages the business and makes operating decisions to allocate resources across departments and functions in line with the Company's strategic goals. The Company operates in one reportable segment which includes all activities related to the research and development of oncology targeted therapies for a range of cancer indications with high unmet medical need. The CODM assesses performance and allocates resources based on comparing actual consolidated net loss to the budget. The measure of segment assets used in determining how to manage and allocate resources is reported within the Company's consolidated balance sheets as cash and cash equivalents and marketable securities.

As a single reportable segment entity, the Company’s segment performance measure is net loss. Significant segment expenses are presented below.

	Year Ended December 31,	
	2024	2023
	(in thousands)	
Clinical, Preclinical, and R&D Operations	$ (49,550)	$ (43,427)
Chemistry, Manufacturing, and Controls	(23,752)	(21,806)
General and Administrative	(22,814)	(19,759)
Other Segment Items [1]	9,197	8,584
Net loss	$ (86,919)	$ (76,408)

(1) Other segment items primarily include interest income, realized gains and losses, and income taxes.

16. Subsequent Events

The Company has not identified any subsequent events that require disclosure.

SIGNATURES

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

Aura Biosciences, Inc.

Date: March 24, 2025 By: /s/ Elisabet de los Pinos

Elisabet de los Pinos
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Elisabet de los Pinos **Elisabet de los Pinos**	President and Chief Executive Officer	March 24, 2025
/s/ Amy Elazzouzi **Amy Elazzouzi**	Senior Vice President, Finance (Interim Principal Financial Officer and Interim Principal Accounting Officer)	March 24, 2025
/s/ David Johnson **David Johnson**	Chairman of the Board of Directors	March 24, 2025
/s/ Giovanni Mariggi **Giovanni Mariggi**	Director	March 24, 2025
/s/ Antony Mattessich **Antony Mattessich**	Director	March 24, 2025
/s/ Sapna Srivastava **Sapna Srivastava**	Director	March 24, 2025
/s/ Karan Takhar **Karan Takhar**	Director	March 24, 2025

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EXECUTIVE OFFICERS

Elisabet de los Pinos, Ph.D.
Chief Executive Officer and President

Amy Elazzouzi
Senior Vice President, Finance

J. Jill Hopkins, M.D.
Chief Medical Officer and President of Research and Development

Conor Kilroy
Chief Legal Officer and Secretary

Mark Plavsic, Ph.D.
Chief Technology Officer

BOARD OF DIRECTORS

David Johnson
Chairman of the Board,
Aura Biosciences, Inc.

Elisabet de los Pinos, Ph.D.
Chief Executive Officer and President,
Aura Biosciences, Inc.

Teresa Marie Bitetti
President of the Global Oncology Business Unit,
Takeda Pharmaceutical Company Limited

Giovanni Mariggi, Ph.D.
Partner, Medicxi

Antony Mattessich
Chief Executive Officer,
Amphista Therapeutics Limited

Sapna Srivastava, Ph.D.
Pharmaceutical Executive (Former)
Independent Board Director

Karan Takhar
Senior Managing Director, Head of Life Sciences Investing,
Matrix Capital Management, L.P.

CORPORATE INFORMATION

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Independent Registered Public Accounting Firm
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